Donation after Circulatory Death

Maastricht Categories III & IV

The Intensive Care Society of Ireland

September 2016
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Organ donation has religious, cultural, ethical and legal dimensions. As clinicians, the public trust in our abilities to respect and uphold the highest ethical standards, to act in accordance with our professional bodies, and to abide by the existing legislative framework.

The donation of organs is an act of altruism and human solidarity that benefits those in medical need and society as a whole. Transplantation affords patients improvement in the duration and also the quality of their lives. In the words of Cardinal Joseph Ratzinger before becoming pope Benedict XVI:

“To donate ones organs is an act of love that is morally licit. As for myself I have agreed to give my organs to whomever may be in need; it is simply an act of love.”

End of life care in the intensive care unit may be an area of significant stress for staff and the process of organ donation, particularly where it is an infrequent event, may compound this stress.

The Guide to Professional Conduct and Ethics for Registered Medical Practitioners (8th edition 2016), specifically refers to the doctor’s responsibilities where organ donation is concerned:

“If patients are diagnosed with a condition which is likely to lead to their death in the near future, and if they are suitable candidates to donate their organs, you should raise this sensibly with them”.

“If a patient is close to death and cannot give their views, you should ask the patient’s family whether the patient had expressed any views about organ or tissue donation or if they might want to donate”(1).

End of life care in general and DCD in particular are areas where ethical challenges do occur. The fundamental ethical pillars of Truth, Autonomy, Beneficence, Nonmaleficence and Justice are respected within these guidelines. A comprehensive discussion of ethics and law in the context of DCD is presented within Transplantation from donors after Deceased Circulatory Death, Chapter 5 available at [www.bts.org.uk/guideline](http://www.bts.org.uk/guideline) The steps described within these guidelines are comparable to the above and other international Guidelines accessible online [www.health.nsw.gov.au/policies](http://www.health.nsw.gov.au/policies) (2-8).

The Irish Human Tissue Act, first drafted in 2009, is on the Department of Health’s legislative program. It addresses several areas pertinent to the field of organ donation and transplantation, specifically in relation to hierarchy of relationships, consent and authorisation for patients who lack capacity. Several revisions are likely before it comes before Dail Eireann for discussion.
The practice of Organ Donation after the Circulatory determination of Death (DCD) is nothing new. Before the widespread adoption of brainstem death criteria DCD represented the only mechanism where a deceased patient could become an organ donor.

These recommendations are based on consultations previously undertaken in response to the first policy of its kind being introduced as outlined below (9).

<table>
<thead>
<tr>
<th>Date</th>
<th>Consultation Undertaken</th>
<th>Response</th>
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<tbody>
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<td>2011</td>
<td>Beaumont Hospital Clinical Ethics Forum</td>
<td>Approved</td>
</tr>
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<td>2011</td>
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<td>2012</td>
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<td>2012</td>
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<td>2012</td>
<td>Division of Nursing and Midwifery of the HSE</td>
<td>Support</td>
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<td>2012</td>
<td>Coroners Society of Ireland</td>
<td>Support</td>
</tr>
<tr>
<td>2011</td>
<td>National Office for Organ Donation and Transplantation (NORDTO)</td>
<td>Support</td>
</tr>
<tr>
<td>2016</td>
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<td>Support</td>
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**Donation after Circulatory Death: Background**

Donation after Circulatory Death (DCD) occurs when a patient donates organs following the determination of death by cardio-respiratory criteria. It is also known as Donation after Cardiac Death (DCD), Donation following the Circulatory Determination of Death (DCDD), or Non Heart Beating Organ Donation (NHBD).

DCD was the standard procedure for organ procurement before the widespread adoption of Brainstem Death (BSD) criteria. DCD was largely abandoned during the 1970’s, the damaging effects of the “warm ischaemic time” (WIT) cited as one major difficulty. Today the incidence of BSD is declining. The reasons for this decline include improvements in safety at work and on the roads and improved neurological Critical Care.

