

Collateral Beauty: Anaesthesia for the Deceased Organ Donor

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INTRODUCTION

Organ donation is an altruistic idea which many aspire to and yet very few achieve. It is now common knowledge that the list of people requiring organ transplants far outweighs the list of potential organ donors, and yet tireless efforts are made by a few to try and grow the list of donors. Due to the paucity in organ donors our exposure to organ retrieval surgery as anaesthetists is also quite restricted. And so often when faced with a patient for planned organ retrieval we might guiltily find ourselves asking the question, 'Do we really need to be involved in this procedure?' The short answer to which is yes. Anaesthetists play an important role in managing and optimizing the deceased donor, establishing specific goals, and implementing certain strategies so as to improve graft survival for the transplanted organs.⁽¹⁾ With the knowledge of the physiological changes that occur after death, they, in effect, perform a balancing act with each of the organs to be harvested before and after the surgery so as to ensure good donor outcomes. An important and crucial skill.

HISTORY (2-4)

1869 – The first human organ transplant – a skin transplant (today commonly known as a skin graft) – was performed by Jaques-Louis Reverdin.
1906 – The next human organ was transplanted – the cornea.
1954 – The first major organ was successfully transplanted – the kidney. This was performed by Dr's Joseph Murray and Hartwell Harrison on live identical twins. Success in this case was brought about by the genetic similarity between the two patients, thus avoiding the complication of graft rejection due to incompatibility.
1962 – The recovery of organs from deceased and brain dead donors began.
1963 – The first lung transplant was done on a prison inmate in Mississippi, USA.
1967 – The first successful liver, pancreas and heart transplants took place.
1985 – Intestinal transplants began

Organ transplantation continued to develop over the late 20th century, and with it came the formation of transplant/organ procurement organizations as well as regulations on the proper conduct of organ donations.

ORGAN DONATION

Organ retrieval for donation is either done from live or deceased patients. It is done with the intention of improving the life of another patient with end-stage organ failure. These patients have chronic disease as a result of environmental and/or genetic factors which their affected organ can no longer recover from. They are frequently on costly medications and therapies, such as renal dialysis, in order to stay alive. Organ transplantation, not only improves the survival rate of such patients, but also improves quality of life and reduces the cost burden on the health sector and the patient.

As it stands, in South Africa, there are about 4300 patients awaiting an organ or cornea transplant. According to the Organ Donor Foundation organ donations have been on the decline since 2009, where 724 organ and cornea transplants were documented to have taken place, to 512 in 2016. Meanwhile the demand for organs steadily rises. A few reasons postulated for this situation are the lack of general public awareness about organ donation and transplantation, the current national policy where organ donation is done on an opt-in basis and where the family of a deceased potential organ donor give the ultimate consent as to whether organ procurement may proceed, the initial exclusion of HIV infected donors, as well as the deficiency of a national database of patients waiting for organ transplants and prospective organ donors. That being said, the insufficient number of available organs to meet the demand is a worldwide problem, which will most likely not be resolved in the near future. For the purpose of this paper, the focus will be on organ retrieval from deceased patients, and how to best anaesthetize these patients in order to ensure a good chance of graft survival in the recipient.

DEFINING DEATH

In order for this process to begin, death needs to be defined or classified. There are two types of death that are described for deceased organ donors. These are: 1) Circulatory death or 2) Brain death. The Academy of Medical Royal Colleges in the United Kingdom defines circulatory death as “the irreversible cessation of circulatory function”, and it defines brain death as “the irreversible loss of function of the brain and brain stem”.⁽⁵⁾ These definitions will be expounded below.

Donation after Circulatory Death

Donation after circulatory death (DCD), previously referred to as donation after cardiac death or non-heart beating donation is further broken down to two categories:

- 1) Uncontrolled DCD, where death occurs unexpectedly or suddenly
- 2) Controlled DCD, where death is expected or planned by withdrawing life-sustaining management.

There is a modified Maastricht classification of DCD recently published in 2013 by an expert European Working Group on the definitions and terminology of DCD donation at the 6th International Conference in Organ Donation in Paris, France. (See Table 1) This classification groups the different types of DCD into 4 categories and describes in more detail the circumstances in which death occurs. Categorizing the different situations in which death occurs allows the transplant team to understand the type of ischaemic insult the organs have undergone, how long the ischaemic time is likely to have been, and subsequently, the probable outcomes for organ donation.

Table 1
The Modified Maastricht Classification of DCD⁽⁶⁾

Category I Uncontrolled	<i>Found Dead</i> IA – Out-of-hospital IB – In-hospital	Sudden unexpected CA without any attempt of resuscitation by a life-medical team; WIT to be considered according to National life-recommendations in place; reference to in- or out-of hospital life-setting
Category II Uncontrolled	<i>Witnessed cardiac arrest</i> IIA – Out-of-hospital IIB – In-hospital	Sudden unexpected irreversible CA with unsuccessful resuscitation by a life-medical team; reference to in- or out-of hospital life-setting
Category III Controlled	<i>Withdrawal of life-sustaining therapy</i>	Planned withdrawal of life-sustaining therapy ^a ; expected CA
Category IV Uncontrolled Controlled	<i>Cardiac arrest while life-brain dead</i>	Sudden CA after brain death diagnosis during donor life-management but prior to planned organ recovery

CA – circulatory arrest; WIT – warm ischaemia time

^a This category mainly refers to the decision to withdraw life-sustaining therapies. Legislation in some countries allows euthanasia (medically assisted CA) and subsequent organ donation described as the fifth category.

