

Donation after Circulatory Death

Maastricht Categories III & IV

The Intensive Care Society of Ireland

September 2016



Intensive Care Society of Ireland

Contents

Page Number

2	Introduction
3	Donation after Circulatory Death: Background
5	Clinical Practice Guideline
8	Appendix A: References
10	Appendix B: Maastricht Categories 2013
11	Appendix C: Decision Algorithm for DCD
12	Appendix D: Process of DCD
13	Appendix E: Pro-forma Observations
14	Appendix F: Antemortem & Postmortem Interventions
16	Appendix G: Support tools for estimating Time of Death

Contributing Authors

Dr J O'Rourke, Dr R Dwyer, Dr B Marsh.

Council Members of the Intensive Care Society of Ireland.

Introduction

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 sensitively with them”.

“If a patient is close to death and cannot give their views, you should ask the patients 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 The steps described within these guidelines are comparable to the above and other international Guidelines accessible online 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.



Provenance of Current Document

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).

Date	Consultation Undertaken	Response
2011	Beaumont Hospital Clinical Ethics Forum	Approved
2011	Beaumont Hospital Executive and Board	Approved
2012	Intensive Care Society of Ireland	Endorsed
2012	Medical Council of Ireland	Welcomed
2012	Division of Nursing and Midwifery of the HSE	Support
2012	Coroners Society of Ireland	Support
2011	National Office for Organ Donation and Transplantation (NODTO)	Support
2016	Organ Donation and Transplantation Ireland	Support

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 SaO₂ 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).

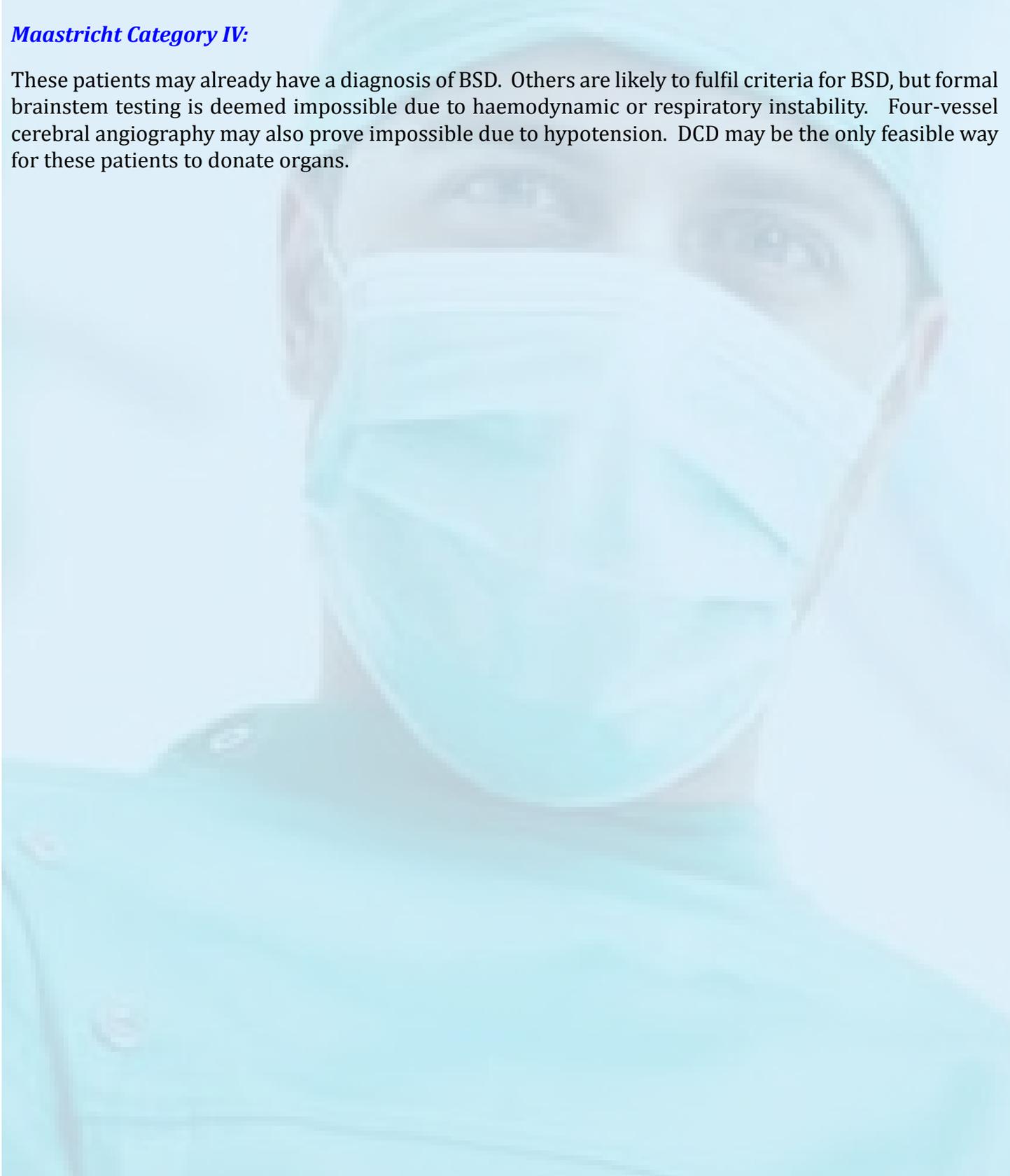
Maastricht Category III:

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 (36,37).

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 Gardai 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

1. Guide to Professional Conduct and Ethics for Registered Medical Practitioners 8th Edition 2016. Section 46.8. Available from: www.medicalcouncil.ie
2. Guidelines relating to solid organ transplants from Non-Heart Beating Donors, British Transplant Society. www.bts.org.uk/guidelines (accessed 10th July 2016)
3. Donation after Circulatory Death: Report of a Consensus Meeting between representatives of The Intensive Care Society, the British Transplantation Society and the NHSBT. www.odt.nhs.uk (accessed 10th July 2016)
4. Shemie S, Baker AJ, Knoll G et al. National Recommendations for donation after Cardiocirculatory death in Canada. *CMAJ*. 2006; 175 (8) s1-24
5. Gries CJ, White DB, Truog RD et al. An Official American Thoracic Society/International Society for Heart and Lung Transplantation/Society of Medicine/Association of Organ and Procurement Organizations/United Network of Organ Sharing Statement: Ethical and Policy Considerations in Organ Donation after Circulatory Determination of Death. *Am J Resp Crit Care Med*. 2013; 188 (1): 103–109
6. Reich DJ, Muligan DC, Abt PL et al. ASTS Recommended Practice Guideline for Controlled Donation after Cardiac Death Organ Procurement and Transplantation. *Am J Transplant*. 2009; 9: 2004-2011
7. Organ Donation after Circulatory Death: NSW Guidelines. www.health.nsw.gov.au/policies (accessed 10th July 2016)
8. National protocol for donation of organs after cardiac death July 2010. Australian Government Organ and Tissue Authority. www.donatelife.gov.au (accessed 10th July 2016)
9. O'Rourke J. Non Heart Beating Organ Donation in Adults: A Clinical Practice Guideline. *Irish Medical Journal*. 2013; 186-188
10. Citerio G, Cypel M, Dobb G et al. Organ Donation in Adults: A Critical Care perspective. *Intensive Care Med*. 2016; 42: 305-315
11. Summers DM, Johnson R, Allen J et al. Analysis of factors that affect outcome after transplantation of kidneys donated after cardiac death in the UK: a cohort study. *Lancet* 2010; 376: 1303-11
12. Shahrestani S, Webster AC, Lam VW et al. Outcomes from pancreatic transplantation after cardiac death: A systematic review and Meta-Analysis. *Transplantation* 2016; (4) DOI: 10.1097/TP.0000000000001084
13. Krutsinger D, Reed RM, Blevins A et al. Lung Transplantation from donation after cardiocirculatory death: A systematic review and meta-analysis. *J Heart Lung Transplant*. 2015; 34: 675-684
14. Cypel M, Levvey B, Van Raemdonck D et al. International Society for Heart and Lung Transplantation Donation after Circulatory Death Registry Report. *J Heart Lung Transplant*. 2015; 34: 1278-1282
15. Taner CB, Bulatoo IG, Willingham DL et al. Events in procurement as risk factors for ischemic cholangiopathy in liver transplantation using donation after cardiac death donors. *Liver Transpl*. 2012; 18: 101-112
16. Thuong M, Ruiz A, Evrard P et al. New classification of Donation after Circulatory Death donors, definitions and terminology. *Transpl Int*. 2016; 27 (7): 749-759
17. Bernat JL, D'Allesandro AM, Port FK et al. Report of a national conference on donation after cardiac death. *Am J Transplant* 2006; 6: 281-291
18. Phua J, Keang Lim T, Zygun D, Doig D. Pro/con debate: in patient who are potential candidates for organ donation after cardiac death, starting medications and or interventions for the sole purpose of making the organs more viable is an acceptable practice. Review article. *Crit Care*. 2007; 11: 211 DOI:10.1186/cc5711