Where DCD is concerned, WIT is the period of hypoperfusion that inevitably occurs following the withdrawal of life-sustaining therapies. The WIT begins when the $\text{SaO}_2$ or Systolic BP fall below 70% or 50mmHg respectively and ends with cold perfusion of the organs (10). With advances in immunosuppression, storage and perfusion of organs, outcome data now demonstrate almost equivalent renal, pancreatic and pulmonary graft survival (11-14). Although hepatic transplantation from DCD donors is associated with an increased incidence of vascular and biliary complications, these may be minimised by stringent donor criteria (15).

**The Maastricht Classification**

Potential donors after circulatory death may be divided into 4 categories, originally described in Maastricht in 1995 and updated in 2013 (Appendix A) (16). These categories define whether the permanence and irreversibility implicit in the declaration of death is based on:

(a) failed CPR efforts: a “cannot resuscitate” situation (Categories I, II & IV),

or

(b) because CPR was deemed inappropriate: a “will not resuscitate” situation (Category III).
**Maastricht Category III:**

These patients die following the elective withdrawal of life-sustaining therapies. The vast majority of these patients have devastating non-recoverable neurological injury, typically secondary to traumatic brain injury or hypoxic ischemic encephalopathy.

Rarely organ donation may occur following the withdrawal of life-sustaining therapies in patients who have not sustained severe neurological injury. Examples may include the withdrawal of cardiovascular supports in Extra-Corporeal Life Support or the withdrawal of respiratory support in high spinal injuries or neuromuscular disorders.

**Maastricht Category IV:**

These patients may already have a diagnosis of BSD. Others are likely to fulfil criteria for BSD, but formal brainstem testing is deemed impossible due to haemodynamic or respiratory instability. Four-vessel cerebral angiography may also prove impossible due to hypotension. DCD may be the only feasible way for these patients to donate organs.
Over-Riding Principles
These Guidelines apply only to patients who may be classified as Maastricht categories III or IV. DCD should only be undertaken when there is consensus among all clinicians and among all family members. Care of the dying patient is of paramount importance and measures to maintain the comfort and dignity of the patient will not be compromised for organ donation. No interventions that could possibly cause pain or distress to the patient before death are acceptable. Blood sampling (to facilitate viral screening and crossmatching) and heparin administration are permissible and should be specifically addressed in the consent process (Appendix E) (12,17-23).

Redirection of care towards palliative measures in the ICU
The decision to withdraw life-sustaining therapies in ICU is normally made by the primary admitting Physician or Surgeon in conjunction with the ICU Consultant. Patient autonomy and their wishes as interpreted and expressed by their families are always respected.

In all patients deemed potential candidates for DCD, the opinion of a second ICU Consultant that life-sustaining therapies are medically inappropriate is required.

(1) Devastating neurological injury
In the vast majority of cases where DCD is considered, the underlying diagnosis is of a neurological condition. In these situations, the opinion of a neurologist or neurosurgeon that life-sustaining therapies are medically inappropriate should be documented before proceeding to DCD.

(1a) Devastating Traumatic Brain Injury or Massive Intracranial Haemorrhage.
These injuries are characterised by definitive structural evidence on CT or MRI. In these situations the neurological (whether neuromedical or neurosurgical) opinion may not necessarily involve an on-site personal review, however, it must be the opinion of a neurological consultant, based on the clinical history and appropriate radiological plus or minus electrophysiological investigations.

(1b) No CT or MRI evidence of devastating neurological injury
Where there is consideration given to WLST in these situations, the personal review and on-site opinion of a consultant neurologist is mandated. This consultant opinion must be attained before any consideration is given to DCD.

(2) Patients without devastating neurological Injury
DCD is occasionally considered in patients without a devastating neurological injury. Death may result from the elective withdrawal of mechanical ventilation in patients with end-stage respiratory failure, high spinal injuries or neuromuscular disorders, or the elective withdrawal of cardiovascular supports such as the discontinuation of ECMO.

In these situations, there should be agreement by two ICU Consultants together with a Consultant Surgeon or Consultant Physician that further life-sustaining therapies are medically inappropriate before DCD is undertaken.