Circulatory death is diagnosed when the following has occurred:

- Central pulse is absent on palpation
- Heart sounds are absent on auscultation
- Asystole is confirmed on a continuous ECG trace
- Pulsatile flow is absent on invasive blood pressure monitoring
- Contractility is absent on echocardiography

When it comes to donation after cardiac death (DCD) it is important to realise that each organ has a different susceptibility to ischaemic injury and thus time till irreversible loss of function will also differ.

Warm ischaemia and **cold ischaemia** are the terms used to describe the types of ischaemia seen in retrieved organs after death of the donor.

Warm ischaemia is subdivided into donor warm ischaemia and recipient warm ischaemia. Donor warm ischaemia occurs from the moment the patient dies (asystole) until cold perfusion of the organs begins. Recipient warm ischaemia occurs from the time the organs are removed from ice up until reperfusion of the organs begins.

Cold ischaemia on the other hand refers to the time in between, where cold perfusion has commenced and the organs are placed in ice, until the organs are removed from ice and recipient warm ischaemia begins.

These times are crucial because prolongation of these times have been shown to increase patient mortality and graft failure rates.^(7, 8) It has however been noted that warm organ ischaemia actually begins in the period preceding cardiopulmonary collapse, when the organs are being under perfused. As a result, the term '**functional warm ischaemia time**' was introduced in order to include this period. This period begins when the systolic arterial pressure of the patient drops below 50mmHg, and/or the arterial oxygen saturation falls below 70%.⁽⁹⁾ The term has its relevance in controlled DCD where cessation of cardiopulmonary support and the subsequent decline in parameters is witnessed and can therefore be accurately timed.

United Kingdom (UK) guidelines for organ-specific acceptable functional warm ischaemia times for DCD organ retrieval are as follows.

Table 2
UK functional warm ischaemia criteria for DCD organ retrieval

Organ	Minimum functional warm ischaemia time (min)	Comments
Kidney	120	Plus a further 120 min in selected donors. DCD kidneys have a higher incidence of delayed graft function, but have similar long-term function to DBD grafts
Liver	30	May be limited to 20 min in sub-optimal donors. Outcomes from DCD liver transplantation are acceptable, but there is greater postoperative morbidity and a higher incidence of graft failure and biliary complications compared with DBD grafts
Lung	60	Time to re-inflation of the lungs rather than cold perfusion. DCD may represent an important source of additional lung grafts, particularly when combined with ex vivo perfusion techniques
Pancreas	30	

Manara et al⁽⁹⁾

In South Africa as well as Australia, warm ischaemia time is considered to begin from the time the donor is extubated. The time cut offs are 1 hour for kidneys and 30 minutes for liver. Currently, in South Africa, only kidneys and livers are procured from donors after circulatory arrest.

With the withdrawal of life-sustaining treatment, asystole or cardiopulmonary arrest does not always follow immediately. When this time is prolonged, the transplant team may be forced to stand down. This time varies in patients which is why the UK has stand downs in 40% of cases where organ retrieval teams are mobilized for possible DCD donations.⁽⁹⁾ NHS guidelines suggest that transplant teams stand down after 60 minutes for liver and pancreas retrieval and 120 minutes for kidney retrieval, with the possibility of waiting another 120 mins after reassessment. In South Africa, the stand-down time is limited to 120 mins.⁽¹⁰⁾ To try and reduce the number of stand downs, criteria have been developed that can be looked at to determine whether time following withdrawal of life-sustaining therapy is likely to be short or prolonged. In doing so, factors which were found to be associated with prolonged time between withdrawal of life-sustaining therapy and circulatory arrest were ⁽¹¹⁻¹³⁾:

- age (younger patients arrest earlier)
- cause of death
- inotropic use (associated with earlier arrest)
- mode of ventilation (those receiving controlled mechanical ventilation arrested earlier)
- fraction of inspired oxygen (those having higher requirements arrested earlier)
- systolic blood pressure and
- arterial pH

Table 3
Stand down time for organ retrieval after withdrawal of life sustaining treatment and asystole⁽¹⁴⁾

Organ	Stand Down Time for organ retrieval	Comments
Liver	60 mins	
Pancreas	60 mins	
Kidney	120 mins	Reassess and possibly wait for another 120 mins

Donation after Brain Death^(15, 16)

Donation after brain death, previously known as heart beating organ donation, refers to organ donation from a donor who is diagnosed with brain death.

Brain death is defined by the American Association of Neurology as:

- 1 – Cessation of brain functioning, including the brainstem;
- 2 – Coma or unresponsiveness; and
- 3 – Apnoea.

The cause of this state must be known and considered to be irreversible.

Brain death is mostly a clinical diagnosis made by performing a number of clinical tests which unveil the absence of brain functioning. Prior to conducting these tests certain prerequisites need to be fulfilled.

Firstly, in the case of a patient going into a coma from an irreversible acute cerebral insult of known aetiology which has affected both hemispheres as well as the brainstem, there must be neuroimaging displaying the acute central nervous system insult that can explain the irreversible loss of neurological functioning.

Secondly, the following conditions, which can mimic brain death, must be excluded:

- i) Un-resuscitated shock
- ii) Hypothermia
- iii) Severe metabolic disorders which can cause a reversible coma
- iv) Peripheral nerve or muscle dysfunction and neuromuscular blockade
- v) Drug intoxication (e.g. Alcohol, hypnotics, barbiturates)

Once these factors have been excluded, clinical neurological examination can continue.

