UC San Diego Health

Normothermic Regional Perfusion (NRP) for controlled DCD

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Organ donation pathways

- **Donation after brain death (DBD)**
  - Neurologic exam consistent with cessation of all brain functions including brain stem
  - Family approached for organ donation
  - Organs evaluated and allocated
  - Donor moved to OR for organ procurement

- **Donation after circulatory death (DCD)** (formerly non-heart beating donation)
  - Neurologic exam ***not*** consistent with complete cessation of all brain function
  - Care team communicate grave prognosis if withdrawal life support
  - Family consent for organ donation obtained
  - Organ evaluation and allocation
  - Withdrawal of life support
  - Death declared after heart stops
  - Stand off period 2-5 min
  - Donor to OR for surgical procurement of organs.

European DCD landscape

Mar Lomero et al Transplant International 2020; 33: 76–88

European DCD features by country

Table 2. Selected features of the regulatory framework and the procedures applied to controlled donation after circulatory death in member states of the Council of Europe.

	Ante mortem substances allowed	Ante mortem cannulation allowed	Most frequent location for WLST	Time waited by recovery teams (h)	Type of in situ preservation and organ recovery procedure applied			
					Rapid recovery	*In situ* cooling	hRP	nRP
Austria	Yes	Yes*	OR	–	X			
Belgium	Yes	Yes	OR	1	X			X‡
Czech Republic	No	No	ICU	2	X	X		
France	Yes	Yes†	ICU	3				X
Ireland	No	No	OR	1.5	X			
Italy	Yes	Yes†	ICU	–				X
Netherlands	No	No	ICU	2	X			X‡
Norway	Yes	Yes†	ICU	1.5				X
Spain	Yes	Yes	OR	2	X	X	X	X
Sweden	No	No	ICU	3	X			

DCD Organ Donation Pathway Techniques

Direct procurement with *ex-situ* machine perfusion of single organs

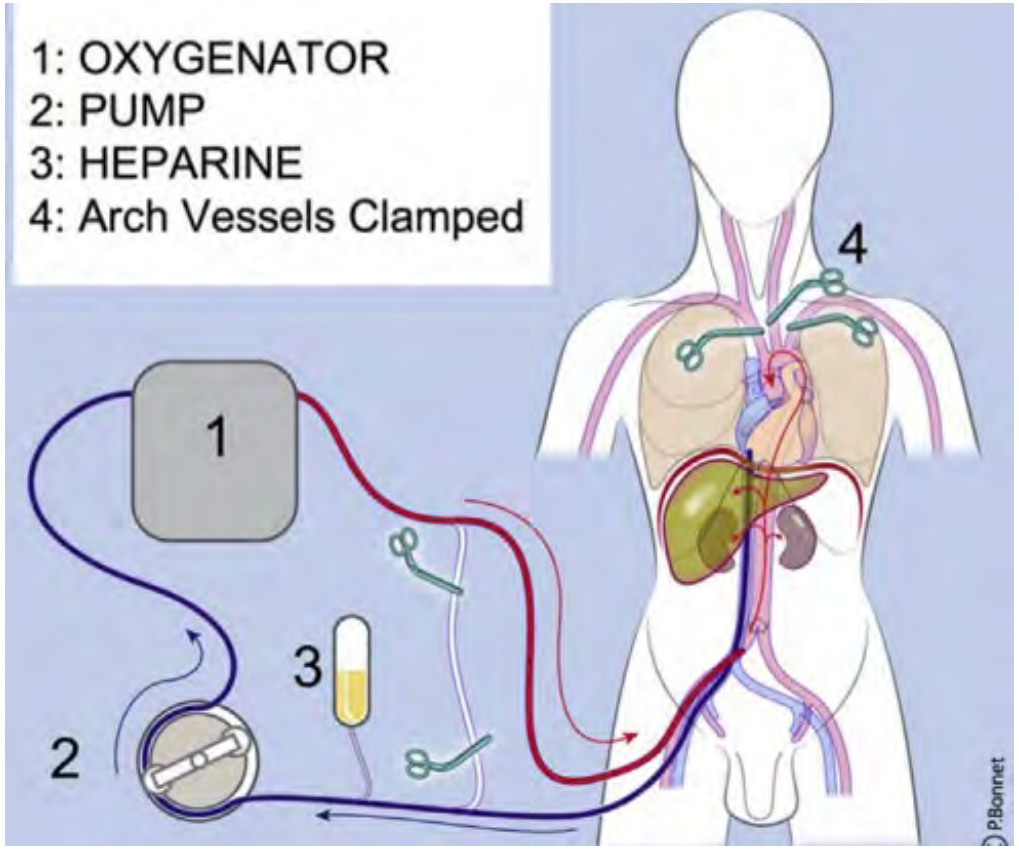
Normothermic regional perfusion - *in-situ* simultaneous machine perfusion of selected organs