Timing of Discussions and Communication with Families
The topic of organ donation should be visited only after a decision has been made to redirect therapies to palliative measures. All healthcare professionals involved should agree that organ donation could be
an appropriate end-of-life care pathway before a patient’s family is approached in situations where DCD is a potential outcome.

Where this agreement exists, it is appropriate to explore with the patient’s family whether the patient had expressed any views about organ or tissue donation, and if donation is likely to be a possibility (1).

Where a family raises the question of organ donation either before a decision to redirect therapies to end-of-life care has been reached or before brain death has occurred, the intensivist should:

“ensure the family understands that the intensivist will revisit the issue of organ and tissue donation without being further prompted should it become appropriate in the future” (24).

**Inclusion and Exclusion Criteria**

The criteria are similar but not identical to those used following BSD. An incidence of delayed graft function is expected and therefore stringent age and comorbidity restrictions should apply.

The patient must be dependent upon ventilation or vasopressors to the extent that they are likely to die within 90 minutes of withdrawal. While there are several predictive tools, the experience and insight of the ICU staff are perhaps most valuable (Appendix F)(25-35).

The agreement of the coroner is required in the vast majority of cases where the potential for organ donation exists. It is reasonable to discuss all potential patients with the coroner.

**Authorisation-Consent**

Every attempt will be made to ascertain the patient’s wishes with respect to organ donation. Unless DCD has the support of all the family, then it should not be pursued. Assurances are given to family members that they may change their minds at any time up to the time of withdrawal of life-sustaining therapies. Premortem blood sampling and systemic heparinisation are specifically addressed. A detailed explanation relating to the withdrawal of life-sustaining therapies and possible **stand-down** after 90 minutes will be given. Information is given on which organs may be retrieved and the subsequent care of the deceased.

**Time-Out Process**

The essential participants include the ICU consultant or consultant Anaesthetist, ICU and theatre nursing staff, the donor co-ordinator and the transplant retrieval teams. Close liaison between the teams will ensure that all expectations are met and all potential outcomes are discussed before withdrawal of life-sustaining therapies.

**Premortem Interventions**

The patient is fully anticoagulated, the standard heparin dose is 300 IU kg⁻¹. The patient may remain in the ICU or be transferred to an appropriate area with privacy for family members where withdrawal of life-sustaining therapies will occur. The administration of heparin has figured prominently in the discussions around DCD and is reviewed in Appendix E.

**Withdrawal of Life-Sustaining Therapies (WLST)**

Mechanical ventilation and inotropic support will be discontinued. Sedative infusions will not be weaned. The ICU doctor will administer sedative, analgesic or antisialogogue medications as appropriate to optimise patient comfort.
Some clinicians recommend the gradual reduction of ventilatory support before terminal extubation to allow time to control tachypnoea through the titration of medications. Many advocate terminal extubation as the chosen method of airway management and argue that palliative goals are best achieved by appropriate pre-emptive sedation (rather than reactively treating tachypnoea) and by reducing technology wherever possible. Survivors of critical illness recall endotracheal tubes and suctioning as being significant sources of discomfort thus reinforcing the argument for removal of artificial airways.

The patient’s vital signs will continue to be monitored and recorded from when life-sustaining therapies are withdrawn to the time of death.

If death does not occur within 90 minutes from the withdrawal of life-sustaining therapies, then it is reasonable to stand-down organ donation as the dying process may be prolonged (Appendix D).

**Determination of death**

This will be in accordance with the criteria defined by Academy of Medical Royal Colleges Criteria (2008) (38):

- Death is certified after 5 minutes of asystole on a continuous ECG display
- OR
- 5 minutes absence of pulsatile flow using direct intra-arterial pressure monitoring.

This should be accompanied by apnoea, absent pupillary reactions, corneal reflexes and absent response to supraorbital pressure.

**Period of Non-intervention**

This is a second 5-minute period after the diagnosis of death. In this time the patient continues to be monitored for evidence of autoresuscitation (defined as the unassisted Return of Spontaneous Circulation (ROSC) after a cardiac arrest). Autoresuscitation may be characterised by the resumption of breathing, a change in neurological status or the return of a pulse or an arterial waveform. Autoresuscitation has never been described in the context of controlled DCD (39). Should this occur however, a further observation period of 5 minutes is mandatory after this activity has disappeared, before proceeding with organ donation. The period of non-intervention may be used to transfer the patient to the theatre where sterile preparation and draping may begin. No incision will be made until this 5-minute period has elapsed.