19. Neyricnk A, Raemdonk DV, Monbaliu D. Donation after Circulatory Death: Current Status. *Curr Opin Anaesthesiol.* 2013; 26: 382-390
20. Cao Y, Shahrestani S, Chee Chew H et al. Donation After Circulatory Death for Liver Transplantation: A Meta-Analysis on the Location of Life Support Withdrawal Affecting Outcomes. *Transplantation.* 2016;100: 1513-1524
21. Sanchez P.G , Rouse M , Pratt D.L et al. Lung Donation after controlled circulatory determination of death: A Review of Current Practices and Outcomes. *Transplant Proc.* 2015; 47: 1958-1965.
22. Mousavi S, Moradi M, Khorshidahmad T, Motamedi M. Anti-Inflammatory Effects of Heparin and Its Derivatives: A Systematic Review. *Advances in Pharmacological Sciences.* 2015. doi:10.1155/2015/507151.
23. Motta ED, The Ethics of Heparin Administration to the non heart beating donor, *J Prof Nurs.* 2005; 21(2): 97-102
24. The ANZICs Statement on Death and Organ Donation 3.2 2013. www.anzics.com.au
25. Bradley JA, Pettigrew GJ, Watson CJ. Time to death after withdrawal of treatment in donation after circulatory death (DCD) donors. *Curr Opin Organ Transplant.* 2013. 18: 133-139
26. Munshi L, Dhanani S, Shemie. Predicting time to death after withdrawal of Life Sustaining therapy. *Intensive Care Med.* 2015: 41: 1014-1028
27. Manara AR, Murphy PG, O'Callaghan G. Donation after Circulatory Death. *Br J Anaesthesia* 2012: 108 ;(S1) 108-121
28. Wind J. Snoeijs M, Brugman C, et al. Prediction of time of death after withdrawal of life-sustaining treatment in potential donors after cardiac death. *Crit Care Med.* 2012; 3: 766-769
29. Brieva J, Coleman N, Lacey J et al. Prediction of Death in Less Than 60 Minutes After Withdrawal of Cardiorespiratory Support in Potential Organ Donors After Circulatory Death. *Crit Care Med.* 2013: 41: 12: 2677-2687
30. Suntharalingham C, Sharples L, Dudley C et al. Time To Cardiac Death after Withdrawal of Life-Sustaining treatment in Potential Organ Donors. *Am J Transplant.* 2009; 9: 2157-2165.
31. Rabinstein AA, Yee AH, Mandrekar J, Prediction of potential for organ donation after cardiac death in patients in neurocritical state: a prospective observational study. *Lancet Neurol.* 2012; 11: 414-419
32. Yee AH, Rabinstein AA, Thapa P et al. Factors Influencing time to death after withdrawal of life support in neurocritical patients. *Neurology* 2010; 74: 1380-1385
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
34. Lewis J, Peltier J, Nelson H, et al. Development of the University of Wisconsin Donation After Cardiac Death Evaluation Tool. *Prog Transplant* 2003;13:265-73
35. De Vita MA, Mori Brooks M, Zawistowski et al. Donors after Cardiac Death: Validation of Identification Criteria for predictors of Rapid Death. *Am J Transplant.* 2008: 8: 432-441
36. Truog RD, Cist AFM, Brackett Se et al. Recommendations for End of Life Care in the Intensive Care Unit: The Ethics Committee of the Society of Critical Care Medicine. *Crit Care Med.* 2001: 29 (12); 2332-2348
37. Truog RD, Campbell ML, Randall Curtis J et al. Recommendations for end-of-life care in the Intensive Care Unit: A Consensus statement by the American College of Critical Care Medicine. *Crit Care Med.* 2008: 36 (3); 953-963
38. A Code of Practice for the diagnosis and confirmation of death. Academy of Medical Royal Colleges.2008. www.aomrc.org.uk/.../code-practice-diagnosis-confirmation-death/ (accessed 18th July 2016)
39. Hornby K, Hornby L, Shemie SD. A systematic review of autoresuscitation after cardiac arrest. *Crit Care Med.* 2010; 38: 1246-1253