Direct Procurement with ex-situ machine perfusion

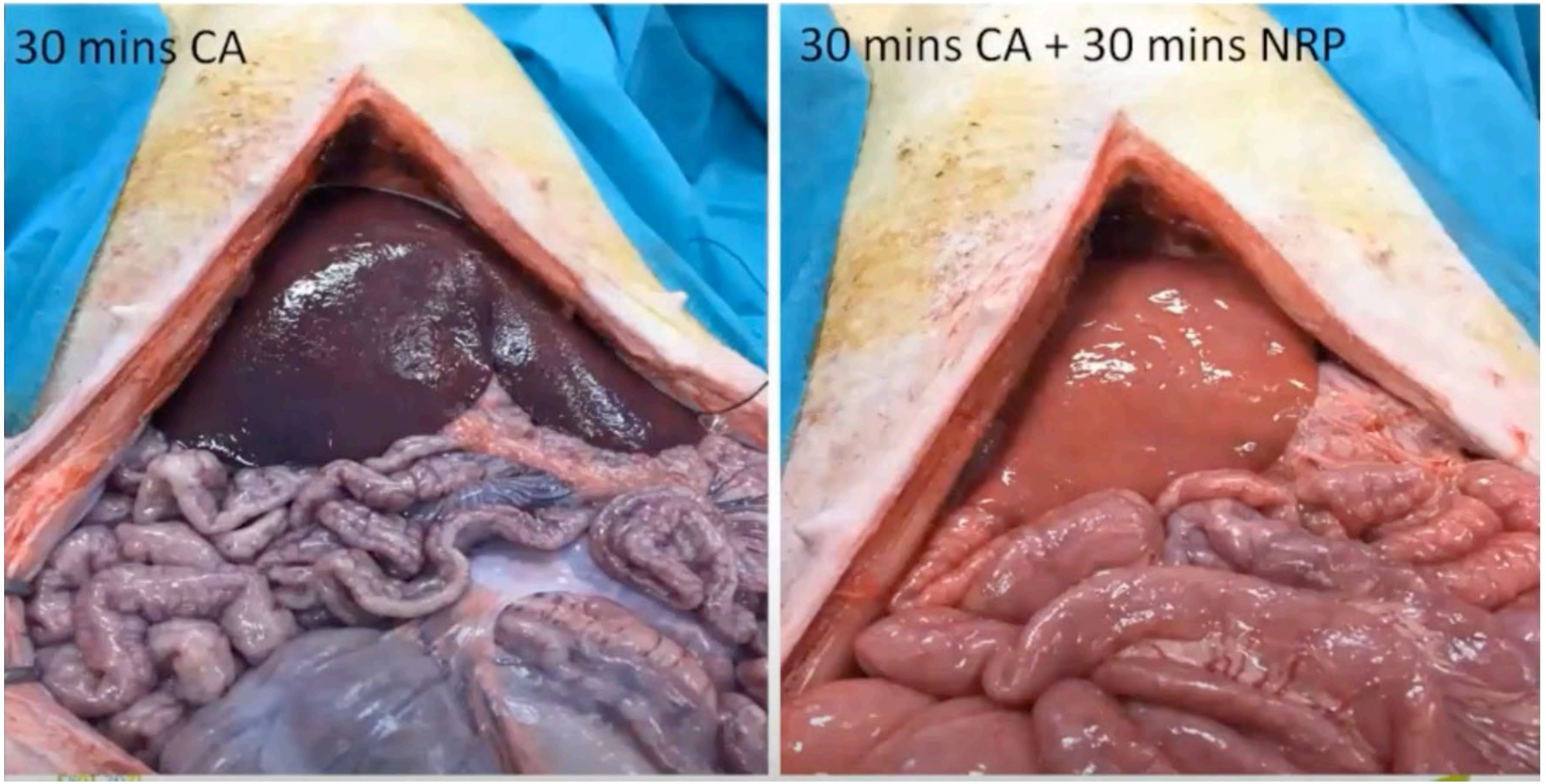
Normothermic Regional Perfusion

Restore flow of **oxygenated blood** following cardiac arrest

Reverse warm ischemic injury of thoraco-abdominal organs after circulatory death



NRP and Ischemic reversal

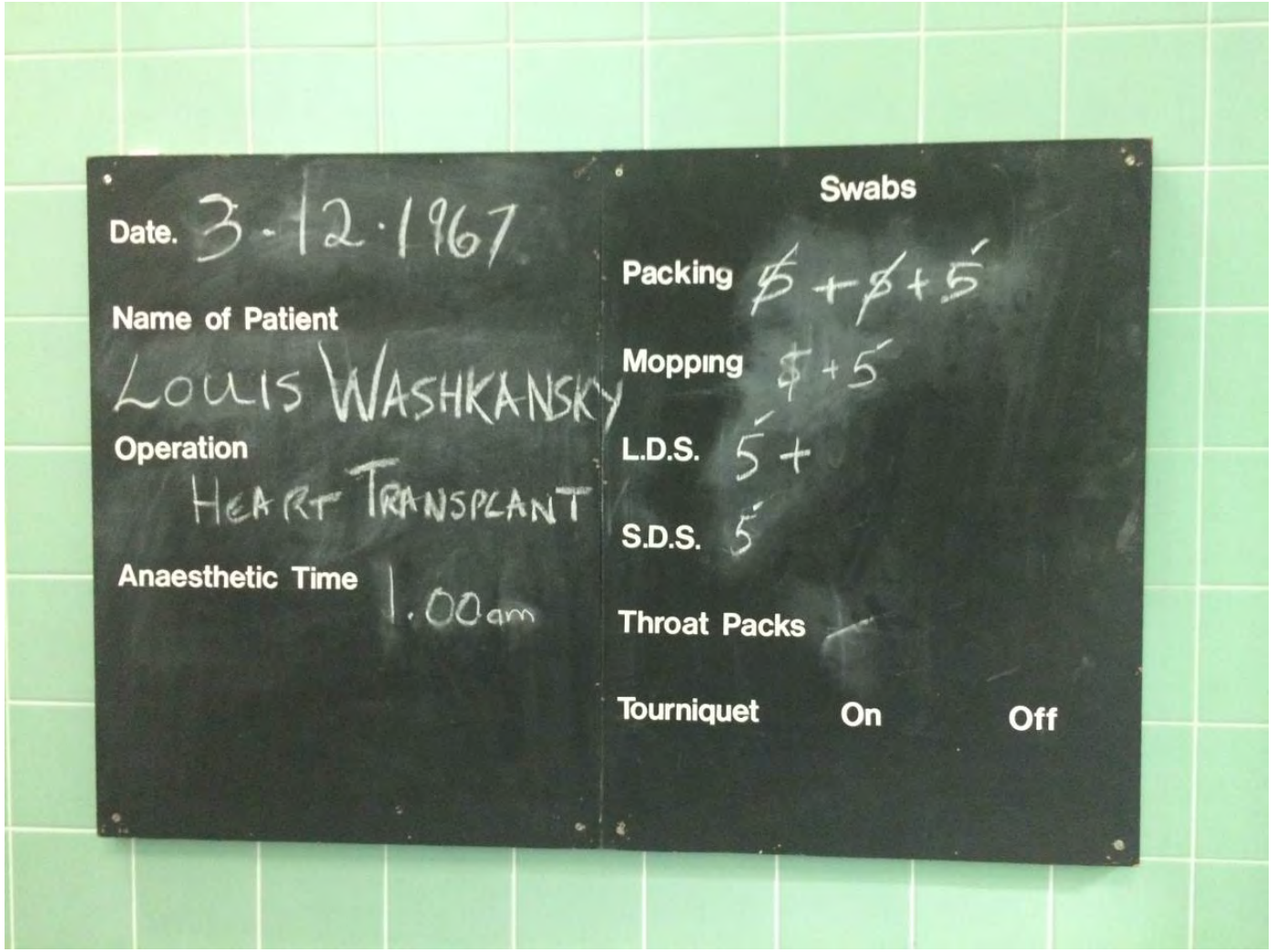


Which organs can be procured with NRP?

- Heart
- Lungs
- Liver
- Kidneys
- Pancreas
- Intestines

Case Presentation

- Recipient is a 58-year-old male patient with ICM and Stage D heart failure who is inotrope dependent in the hospital.
- Donor is 26-year-old female with TBI following MVA
- DCD donation consent was obtained and NRP technique was used to procure heart.
- Transplant was successful with short ischemic time
- Recipient extubated POD 1
- Developed pneumonia on POD 16 and expired on POD 18.
- What was the date of this case?


Date. 3-12-1967
Name of Patient
Louis WASHKANSKY
Operation
HEART TRANSPLANT
Anaesthetic Time 1.00 am
Swabs
Packing 5 + 5 + 5
Mopping 5 + 5
L.D.S. 5 +
S.D.S. 5
Throat Packs
Tourniquet On Off

Department of Surgery
University of Cape Town Medical School
Observatory
CAPE TOWN.

Cardiothoracic Surgery
Groote Schuur Hospital
Observatory
CAPE TOWN.