**Care of the body of the deceased patient**

The remains of the deceased patient are cared for in accordance with normal practice. The patient’s family may wish to spend time with the deceased before the remains are taken to the mortuary. Where a postmortem is required by the Coroner, formal identification with the Gardaí is required. This may occur after the organ donation operation has been completed or later in the mortuary.

**Education, Audit and Clinical Governance**

While DCD is not new (and was indeed the route for organ procurement in the early days of transplantation), most medical and nursing staff will not be familiar with the processes involved. It is an important end-of-life care pathway when criteria for brainstem death are not fulfilled. It will be sustained within any hospital by the development of a locally agreed policy, education, after-event reviews and audit.
Appendix A: References


33. Yorick J, de Groot, MD; Hester F. Lingsma, PhD; External validation of a prognostic model predicting time of death after withdrawal of life support in neurocritical patients* Crit Care Med.* 2012: 40 (1); 233-238


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### Appendix B: Maastricht Classification

#### The modified Maastricht Classification for DCD: Paris 2013 (15)

<table>
<thead>
<tr>
<th>Category</th>
<th>Clinical Scenario</th>
<th>Location</th>
<th>Circulatory Death uDCD or cDCD</th>
<th>Warm Ischaemic Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ia</td>
<td>Found Dead</td>
<td>Out of hospital</td>
<td>Uncontrolled</td>
<td>Approximate calculation</td>
</tr>
<tr>
<td></td>
<td>Unwitnessed</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ib</td>
<td>Found Dead</td>
<td>In-hospital</td>
<td>Uncontrolled</td>
<td>Approximate calculation</td>
</tr>
<tr>
<td></td>
<td>Unwitnessed</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Iia</td>
<td>Witnessed Cardiac Arrest</td>
<td>Out of hospital</td>
<td>Uncontrolled</td>
<td>Approximate calculation</td>
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<td></td>
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</tr>
<tr>
<td>Iib</td>
<td>Witnessed Cardiac Arrest</td>
<td>In-hospital</td>
<td>Uncontrolled</td>
<td>Approximate calculation</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>Withdrawal of Life-Sustaining-Therapy</td>
<td>In-hospital</td>
<td>Controlled</td>
<td>Known Exactly</td>
</tr>
<tr>
<td>IV</td>
<td>Cardiac Arrest during or after criteria for BSD completed</td>
<td>In-hospital</td>
<td>Controlled/Uncontrolled</td>
<td>Known Exactly</td>
</tr>
</tbody>
</table>

Uncontrolled (uDCD): Permanent and irreversible circulatory death determined on the basis that patient *cannot* be resuscitated - failed resuscitation.

Controlled (cDCD): Permanent and irreversible circulatory death determined on the basis that patient *will not* be resuscitated - Do Not Attempt Resuscitation order in place.

The terms “Controlled” and "Uncontrolled” are not used as a measure of clinical coordination, rather to reflect the applicable time constraints for authorisation or consent and the logistics of organising retrieval teams and theatre (4).
Appendix C: Decision Algorithm for DCD

Patient with Severe TBI or Severe Hypoxic Ischaemic Encephalopathy
Decision to redirect therapy towards end-of-life care by Admitting
Consultant and ICU consultant

Controlled Withdrawal of Life-Sustaining therapies considered

Patient deemed a potential candidate for DCD

Second Medical opinion regarding Withdrawal of Life-Sustaining Treatments where admitting consultant is not a Neurosurgeon or Neurologist

Second ICU Consultant opinion

Discussion with Coroner “Lack of Objection” to Organ Donation

Consensus that Withdrawal of Life Sustaining therapies is appropriate between Admitting Consultant + Neurological Opinion + 2 ICU Consultants