The diagnostic criteria mentioned in the 2010 Neurology International Journal describe that the patient needs to be in a deep unresponsive coma, meaning that they do not demonstrate any spontaneous movement, neither do they produce a motor response to stimuli in the cranial nerve distribution. Some patients, although brain dead, may have spinal reflexes remaining, but these are confined to the spinal distribution and do not prevent the diagnosis of brain death. Importantly, brainstem reflexes must be absent, as these are the main indicators for the presence of brainstem function.

Cranial nerve (CN) tests are used to assess for brainstem death.

1. Pupillary reflex (*Afferent CN II and Efferent CN III*): dilated, medium-sized or small pupils may be found together with the absence of reactivity to bright light in both eyes

2. Corneal reflex (*Afferent CN V1 and Efferent CN VII*): bilateral reflexive closure of the eyelids in response to stimulation of the cornea with a cotton swab or upward deviation of the eye (Bell's phenomenon) is absent
3. Oculo-cephalic (Doll's eyes) and oculo-vestibular (Caloric test) responses (*Afferent CN VIII and Efferent CN III and VI*): where eyes would move conjugately in opposing direction to brisk turning of the head – Doll's eyes, or move towards the side of ice-cold water stimulation of the ear's tympanic membrane – Caloric test; these are not seen in brainstem death
4. Gag and cough response (*Afferent CN IX and Efferent CN X*): this is tested by passing a suction catheter through the endotracheal tube and applying negative pressure for several seconds. Absence of a cough reflex from this stimulation suggests brainstem death

The Atropine test is another method for examining brain death, specifically the presence of bulbar parasympathetic activity on cardiac activity. A negative Atropine test suggests brain death. The test is performed by administering 2mg of Atropine intravenously while a continuous ECG is monitored, for 10 minutes. What is expected is that the heart rate will increase. The test is considered to be negative if the heart rate does not increase by more than 3% of baseline rate, as this confirms the absence of vagal tone from a functional bulbar parasympathetic activity on the heart.^(16, 17)

Lastly, the Apnoea test is performed to clinically demonstrate the presence of brain death through the absence of respiratory effort, even though it has been regarded as controversial for its potential to worsen patient condition. In South Africa the apnoea test is performed by first ventilating the patient with 100% oxygen for 10 minutes, and ensuring that the PaCO₂ at this time is within normal limits (35 – 45mmHg). The patient is then disconnected from the ventilator and placed on a T-piece with oxygen flow rate running at 15 L/min. During this time, the PaCO₂ rapidly rises at a rate of about 3mmHg/min, and should, provided there is brainstem function, stimulate the respiratory centre to start respiration. If, however, no respiratory movements are seen over the next 10 mins, and the PaCO₂ has risen to above 50mmHg or to more than 20mmHg above baseline, then the test is considered to be positive and the patient is declared brain-dead. If, however, the patient starts to desaturate and become haemodynamically unstable during this period, they may be returned back onto the ventilator, whilst a blood gas is taken to check the level of PaCO₂ from the period of apnoea. If the level is above 50mmHg, and there remains no spontaneous ventilation, the patient may also be declared brain dead.⁽¹⁸⁾ After a positive finding, a second apnoea test may or may not be performed to confirm the previous findings, depending on the accepted protocol in the country.

In the UK, the second apnoea test is performed after patient ventilation has been resumed and the blood gas has normalized. In the United States, the apnoea test is done only once, after confirmatory tests have been done showing the absence of brain recovery.

A number of ancillary tests may be done if there is any uncertainty pertaining the diagnosis of brain death or if neurological tests were unable to be completed. These tests are grouped into two groups:

- 1) *Cerebral perfusion tests*: These aim to demonstrate the absence of blood flow to brain tissue, which would undoubtedly prove that the brain cells are dead by virtue of not getting oxygen delivery.
 - a) **Cerebral angiography** - This is the gold standard test used for looking at cerebral perfusion. Cerebral angiograms can be done by computed tomography (CT), by digital subtraction (DS), by intravenous radionuclide or by magnetic resonance imaging (MRI). CT angiography (CTA) has been shown to have a high sensitivity as well as a wide safety margin when it comes to diagnosing brain death. A retrospective study done in Canada which looked at 4-vessel DS angiography in brain death suggested that the absence of cerebral deep venous drainage or intracranial capillary blood flow might be

a better objective study than the 4-vessel angiogram at demonstrating cerebral circulatory arrest for brain death diagnosis.⁽¹⁹⁾

b) **Transcranial Doppler (TCD)** – This test has the advantage of being a non-invasive test. TCD looks at local blood flow in the proximal area of large intracerebral arteries. By using the transtemporal acoustic window, the middle, anterior and posterior cerebral arteries, as well as the posterior communicating artery may be located and velocities obtained if present. However, its main limiting factor is that it is very operator dependent.

1) *Neurological electrical activity tests*: These tests aim to demonstrate the absence of neurological electrical activity in order to confirm brain death.

a) **Electroencephalogram (EEG)**: This test looks for an isoelectric EEG trace to confirm brain death, however it is sensitive to hypothermia, extreme hypotension, drugs and electrical interference. Due to these factors it is not recommended that the EEG be used in isolation.

b) **Multimodality evoked potentials (MEP) and electroretinography (ERG)**: These tests have the advantage over the EEG of being resistant to the effects of hypothermia and drugs. But they too have their own limitations, and therefore also cannot be used as single tests in the confirmation of brain death.

It is thus recommended that if EEG is used to confirm brain death, that it either be used in conjunction with other bioelectrical tests such as MEP and ERG, or together with the cerebral perfusion tests such as TCD.