Appendix B: Maastricht Classification

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

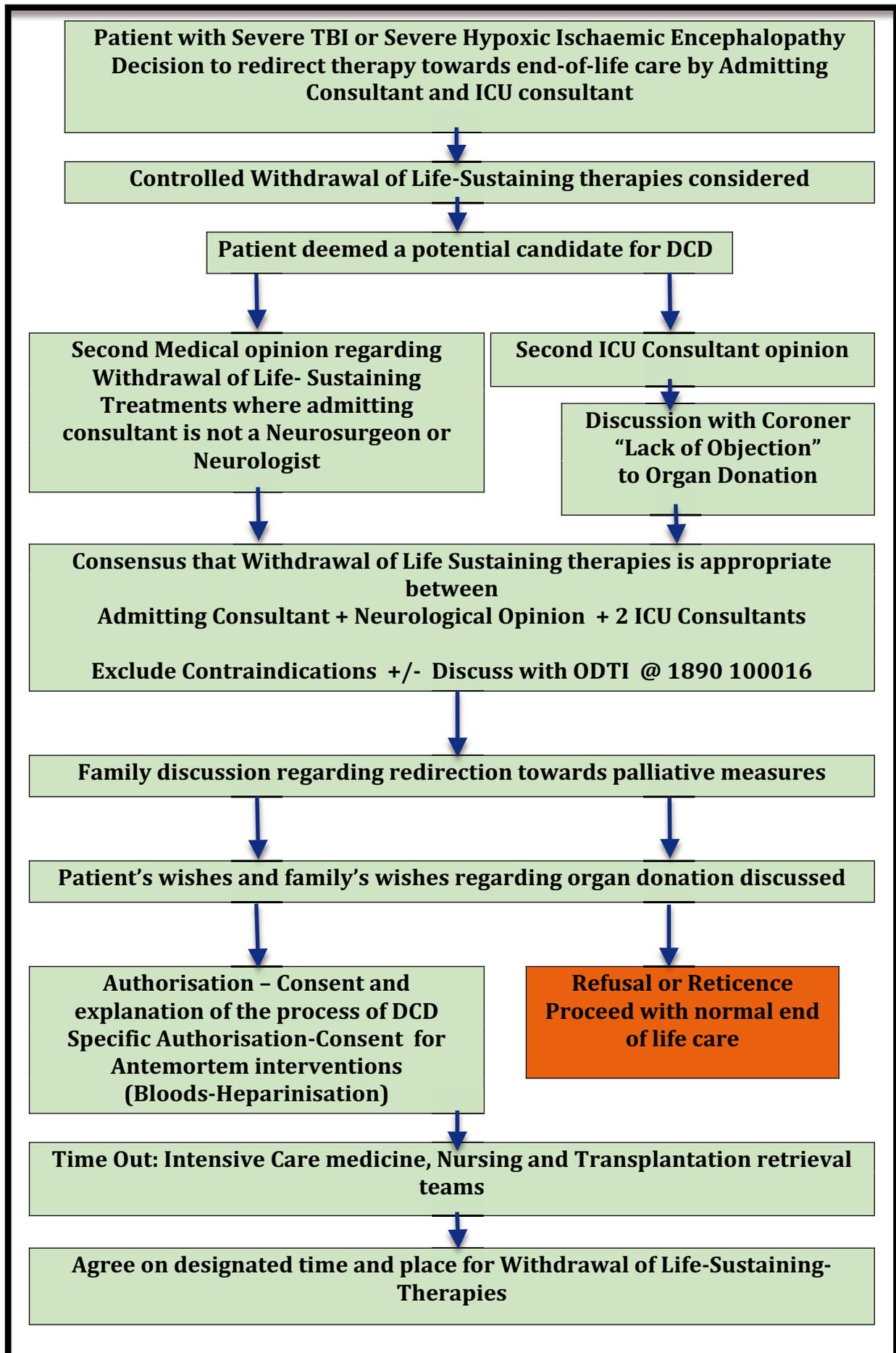
Category	Clinical Scenario	Location	Circulatory Death uDCD or cDCD	Warm Ischaemic Time
Ia	Found Dead Unwitnessed	Out of hospital	Uncontrolled	Approximate calculation
Ib	Found Dead Unwitnessed	In-hospital	Uncontrolled	Approximate calculation
IIa	Witnessed Cardiac Arrest	Out of hospital	Uncontrolled	Approximate calculation
IIb	Witnessed Cardiac Arrest	In-hospital	Uncontrolled	Approximate calculation
III	Withdrawal of Life- Sustaining-Therapy	In-hospital	Controlled	Known Exactly
IV	Cardiac Arrest during or after criteria for BSD completed	In-hospital	Controlled/Uncontrolled	Known Exactly