Exclude Contraindications +/- Discuss with ODTI @ 1890 100016

Family discussion regarding redirection towards palliative measures

Patient’s wishes and family’s wishes regarding organ donation discussed

Authorisation – Consent and explanation of the process of DCD Specific Authorisation-Consent for Antemortem interventions (Bloods-Heparinisation)

Refusal or Reticence Proceed with normal end of life care

Time Out: Intensive Care medicine, Nursing and Transplantation retrieval teams

Agree on designated time and place for Withdrawal of Life-Sustaining-Therapies
Appendix D: Process of DCD

T1: Remain in ICU or Transfer to Area where WLST to take place

T2: On Arrival
- Heparin 300 IU kg⁻¹,
- Pre-emptive sedation bolus before WLST or
- Reactive bolus after WLST

T3: WLST,
- Stop Ventilation, Inotropes, Extubate

T4: Warm Ischaemic Time begins (WIT)
- SpO₂ <70% or SBP < 50mmhg
- Maximum wait period
  - 90 minutes

Potential Outcomes

- Patient dies within 90 minutes of WLST
  - T5: Time of Death (TOD)
    - is after 5 minutes of Pulselessness and Apnoea
    - other AoRMC Criteria
    - No Evidence of ROSC

- Patient does not die within 90 minutes of WLST
  - Stand-Down time
  - Patient transferred back to ICU to continue EOL care
  - T6: Period of Non-intervention (5 minutes)
    - Patient transferred to Theatre
    - Prepped, Draped,
    - Examine for signs of Autoresuscitation

T7: Organ Donation Operation Begins

T8: Cold perfusion fluid begins
- Warm Ischaemic time ends (WIT)
### Donation after Circulatory Death

*To be completed by doctor caring for patient during WLST*

<table>
<thead>
<tr>
<th>Adressograph</th>
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</table>

**Diagnosis:**

**Admitting Consultant:**
Diagnosis and prognosis consistent with WLST and DCD:

**ICU Consultant Opinions:**
Diagnosis and prognosis consistent with WLST and DCD:

**Neurological opinion (where applicable):**
Diagnosis and prognosis consistent with WLST and DCD:

**Case Discussed with Coroner:**

**Consent from Next of Kin:**

**Consent for Antemortem interventions:**
- Bloods for Crossmatch & Viral screens
- Heparin 300 IU kg⁻¹

**Timeout procedure with teams:**

**Consultant responsible for care during withdrawal period:**

**ICU Staff nurse responsible for care during withdrawal period:**

<table>
<thead>
<tr>
<th>T1:</th>
<th>Ventilation settings prior to WLST</th>
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<tbody>
<tr>
<td></td>
<td>Sedative Infusions</td>
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<table>
<thead>
<tr>
<th>T2:</th>
<th>Heparinisation 300 IU kg⁻¹</th>
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<table>
<thead>
<tr>
<th>T3:</th>
<th>Withdrawal of Life Sustaining therapies</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Date</td>
</tr>
<tr>
<td></td>
<td>Time</td>
</tr>
<tr>
<td></td>
<td>Location</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>T4:</th>
<th>WIT begins</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>SaO₂ &lt;70% or SBP &lt;50mmHg</td>
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</tbody>
</table>

**Medications Administered before and after WLST**

<table>
<thead>
<tr>
<th>Time</th>
<th>Medication</th>
<th>Dose</th>
</tr>
</thead>
</table>

**Criteria for diagnosis of Cardiorespiratory Death**
Determined: After 5 minutes Asystole on ECG  **OR** After 5 minutes of pulselessness on Arterial line

- Pulseless - flat arterial waveform trace  Y/N
- Absent Heart sounds                      Y/N
- Apnoea                                  Y/N
- Pupils fixed with no reaction           Y/N
- Response to supra-orbital pressure      Y/N
- Corneal reflexes                        Y/N

<table>
<thead>
<tr>
<th>T5:</th>
<th>Time of Death</th>
</tr>
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</table>

<table>
<thead>
<tr>
<th>T6:</th>
<th>Period of Non-intervention (5 minutes)</th>
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<tbody>
<tr>
<td></td>
<td>Re-examine for signs of autoresuscitation</td>
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<table>
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<tr>
<th>T7:</th>
<th>Organ donor operation Begins</th>
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<table>
<thead>
<tr>
<th>T8:</th>
<th>Cold perfusion fluid begins</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>WIT ends (Cold Ischaemic time begins)</td>
</tr>
</tbody>
</table>

**Signature:**

**IMC Registration Number:**

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Antemortem and Postmortem Interventions

There should be no medical interventions before withdrawal of life sustaining therapies that are likely to cause discomfort, harm or place that patient at risk of adverse events. Specific examples of such interventions include the administration of phentolamine or thrombolytic agents or premortem femoral cannulation.