UNSUITABLE DONORS

(CONTRA-INDICATIONS FOR ORGAN DONATION FROM DECEASED DONORS)

When it comes to exclusion criteria for deceased donors, different countries have their own protocols as to who can be included as a donor and who cannot. But there are a few constants that remain the same throughout the differing protocols.

The Council for Medical Schemes in SA lists the following as exclusion criteria for deceased donors:

- Donors above the age of 70yrs and babies under 500g in weight
- Donors with a malignancy or with a previous metastasized malignancy
- Donors with aplastic anaemia or with a haematological malignancy
- Donors in multiple organ failure
- Donor with the following infections:
 - Tuberculosis
 - Intra-abdominal sepsis
 - HIV*
 - Rabies
 - Hepatitis B**
 - Human T-cell lymphotropic Virus
 - Viral encephalitis or meningitis
 - Active Herpes or Cytomegalovirus infections
 - Acute Epstein-Barr Virus
 - West Nile Virus infection
 - SARS

- Active Cryptococcus, Aspergillosis, Histoplasma, Coccidioides, Candida or invasive yeast infection
- Active parasitic infections: Trypanosoma cruzi, Leishmania, Strongyloides or Malaria
- Creutzfeldt-Jacob disease

*Donors with HIV infection can be have their organs procured for transplantation into suitable HIV infected recipients.

**It is now acceptable for a donor with Hepatitis B surface antigen (HBsAg) to have their organs transplanted in recipients who are HBsAg + or who have developed immunity against Hep B by either immunization or previous infection as demonstrated by a Hepatitis B surface antibody (HBsAb) titre of >10IU/ml.⁽²⁰⁾

CONSENT FOR ORGAN DONATION – WHAT DOES THE LAW STATE? ⁽²¹⁾

Once death has been confirmed, whether circulatory or brain death, and exclusion criteria excluded, consent is required in order to proceed with organ retrieval. It is noted in South Africa's National Health Act that the diagnosis of brain death prior to organ donation needs to be determined by two doctors, of whom one must have been qualified for at least 5 years. Neither of the certifying doctors may be part of the transplant team.

When it comes to the issue of consent, the National Health Act states that a will or document signed by the deceased and witnessed by two competent witnesses is acceptable as consent to organ donation. It is required that the institution or the specific recipient to whom the organs are being donated (termed as the 'donee') be specified in the will or document, or else the donation is considered null and void. However, in the case of organ donation for transplantation, this rule does not apply. If a donee institution or person has not been specified, regulations state that the institution nearest to the place where the deceased donor is kept shall be considered as the donee.

Where the deceased has not documented their wish to donate their organs, and neither have they expressed any objection to it whilst still alive, consent to donation may be given by a relative. The hierarchical order provided in the act in which specific relatives may give consent is firstly spouse, then partner, major child, parent, guardian, major brother or major sister of the deceased. If, however, the persons who can provide consent on behalf of the deceased cannot be located at the time of death after all steps to try and locate them have been taken, the Director-General of Health is authorized to donate any tissue of that person to an institution or person.

The National Act further states that human tissue retrieval must occur within a 24 hour period after the donor's death, with the exception where a whole-body donation has been made to an institution for tissue harvesting.

It is important to take these laws into account as failure to comply with them when retrieving organs from a deceased individual for donation is considered an offence which if convicted, may result in imprisonment (not more than 5 years) or a fine or both.

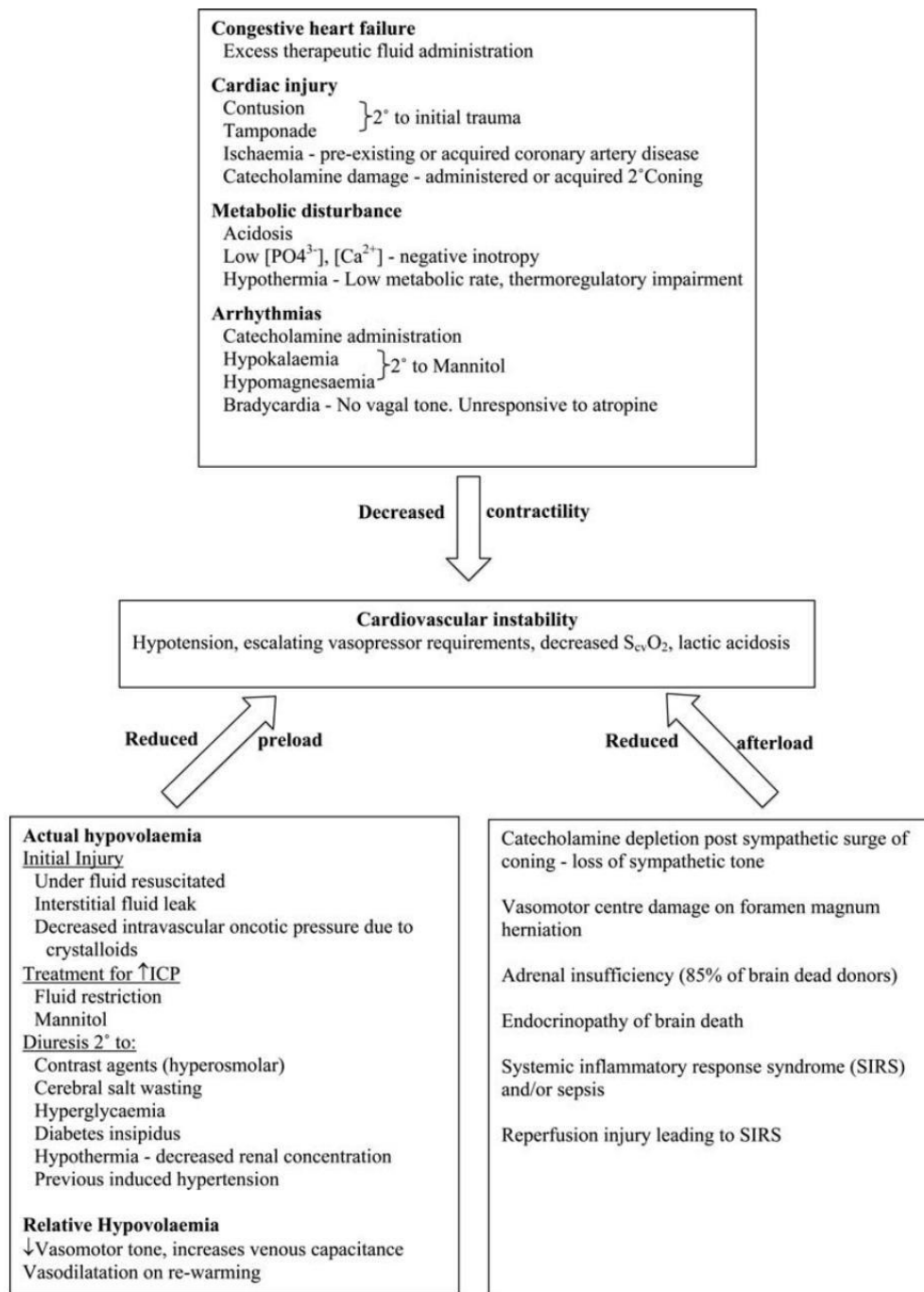
PHYSIOLOGICAL CHANGES AFTER BRAIN DEATH AND ANAESTHETIC CONSIDERATIONS ^(22, 23)