OPERATION REPORT

PATIENT: LOUIS WASHKANSKY BYPASS CASE No. 971.
Hospital No. 61/003-908 Age: 54 Sex: M Wt. 128½ lbs.

Date of Operation: December 3, 1967.

Lesion: CORONARY ARTERY DISEASE WITH LEFT VENTRICULAR ANEURYSM.

Incision: Median sternotomy

Findings: The aorta was dilated and slightly atherosclerotic. The pulmonary artery was dilated. The right ventricular muscle was hypertrophied. The left atrial wall was hypertrophied and the left atrium was slightly dilated. The right atrium was also dilated and hypertrophied to some extent. The left ventricle was considerably dilated and 80% of the left ventricular muscle was fibrous, forming a large left ventricular aneurysm.

Operation: MEDIAN STERNOTOMY. PARTIAL EXCISION OF PATIENT'S HEART PRESERVING PORTIONS OF THE LEFT ATRIUM (WITH THE PULMONARY VEINS) AND THE RIGHT ATRIUM (WITH THE VENA CAVAE) AND PRESERVING THE ASCENDING AORTA AND MAIN PULMONARY ARTERY. REPLACEMENT OF THE HEART WITH A DONOR HEART BY ANASTOMOSES AS DESCRIBED BELOW. THIS WAS DONE USING TOTAL CARDIOPULMONARY BYPASS WITH THE PUMP OXYGENATOR, PROFOUND HYPOTHERMIA AND CONTINUOUS PERFUSION OF THE DONOR HEART.

Procedure:

The donor was a young woman (Denise Ann Darvall, aged 25 years) who had been fatally injured in a motor accident and had extensive brain damage and fractures of the pelvis and lower limbs. She had fixed, dilated pupils, areflexia and respiration was slow and irregular on

was A Rh positive). ... Netherlands) revealed no significant histoincompatibility. She was taken to the operating theatre on supportive therapy. The anterior chest wall was prepared and the usual sterile drapes were applied. When there had been no activity on the electrocardiogram, absence of breathing and absence of all reflexes for 7 minutes, she was declared dead. The heart was rapidly exposed through a median sternotomy. The donor was heparinised and connected to the heart lung machine by cannulating the ascending aorta for arterial return and the right atrium for venous drainage. A vent was placed in the left ventricle to decompress the heart. The heart-lung machine was started and the body was cooled. As soon as the ascending aorta was isolated and looped, the cannula in the aorta was placed to point towards the aortic valve. A clamp was then applied distal to the cannula and perfusion of the myocardium alone was continued. When the heart had been cooled to about 16°C, the perfusion was discontinued and the heart was excised as follows.