Although it is important to estimate the likely timeframe from WLST to death (Appendix F), the temporary withdrawal of mechanical ventilation as required by the Wisconsin and UNOS DCD support tools is within the category of antemortem interventions, and cannot be recommended. While these tools have merits, partial scores may be calculated without ventilator disconnection and together with the other parameters described, the clinician may decide suitability for DCD.

No procedure is permissible after the diagnosis of death that has the potential to restore cerebral circulation. Re-intubation is required where the lungs are being retrieved; the lungs should not be re-inflated until after isolation of the cerebral circulation (usually by aortic or bilateral carotid arterial cross-clamp).

Heparinisation

Risks

Systemic heparinisation may incur a significant risk of bleeding and this risk must be determined on an individual patient basis. Clearly where the patient is bleeding, has a significant DIC or coagulopathy, this risk is compounded and heparin is contraindicated.

Ethical Aspects

While the risks presented must be considered closely:

“In the context of DCD there is no evidence that administering 20000 units of heparin at the time of withdrawal of ventilatory and cardiovascular support or when the patient has become hypoxic but still has a detectable circulation has any impact on the patient or fore-shortens the patients life” (16).

Others state:

“We reiterate that any bad effects of heparin must not be exaggerated without medical evidence. These interventions benefit DCD by improving organ viability, not by causing ‘a more rapid death’ “ (17).

A third group have examined the risk-benefit profile of premortem systemic heparinisation and concluded that:

“so far, no data support a potential hastening of death due to heparin” (18).

Scientific benefits of Heparin in DCD

The principle effect of heparin in the context of DCD is to prevent intravascular thrombosis. The pre-mortem use of heparin in DCD is advocated by the vast majority of transplant surgeons. Some clinicians argue that the post-mortem administration of heparin is sufficient, the evidence suggests pre-mortem heparinisation is superior and will result in better outcomes from all organs (19).

One large meta-analysis examined outcomes from DCD and DBD liver transplants (N= 1184 & 7847 respectively). This analysis strongly supported the antemortem use of heparin in liver transplantation.
from DCD donors. Pre-mortem administration of heparin before withdrawal of life support reduced the incidence of primary non-function of the allograft from 11% to 3.4% (19).

Lung transplant surgeons also advocate for the use of antemortem heparin in DCD, this is combined with retrograde and anterograde flushing. Heparinisation and flushing will effectively remove thrombi that may form during the donation process (20).

In a systematic review and meta-analysis of DCD versus DBD pancreatic transplants, although graft survival was equivalent up to 10 years; the odds ratio of graft thrombosis was 1.67 times higher in the DCD cohort. This difference disappeared in patients whose donor had received heparin prior to withdrawal of life sustaining therapies (11).

Although numerous case series describe excellent outcomes in recipients of kidney transplants where the donor did not receive heparin, it is recommended by the majority of organ procurement organizations. Heparinisation has been shown to result in improved machine perfusion indices and its use may obviate the need for subsequent TPA or streptokinase for glomerular thrombi.

Heparin is also known to possess anti-inflammatory effects; these effects however are unproven in the context of organ donation (21).