A number of changes occur as a result of brain stem death which have the potential of damaging potential transplant organs. Being aware of these changes allows the critical care team and anaesthetist to optimize the physiological condition of the vital organs so they may still be in good condition at the time of procurement.

These changes occur in the following systems:

- 1) **Cardiovascular.** An initial hyper-adrenergic state or 'catecholamine storm' caused by ischemia of the pons during brain herniation leads to pulmonary and systemic hypertension and a resultant increase in afterload to both the right and left ventricles. This situation leads to myocardial ischaemia from increased oxygen consumption with subsequent reduction in myocardial function. The associated myocardial injury that occurs can result in left ventricular failure with a reduction in cardiac output. The Cushing's reflex can also occur during this time, where hypertension with bradycardia is seen as a result of reflex baroreceptor activation and/or midbrain activation of the parasympathetic nervous system. Brain stem herniation through the foramen magnum further results in the loss of spinal cord sympathetic reflexes. This causes vasoplegia and further reduced cardiac output. Subsequently, this next phase, which often occurs several hours later, demonstrates an ensuing drop in preload and afterload which also compromises myocardial perfusion and jeopardizes haemodynamic stability. Arrhythmias also occur due to a number of factors such as electrolyte imbalances and acid-base disturbances.

Hypovolaemia is often seen after brain death and may be aggravated by the operation itself because of the fluid shifts which occur during thoracic and abdominal incisions and due to evaporative losses while the organs are exposed. Polyuria from Diabetes Insipidus also contributes to the hypovolaemia.



Factors causing cardiovascular instability in the potential organ donor.

The anaesthetic management of these cardiovascular problems entails the administration of intravenous fluids. It is crucial to keep in mind that whilst a moderate amount of IV fluid may be acceptable for maintaining liver and kidney perfusion, it may be damaging to organs such as the lungs and pancreas. Therefore, in order to improve organ perfusion by counteracting the vasoplegic effects of brainstem death vasopressors may be used judiciously. Dobutamine, adrenaline, noradrenaline, phenylephrine or vasopressin may be used. Of these vasopressors, vasopressin is generally preferred because of its co-management of the diabetes insipidus seen in these patients. It is however understood that the risk undertaken by giving vasopressors is that of vasoconstriction and reduction of blood flow to the organs and hence large doses should be avoided. Appropriate cardiovascular goals are outlined in table 5.

The IV fluid of choice to use during organ procurement surgery depends largely on whether the lungs will be harvested. If lungs are to be harvested, colloids are preferred so as to maintain the integrity of the lung tissue. If the lungs are not being harvested, then crystalloids may be used, but the infusion of large volumes of 0.9% sodium chloride is to be avoided because of the complication of developing hyperchloremic metabolic acidosis. It has been suggested that the use of hydroxyethyl starches (HES) as colloids can lead to impaired renal function in kidney transplant patients, however in a recent study by Limnell and Schramko, it was shown that the use of crystalloids alone when compared with the use of crystalloids with colloids increased the risk of developing delayed graft failure. Although the colloid used in this study was Gelatin and not HES, it is mentioned that the newer 3rd generation HESs (e.g. Voluven) cause less colloid-induced kidney injury than the older generations.⁽²⁴⁾

- 2) **Respiratory:** Neurogenic pulmonary oedema may occur after brain stem death due to a number of factors.

The initial catecholamine surge causes a cytokine release which increases the permeability of the pulmonary vasculature.

The increased systemic vascular resistance (SVR) also contributes by increasing the pulmonary venous blood volume and subsequently overloading the lungs.

Lastly excessive crystalloid administration during the resuscitative phase can increase pulmonary hydrostatic pressures and add to the development of pulmonary oedema.

The early administration of methylprednisolone has been shown to minimize the accumulation of extravascular lung water. That, together with the avoidance of intravenous fluid overloading can improve the retrieval rate of lungs for transplant. The ventilation strategy that must be considered given this condition is that of lung protective ventilation.