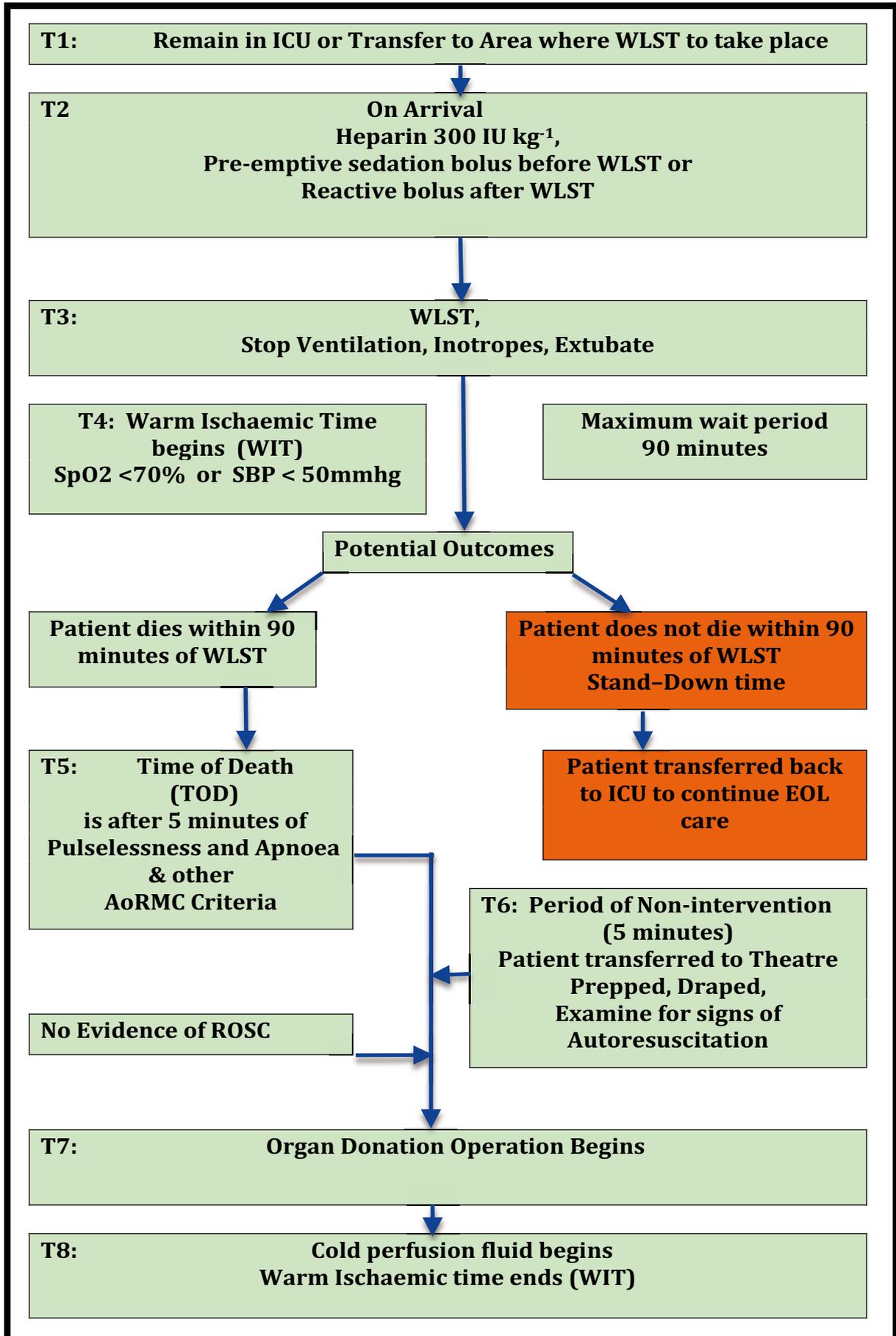
Uncontrolled (uDCD): Permanent and irreversible circulatory death determined on the basis that patient cannot be resuscitated - failed resuscitation.