In summary, the administration of heparin is contentious. While both approaches are used internationally, the final decision should be based on the ICU doctor’s assessment of whether the clear benefits of heparin will constitute a greater than negligible complication rate in the potential organ donor patient (22).
Predicting the Time of Death following the Withdrawal of Life-Sustaining therapy

Rationale:
Individual organs tolerate warm ischaemia to varying extents. Typical sequelae of a prolonged ischaemic time are acute tubular necrosis in renal transplantation, ischaemic cholangiopathy in liver transplantation and endothelial injury in pulmonary grafts. The maximum acceptable warm ischaemic time varies for different organs and organisations vary in their individual tolerance of the WIT. The Warm Ischaemic time begins with \( \text{SaO}_2 < 70\% \) and \( \text{SBP} < 50\text{mmHg} \) (25).

Where the WIT is prolonged the organs may be rendered unusable. Between 20 - 40% of patients referred for DCD within Maastricht Category 3 do not die within the potential window where organs were considered viable and therefore the process was "stood-down"(26,27). Maximal tolerable WIT limits must be considered in the context of the age and physical fitness of the potential donor patient. The upper limits of tolerable WIT are patient specific and are generally set by the transplant surgeons. These timelines may be significantly shorter than those outlined below.

Maximum tolerable Warm Ischaemic Times

<table>
<thead>
<tr>
<th>Organ</th>
<th>Australian (7)</th>
<th>British (3)</th>
<th>Canadian (5)</th>
<th>USA (6, 12,13)</th>
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<tr>
<td></td>
<td>\textit{Minutes}</td>
<td>\textit{Minutes}</td>
<td>\textit{Minutes}</td>
<td>\textit{Minutes}</td>
</tr>
<tr>
<td>Kidney</td>
<td>60 (240 in selected patients)</td>
<td>120</td>
<td>120</td>
<td>45-60</td>
</tr>
<tr>
<td>Liver</td>
<td>30</td>
<td>20</td>
<td>30</td>
<td>30</td>
</tr>
<tr>
<td>Lungs</td>
<td>90</td>
<td>60</td>
<td>60</td>
<td>60</td>
</tr>
<tr>
<td>Pancreas</td>
<td>60</td>
<td>30 (60 for Islets)</td>
<td>60</td>
<td>60</td>
</tr>
</tbody>
</table>

This appendix outlines variables that may be utilised to support a clinical judgement in relation to the Time of Death (TOD) following the WLST.

(1) Independent variables (2) Groups of variables (3) Decision-Support tools

(1) Independent Variables

- The Opinion of the Intensive Care Physician

In one study, the clinical judgment of the intensivist predicted death within 60 minutes with a sensitivity of 73% and 89% and at 120 minutes with a specificity of 56% and 25%. Although the opinion of the intensivist was valuable, the sensitivity and specificity were considered too low by the authors to be useful in clinical practice (28). The authors suggest combining this prediction with a combination of physiological variables and clinical support tools.

Others attempting to predict death within 60 minutes from WLST based on intensivist opinion alone, demonstrated an efficiency of 0.82, sensitivity 0.81 and positive predictive value 0.83 (29).
Independent predictors that have been shown on multivariate analysis to correlate with time from WLST to death include (30):

a) Aetiology of Neurological Injury: TBI<ICH<HIE

Patients with neurological injury due to Traumatic Brain Injury die more quickly than patients who have suffered Intracranial Haemorrhage. The longest period from WLST to death is seen in patients who have suffered Hypoxic Ischaemic Encephalopathy.

b) Glasgow Coma Scale
c) Hypoxia and Increased FiO₂ requirements
d) Acidosis at the time of WLST
e) Ventilation mode – an impaired respiratory drive
f) Inotropic support
g) Planned airway management

(2) Groups of variables:

• Combinations of physiological variables correlating with time from WLST to death

In potential DCD donors, useful predictors of death within 60 minutes after WLST include:

• the opinion of the intensive care specialist
• the level of respiratory support required
• the degree of neurological impairment
• the level of cardiorespiratory support

These variables should be considered before discussing organ donation with families of potential organ donor patients (29).

Two Sets of Characteristics predicted death within 60 minutes of WLST

• Significant ventilation requirements, a low spontaneous respiratory rate and a high PEEP
• A combination of Impaired respiratory drive, (low SRR), coma (low GCS) and high circulatory support requirements

(3) Scoring Systems: Decision Support Tools

The DCD N Score:

This score has been validated within a neurocritical care population. Four clinical variables predict time of death (31-33). One point is allocated to an absent corneal reflex, an extensor or absent motor response and an oxygenation index of > 3.0. and two points to an absent cough reflex (maximum score = 5).