Listed in table 4 below are targets that should be aimed for when mechanically ventilating donor lungs.

Table 4
Mechanical ventilation targets ⁽¹⁴⁾

Ventilation parameter	Target range
Tidal volume	6–8 ml kg ⁻¹
PEEP	>5 cm H ₂ O
Peak inspiratory pressure	<25 cm H ₂ O
pH	7.35–7.45
<i>P</i> _{aCO₂}	4.5–6.0 kPa
<i>P</i> _{aO₂}	≥10 kPa
<i>S</i> _{pO₂}	≥95% for the lowest <i>F</i> _{I_{O₂}} , ideally <0.4

- 2) **Endocrine:** As a result of pituitary ischaemia, diabetes insipidus (DI) occurs from the underproduction of antidiuretic hormone (ADH). This leads to polyuria (urine output >4ml/kg/hr), hypernatremia (serum sodium >145 mmol/L), with a high serum osmolality (>300 mOsm/kg) and a low urine osmolality (<200 mOsm/kg). To replace fluid losses, low sodium-containing IV fluids are administered. Earlier use of Vasopressin to support the cardiovascular system may prevent the need to treat DI. Desmopressin is given as a 1-4 mcg bolus followed by 1-2 mcg doses 6 hourly if DI persists.

There is also decreased production of adrenocorticotrophic hormone (ACTH) which causes low circulating levels of cortisol that further aggravate hypotension. Methylprednisolone 15mg/kg daily is given to manage this.

Hypothalamic dysfunction also occurs, resulting in loss of thermoregulation, functional hypothyroidism and vasodilation. Some centres will administer T3 intravenously in order to manage the effects of hypothyroidism.

Lastly, hyperglycaemia can occur and frequently does. An insulin infusion is then run to maintain blood glucose levels between 4.0 and 8.0 mmol/L.

- 3) **Coagulation:** Abnormalities in coagulation can occur secondary to hypothermia, metabolic acidosis and the effects of catecholamines on platelet function. Damaged brain tissue also causes the release of plasminogen activator and thromboplastin. These changes can lead to a disseminated intravascular coagulopathy. If signs of active bleeding are seen then the patient's coagulation should be corrected.⁽²⁵⁾
- 4) **Musculoskeletal:** Reflex somatic movements can occur as a result of residual spinal reflexes. This is seen as a spontaneous movement of the arms and hands towards the body and is also known as the 'Lazarus sign'. This is disturbing to witness, therefore a dose of muscle relaxant is given on commencement of organ procurement to prevent it.

Table 5
Anaesthetic considerations^(9, 26)

<u>Systems</u>	<u>Recommended Anaesthetic Management of Physiological Changes</u>
Cardiac	Restore intravascular volume
	Use vasopressors as necessary to maintain adequate organ perfusion
	Maintain SBP>100mmHg, MAP>70mmHg, HR 60-120beats/min
Respiratory	Lung protective ventilation strategy: TV 6-8ml/kg of predicted body weight, PEEP 8-10 cmH2O
	Judicious intravenous fluid; CVP 4-8 (<10) mmHg
Endocrine	Vasopressin to support haemodynamics and control polyuria
	Insulin infusion to maintain serum glucose <10mmol/L
	Consider hormone replacement: Thyroxine or T3 infusion; Corticosteroids (Methylprednisolone)
Hematologic	Transfuse for Hb <7 or 8 g/dL to optimize oxygen delivery to organs
	Correct coagulopathy with clotting factors &/or platelets if evidence of ongoing bleeding
Musculoskeletal	Skeletal muscle paralysis

Extrapolated from T. A. Anderson et al⁽¹⁾

SBP – systolic blood pressure; MAP – mean arterial pressure; HR – heart rate; TV – tidal volume; PEEP – positive end expiratory pressure; CVP – central venous pressure.

Specific organ considerations (1, 15, 25)

Heart

In the case of brain dead donors the evaluation for potential heart donors must include the following investigations:

- ✓ 12-lead ECG
- ✓ chest X-ray
- ✓ echocardiogram
- ✓ CK-MB and troponin levels
- ✓ Cardiac catheterization for males above 40 years of age or females above 45 years of age, and younger patients if they have cardiovascular risk factors.

Hearts of DCD donors are only allowed 30 minutes of warm ischemia time to be considered for transplant.

Lungs

Assessment during consideration for lung donation involves doing a chest x-ray and bronchoscopy to examine the general integrity of the lung. In cases of lung retrieval, the extubated patient requires re-intubation by the anaesthetist. This is followed by a single recruitment manoeuvre, after which 10 cmH₂O of continuous positive airway pressure (CPAP) is maintained. At this point, mechanical ventilation should not be restored until the aortic arch vessels have been clamped, and cerebral circulation isolated as this increases the risk of cerebral oxygen delivery occurring. When mechanical ventilation is restarted acute lung injury must be prevented through lung protective ventilation methods.

Liver

In the evaluation of a potential liver donor the following tests are performed:

- ✓ Liver function tests,
- ✓ Prothrombin time (PT),
- ✓ Activated partial thromboplastin time (aPTT) and
- ✓ Liver biopsy for patients with a BMI >32, age >70 and a medical history suggestive of liver disease.

With liver retrieval it is important to note that there is a high risk of biliary complications, more so in the DCD organs, which may result in graft failure. Above that, the haemodynamic changes brought about by brain death can cause injury to the liver. A release of cytokines is seen surrounding the time of liver retrieval and administering methylprednisolone assists with reducing this cytokine release before and during retrieval.