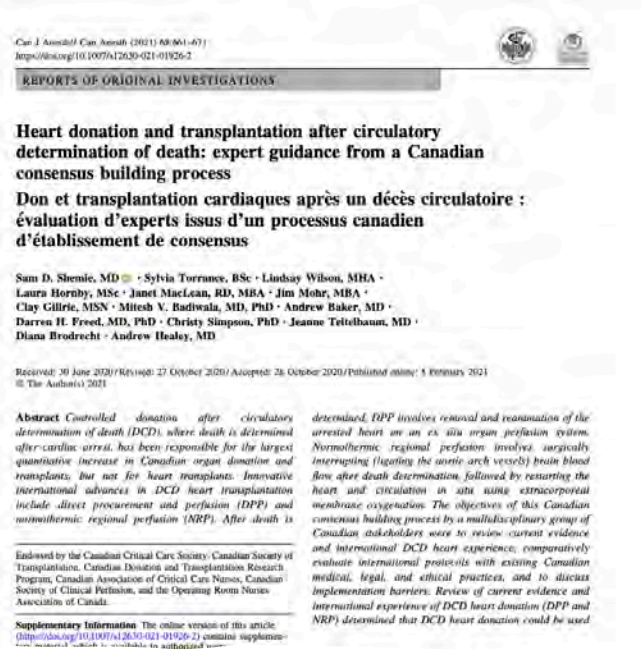
... and the superior vena cava ... vein. The right and left pulmonary arteries were divided and the main pulmonary artery was freed. The left atrium was mobilised by incising the four pulmonary veins. The heart was now free and was taken to the adjoining theatre, to the recipient. Perfusion of the aorta was recommenced immediately by connecting the arterial catheter to a coronary perfusion pump and, as soon as the aorta had filled, it was clamped distal to the perfusion cannula so that the coronary arteries would be perfused. The heart was vented throughout this procedure and care had been taken not to allow air to enter it.

Is the donor truly deceased after NRP?

- An individual is dead who has sustained either
  - irreversible cessation of circulatory and respiratory functions, or
  - irreversible cessation of all functions of the entire brain, including the brainstem.
- Circulatory death declaration confirms cessation of circulation and therefore absence of brain circulation, thus both circulatory and brain death is present
- NRP head vessel clamping and venting ensure that absence of brain circulation and therefore brain death is not disturbed during machine perfusion of thoraco-abdominal organs

Has the Ethics of NRP been debated in peer reviewed literature?

Yes



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https://doi.org/10.1007/s12630-021-01926-2

REPORTS OF ORIGINAL INVESTIGATIONS

Heart donation and transplantation after circulatory determination of death: expert guidance from a Canadian consensus building process

Don et transplantation cardiaques après un décès circulatoire : évaluation d'experts issus d'un processus canadien d'établissement de consensus