<table>
<thead>
<tr>
<th>Absent corneal reflex</th>
<th>Absent cough reflex</th>
<th>Extensor or absent motor response</th>
<th>Oxygenation index &gt;3·0</th>
<th>Score</th>
<th>Probability</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>0</td>
<td>0·08</td>
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<tr>
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<td>No</td>
<td>No</td>
<td>Yes</td>
<td>1</td>
<td>0·16</td>
</tr>
<tr>
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<td>No</td>
<td>No</td>
<td>No</td>
<td>1</td>
<td>0·18</td>
</tr>
<tr>
<td>No</td>
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<td>Yes</td>
<td>No</td>
<td>2</td>
<td>0·26</td>
</tr>
<tr>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>2</td>
<td>0·34</td>
</tr>
<tr>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>2</td>
<td>0·37</td>
</tr>
<tr>
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<td>No</td>
<td>Yes</td>
<td>No</td>
<td>2</td>
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<tr>
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<td>No</td>
<td>Yes</td>
<td>3</td>
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<td>No</td>
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<td>No</td>
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</tr>
<tr>
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<td>Yes</td>
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<td>Yes</td>
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<td>Yes</td>
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<td>Yes</td>
<td>No</td>
<td>4</td>
<td>0·74</td>
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<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>5</td>
<td>0·87</td>
</tr>
</tbody>
</table>
Using the oxygenation index as a continuous variable rather than a categorical variable increases the sensitivity and specificity.

**The Wisconsin DCD Evaluation Tool**

This prediction tool requires temporary disconnection from the ventilator to assess the probability of asystole after WLST. The developers of this tool reported a specificity and sensitivity as 0.83 & 0.84 when predicting death within 60 minutes of WLST in a neurocritical population (34). These results could not be externally validated in a general ICU population and consequently this tool should only be used in for neurological critical care (26,34).
**The UNOS Criteria**

This tool also relies on a disconnection of the patient from the ventilator to determine spontaneous respiratory drive and oxygenation.

It is perhaps most applicable within advanced cardiovascular supports such as those available only within a centre capable of delivering advanced extracorporeal life support.

Patients with two or more criteria may be considered as potential DCD donors based on an external validation study. Patients who had zero, one, two or three criteria had a probability of dying within 60 minutes of 29%, 52%, 65% and 82% respectively (35).

<table>
<thead>
<tr>
<th>Respiratory Drive</th>
<th>Pressure Cost of Oxygenation</th>
<th>Invasive CVS Supports</th>
<th>Vasopressors</th>
<th>IABP &amp; Cardiac Index</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apnoea</td>
<td>PEEP $\geq$ 10 &amp; SaO$_2$ $\leq$ 92%</td>
<td>LVAD</td>
<td>High Dose Vasopressors Noradrenaline Adrenaline or Phenylephrine $\geq$ 0.2 mcgs/kg/min</td>
<td>IABP 1:1 or Dobutamine $&gt; 10$ mcgs/kg/min CI $&lt; 2.2$ l min$^{-1}$</td>
</tr>
<tr>
<td>RR $&lt; 8$</td>
<td>FiO$_2$ $&gt; 0.5$ &amp; SaO$_2$ $\leq$ 92%</td>
<td>RVAD</td>
<td>Dopamine $\geq$ 15 mcgs/kg/min</td>
<td>IABP 1:1 &amp; CI $&lt; 1.5$ l min$^{-1}$</td>
</tr>
<tr>
<td>RR $&gt; 30$ during trial off ventilation</td>
<td></td>
<td>VA ECMO</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Pacemaker with unassisted rhythm $&lt; 30$</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Conclusions**

It is important that the physician considers multiple factors when determining whether a patient is likely to die within 90 minutes from WLST.

It may be prudent to combine clinical expertise and a consensus of medical opinions with individual predictors, groups of predictors and scoring tools before a final decision regarding suitability for DCD is taken.