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





Donation after Circulatory Death

To be completed by doctor caring for patient during WLST

Adressograph

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:

T1:	Ventilation settings prior to WLST Sedative Infusions
T2:	Heparinisation 300 IU kg ⁻¹
T3:	<i>Withdrawal of Life Sustaining therapies</i> Date Time Location
T4:	WIT begins SaO ₂ <70% or SBP <50mmhg

Medications Administered before and after WLST

Time	Medication	Dose

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
• Apnoeic	Y/N
• Pupils fixed with no reaction	Y/N
• Response to supra-orbital pressure	Y/N
• Corneal reflexes.	Y/N
T5:	Time of Death
T6:	Period of Non-intervention (5 minutes) Re-examine for signs of autoresuscitation
T7:	Organ donor operation Begins
T8:	Cold perfusion fluid begins WIT ends (Cold Ischaemic time begins)

Signature:

IMC Registration Number:

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 pre-mortem 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 pre-mortem 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 SaO₂ < 70% and SBP < 50mmhg (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

Organ	Australian (7)	British (3)	Canadian (5)	USA (6, 12,13)
	<i>Minutes</i>	<i>Minutes</i>	<i>Minutes</i>	<i>Minutes</i>
Kidney	60 (240 in selected patients)	120	120	45-60
Liver	30	20	30	30
Lungs	90	60	60	60
Pancreas	60	30 (60 for Islets)	60	60

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).

Absent corneal reflex	Absent cough reflex	Extensor or absent motor response	Oxygenation index >3.0	Score	Probability
No	No	No	No	0	0.08
No	No	No	Yes	1	0.16
Yes	No	No	No	1	0.18
No	No	Yes	No	1	0.20
No	Yes	No	No	2	0.26
Yes	No	No	Yes	2	0.34
No	No	Yes	Yes	2	0.37
Yes	No	Yes	No	2	0.40
No	Yes	No	Yes	3	0.45
Yes	Yes	No	No	3	0.48
No	Yes	Yes	No	3	0.51
Yes	No	Yes	Yes	3	0.61
Yes	Yes	No	Yes	4	0.68
No	Yes	Yes	Yes	4	0.71
Yes	Yes	Yes	No	4	0.74
Yes	Yes	Yes	Yes	5	0.87

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).



UW Donation After Cardiac Death (DCD) Evaluation Tool

Criteria	Assigned Points	Pt. Score
Spontaneous Respirations after 10 min.	-	
Rate >12	1	
Rate <12	3	
TV >200 cc	1	
TV <200 cc	3	
NIF > 20	1	
NIF <20	3	
No Spontaneous Respirations	9	
BMI		
< 25	1	
25-29	2	
> 30	3	
Vasopressors		
No Vasopressors	1	
Single Vasopressor	2	
Multiple Vasopressors	3	
Patient Age		
0-30	1	
31-50	2	
51 +	3	
Intubation		
Endotracheal tube	3	
Tracheostomy	1	
Oxygenation After 10 minutes		
O2 Sat >90%	1	
O2 Sat 80-89%	2	
O2 Sat <79%	3	
	Final Score	
Date of Extubation	Time of Extubation	
Date of Expiration	Time of Expiration	
	Total Time	

Scoring

- 8-12 High Risk for continuing to breath after extubation
- 13-18 Moderate risk for continuing to breath after extubation
- 19-24 Low risk for continuing to breath after extubation

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).

Respiratory Drive	Pressure Cost of Oxygenation	Invasive CVS Supports	Vasopressors	IABP & Cardiac Index
Apnoea	PEEP \geq 10 & SaO ₂ \leq 92%	LVAD	High Dose Vasopressors Noradrenaline Adrenaline or Phenylephrine \geq 0.2 mcgs/kg/min	IABP 1:1 or Dobutamine > 10mcgs/ kg/min CI < 2.2 l min ⁻¹
RR < 8	FiO ₂ \geq 0.5 & SaO ₂ \leq 92%	RVAD	Dopamine \geq 15 mcgs/ kg/min	IABP 1:1 & CI < 1.5 l min ⁻¹
RR > 30 during trial off ventilation		VA ECMO		
		Pacemaker with unassisted rhythm < 30		

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.