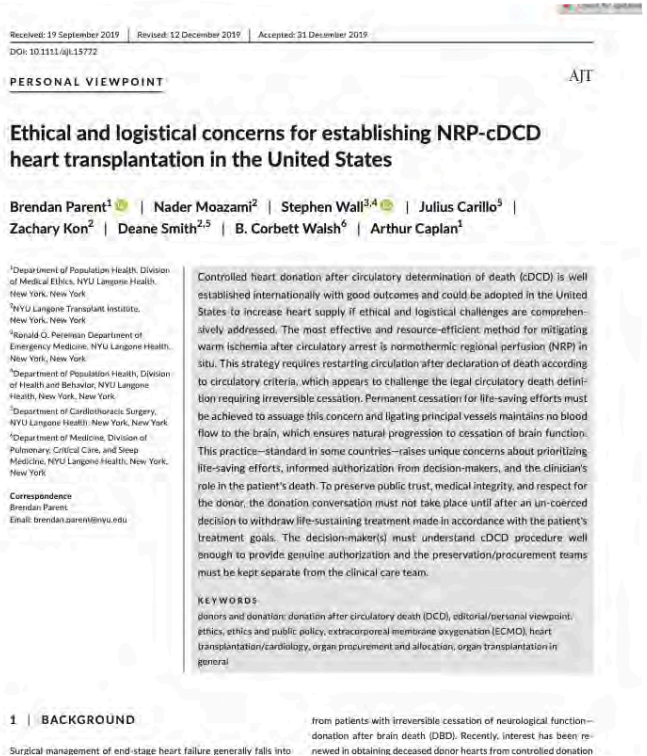
Sam D. Shemie, MD · Sylvia Torrance, BSc · Lindsay Wilson, MBA · Laura Hornby, MSc · Janet MacLean, RD, MBA · Jim Mohr, MBA · Clay Gillrie, MSN · Mitesh V. Badiwala, MD, PhD · Andrew Baker, MD · Darren H. Freed, MD, PhD · Christy Simpson, PhD · Jeanne Teitelbaum, MD · Diana Brodrecht · Andrew Healey, MD

Received: 30 June 2020 / Revised: 27 October 2020 / Accepted: 28 October 2020 / Published online: 5 February 2021

Abstract *Controlled donation after circulatory determination of death (DCD), where death is determined after cardiac arrest, has been responsible for the largest quantitative increase in Canadian organ donation and transplants, but not for heart transplants. Innovative international advances in DCD heart transplantation include direct procurement and perfusion (DPP) and normothermic regional perfusion (NRP). After death is determined, DPP involves removal and reanimation of the arrested heart on an ex situ organ perfusion system. Normothermic regional perfusion involves surgically interrupting (ligating the aortic arch vessels) brain blood flow after death determination, followed by restarting the heart and circulation in situ using extracorporeal membrane oxygenation. The objectives of this Canadian consensus building process by a multidisciplinary group of Canadian stakeholders were to review current evidence and international DCD heart experience, comparatively evaluate international protocols with existing Canadian medical, legal, and ethical practices, and to discuss implementation barriers. Review of current evidence and international experience of DCD heart donation (DPP and NRP) determined that DCD heart donation could be used*

Endorsed by the Canadian Critical Care Society, Canadian Society of Transplantation, Canadian Donation and Transplantation Research Program, Canadian Association of Critical Care Nurses, Canadian Society of Clinical Perfusion, and the Operating Room Nurses Association of Canada.

Supplementary Information The online version of this article (https://doi.org/10.1007/s12630-021-01926-2) contains supplementary material, which is available to authorized users.



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PERSONAL VIEWPOINT

AJT

Ethical and logistical concerns for establishing NRP-cDCD heart transplantation in the United States

Brendan Parent[1] | Nader Moazami[2] | Stephen Wall[3,4] | Julius Carillo[5] | Zachary Kon[2] | Deane Smith[2,5] | B. Corbett Walsh[6] | Arthur Caplan[1]