Kidney

Potential kidney donors are assessed using serum urea, creatinine and electrolyte levels. Kidney transplants require that a negative fluid balance be avoided during organ procurement. However, fluid overloading may be detrimental to the condition of other organs in a multi-organ retrieval situation. Dopamine is considered the inotrope of choice in some organ donor protocols because of its beneficial effects on renal grafts. This is supposedly due to its reduction of preservation injury and inflammation, as well as its cardiovascular effects rather than any direct renoprotective effect.

Pancreas

Pancreas donations from deceased donors are generally considered if:

1. There has been no trauma to the pancreas itself,
2. the donor is < 55 years of age,
3. the donor's body mass index is < 30kg/m²,
4. the donor is not diabetic and
5. does not have pancreatitis.

CONSIDERATIONS AFTER CARDIAC DEATH ⁽⁹⁾

When dealing with circulatory death it becomes more difficult to maintain certain physiological parameters given that, unlike with brain death, circulation is required to have come to a complete stop in order to diagnose death. This prerequisite affects the warm ischaemia time and thus the integrity of the organs for donation. There have been debates as to the acceptable amount of time required to have passed from the moment of circulatory arrest to proceeding with the organ procurement process. These have culminated in a generally accepted minimum time of 5 minutes of continuous cardiorespiratory arrest to allow for any possibility of spontaneous return of circulation to pass. It is however emphasized that during this time, no efforts or procedures that might result in the restoration of cerebral blood flow be allowed. Such efforts would include cardiopulmonary resuscitation, cardiopulmonary bypass, and other procedures which may inadvertently restore blood flow to the brain, such as perfusion of the body regionally or systemically with blood-containing fluids (e.g. ECMO), mechanical ventilation with oxygen, or patient movement during transfer to theatre and onto the theatre table. Once this specified time has passed the team is then allowed to commence organ preservation methods. These generally consist of arterial and venous femoral cannulation and extra-corporeal membrane oxygenation (ECMO) which represents the re-initiation of circulation with an oxygen-rich solution.

THE ORGAN PROCUREMENT PROCEDURE ⁽²⁷⁾

Once in theatre, multi-organ procurement requires that there be good communication between the different surgical teams so that techniques and sequences to be followed are clear to all and a smooth, timeous process is undertaken in order to minimize organ damage.

The surgery begins with an incision made from the suprasternal notch to the pubis. This is done so that the thoracic and abdominal organs can all be visualized by the procurement coordinator who then relays information on the general condition of the organs to the different recipient teams. Thereafter the aorta is exposed at the level of the diaphragm and encircled just below or above the diaphragm. The origin of the inferior mesenteric artery is also exposed, then tied and divided. The aorta is then encircled at this level and prepared for cannulation. The inferior mesenteric vein is also encircled and cannulated.

Next, the common bile duct is tied off and divided so the gallbladder can be incised and washed out to avoid autolysis of the biliary tract mucosa. This completes the initial dissection, and the thoracic team is then able to prepare the chest for organ removal. This process involves mediastinal dissection and opening up of the pleural spaces. Sutures are placed in the superior vena cava (SVC), inferior vena cava (IVC) and proximal aorta in preparation for aortic cannulation for cardioplegia. They may also be placed in the main pulmonary artery if the lungs are also being harvested. At this point the lungs may be examined quickly through the pleural spaces.

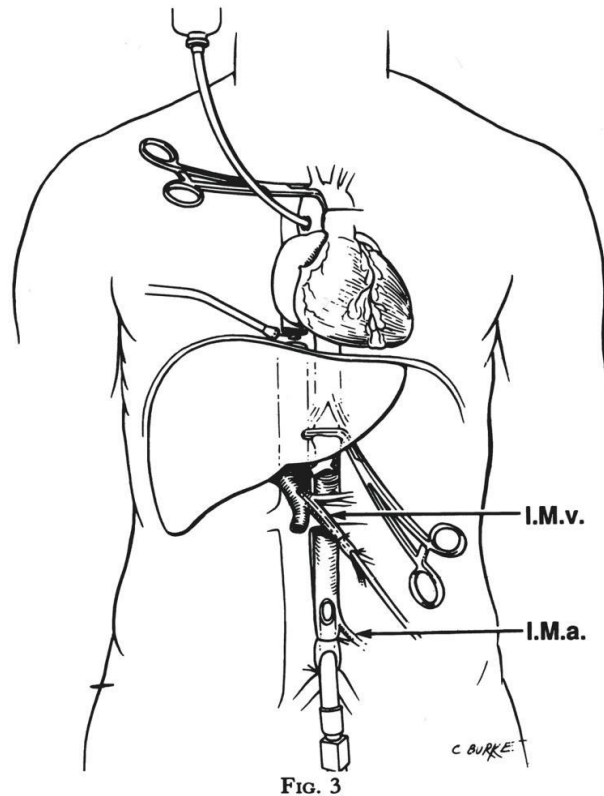


Fig. 3.
Cross clamping of aorta at the time of rapid infusion. *I.M.v.*, Inferior mesenteric vein, and *I.M.a.*, inferior mesenteric artery.

Once thoracic dissection is complete, 300-500units/kg of Heparin is administered intravenously, and the aorta is ligated distal to the inferior mesenteric artery and cannulated. This is followed immediately by tying off the SVC, and simultaneously clamping the proximal aorta and the descending aorta at the level of the diaphragm. Cold infusion with University of Wisconsin (UW) solution is commenced while the heart is perfused separately with cold cardioplegia. The IVC vents the solutions. Once arrested, the heart is removed first. If the lungs are being procured, then cold flush is perfused through the main pulmonary artery and vented out through the left atrial appendage. When the aorta has been transected the pulmonary cold flush will be allowed to vent through the open aorta. After removal of the heart, the lungs are then extracted. Only once this is done is the abdominal team able to commence with organ dissection and removal of the liver, pancreas, intestine and kidneys. It is advised that long segments of major vessels such as the iliac arteries and veins, the IVC and aorta are removed and stored under hypothermic conditions in case vascular problems are met during the transplant operations. The remaining body is then sutured closed and disposed according to the wishes of the family.

ANAESTHESIA FOR ORGAN RETRIEVAL

A checklist is suggested by Gelb and Robertson in an article in the Canadian Journal of Anaesthesia in order to ensure proper preparation of the theatre and to have important drugs ready and available once the procedure starts.⁽²⁸⁾

1. *Check:*
 Consent for organ donation
 Declaration of brain death
 Laboratory tests (electrolytes, haemoglobin and blood gases)

2. *Monitors:*
 - ECG
 - Capnography
 - Pulse oximetry
 - Intra-arterial blood pressure
 - Central venous pressure
 - Urine output
 - Temperature

3. *Drugs:*
 - Vasoactive drugs (adrenaline, noradrenaline, dopamine, isoproterenol)
 - Lignocaine
 - Desmopressin
 - Diuretics (furosemide, mannitol)
 - Heparin
 - Antibiotics
 - Other drugs as requested by the transplant team

4. *Other:*
 - Warming blanket
 - Fluid warmer
 - IV fluids (crystalloids, colloids, blood)

There is no national standard pre-operative checklist for preparing for organ retrieval surgery currently available in South Africa, but different institutions will have their own checklists, such as the WHO checklist, modified for the organ procurement surgery.

As the anaesthetist involved during procurement surgery, besides having to administer Heparin at a given time, it may be required that blood samples be taken for further lab studies such as irregular antibodies. Other than those, it is usually not necessary to take further investigative samples.

There is often a haemodynamic response seen after surgical stimulation, which is the result of spinal reflex activation. This is frequently observed as an initial rise in heart rate and blood pressure mimicking a pain response. To attenuate this a short-acting opioid may be given on induction, or else a short-acting beta-blocker that can be stopped should the haemodynamic response change. If a bradyarrhythmia occurs intraoperatively, a direct acting beta agonist is used. Atropine does not demonstrate any response in the brain dead patient.

Ventilation strategy is continued from ICU through to theatre. Air and oxygen is used to ventilate the patient. There has been evidence showing the benefit of giving volatiles such as Sevoflurane during organ procurement surgery.⁽²⁹⁾ Volatile agents cause ischaemic pre-conditioning of organs which has been suggested to improve graft organ functioning. Finally, ventilation is discontinued once the aorta is cross-clamped. This time should be documented on the anaesthetic chart.

PSYCHOLOGICAL ASPECTS OF ORGAN RETRIEVAL ⁽³⁰⁾

The organ procurement process has been tailored over the years to become a highly organized procedure involving transplant teams with much experience on the on-goings from death declaration right through to termination of ventilation. However, what often occurs is that the organ procurement operation is done in a health care facility where there are bound to be inexperienced team members who will most likely be affected by the events which unravel before them.

In 1992 K. L. Kawamoto described the implications of organ procurement surgery for the perioperative care team in the operating room (OR) in an article in the Association of Perioperative Registered Nurses Journal. This article revealed that “staff members may have underlying concerns that organ donors are not dead, despite a declaration of brain death”, which meant that in their minds the organ retrieval process may in fact be killing the donor patient. These thoughts, together with the exposure to the process of removing organs which are rarely seen removed from patients in the OR e.g. heart and lungs, can be particularly stressful for the centre's OR team. Other stressors on staff that have been identified are the lack of certainty regarding the diagnosis of brain death, which the operating team is usually not involved in. Also, the effect of experiencing a death on table, an experience commonly interpreted by OR staff as a failure. That being realised, staff members often find themselves putting aside their feelings of anxiety and distress in order to get through the procedure and hopefully forget about it. This is often done to the detriment of the individual member and the team dynamics. It has also been shown in studies that organ donation and transplant professionals are also likely to suffer from burn out and traumatic stress as a result of their involvement⁽³¹⁾. What this highlights is the dire need for a support system for the health care professionals involved in the organ procurement process, especially when it occurs in centres that do not frequently have organ procurement surgery done. It has been suggested that a member of the transplant organization remain behind after the rest of the team has left with the donor organs, to assist with the post-mortem care of the donor body and meanwhile address any questions or concerns the theatre personnel may have. Thereafter, a debriefing session should be scheduled for the ICU and OR team at a later stage, at which time any emotional or technical issues may also be addressed.

CONCLUSION

Organ procurement surgery, although not frequently done in our setting, requires an intricate knowledge of the physiological changes a patient goes through after brain death, and to a lesser extent, circulatory death. It also requires that one carefully manages the haemodynamics for the relevant organs to ensure good perfusion before the organs are removed. This becomes important in ensuring better outcomes for organ survival in the transplant recipient. The role we play as physicians during this process not only allows improved graft survival, but also helps families and the general public appreciate more the good that can come from donating their own organs or organs of deceased loved ones. This will go a long way towards increasing the number of potential donors on our list.

Finally, the psychological aspect of such a procedure must not be forgotten, and attention needs to be paid to the involved staff members, especially in institutions where organ procurement surgery is not frequently done.

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