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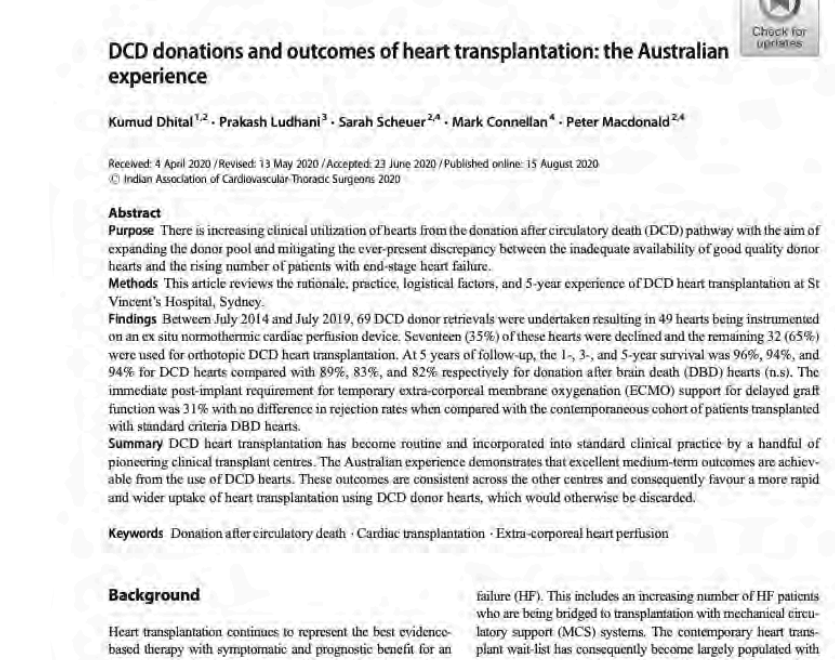
Controlled heart donation after circulatory determination of death (cDCD) is well established internationally with good outcomes and could be adopted in the United States to increase heart supply if ethical and logistical challenges are comprehensively addressed. The most effective and resource-efficient method for mitigating warm ischemia after circulatory arrest is normothermic regional perfusion (NRP) in situ. This strategy requires restarting circulation after declaration of death according to circulatory criteria, which appears to challenge the legal circulatory death definition requiring irreversible cessation. Permanent cessation for life-saving efforts must be achieved to assuage this concern and ligating principal vessels maintains no blood flow to the brain, which ensures natural progression to cessation of brain function. This practice—standard in some countries—raises unique concerns about prioritizing life-saving efforts, informed authorization from decision-makers, and the clinician's role in the patient's death. To preserve public trust, medical integrity, and respect for the donor, the donation conversation must not take place until after an un-coerced decision to withdraw life-sustaining treatment made in accordance with the patient's treatment goals. The decision-maker(s) must understand cDCD procedure well enough to provide genuine authorization and the preservation/procurement teams must be kept separate from the clinical care team.

KEYWORDS
donors and donation: donation after circulatory death (DCD), editorial/personal viewpoint, ethics, ethics and public policy, extracorporeal membrane oxygenation (ECMO), heart transplantation/cardiology, organ procurement and allocation, organ transplantation in general

1 | BACKGROUND

Surgical management of end-stage heart failure generally falls into

from patients with irreversible cessation of neurological function—donation after brain death (DBD). Recently, interest has been re-



Check for updates

DCD donations and outcomes of heart transplantation: the Australian experience

Kumud Dhital[1,2] · Prakash Ludhani[3] · Sarah Scheuer[2,4] · Mark Connellan[4] · Peter Macdonald[2,4]

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Abstract
Purpose There is increasing clinical utilization of hearts from the donation after circulatory death (DCD) pathway with the aim of expanding the donor pool and mitigating the ever-present discrepancy between the inadequate availability of good quality donor hearts and the rising number of patients with end-stage heart failure.
Methods This article reviews the rationale, practice, logistical factors, and 5-year experience of DCD heart transplantation at St Vincent's Hospital, Sydney.
Findings Between July 2014 and July 2019, 69 DCD donor retrievals were undertaken resulting in 49 hearts being instrumented on an ex situ normothermic cardiac perfusion device. Seventeen (35%) of these hearts were declined and the remaining 32 (65%) were used for orthotopic DCD heart transplantation. At 5 years of follow-up, the 1-, 3-, and 5-year survival was 96%, 94%, and 94% for DCD hearts compared with 89%, 83%, and 82% respectively for donation after brain death (DBD) hearts (n.s). The immediate post-implant requirement for temporary extra-corporeal membrane oxygenation (ECMO) support for delayed graft function was 31% with no difference in rejection rates when compared with the contemporaneous cohort of patients transplanted with standard criteria DBD hearts.
Summary DCD heart transplantation has become routine and incorporated into standard clinical practice by a handful of pioneering clinical transplant centres. The Australian experience demonstrates that excellent medium-term outcomes are achievable from the use of DCD hearts. These outcomes are consistent across the other centres and consequently favour a more rapid and wider uptake of heart transplantation using DCD donor hearts, which would otherwise be discarded.

Keywords Donation after circulatory death · Cardiac transplantation · Extra-corporeal heart perfusion

Background

Heart transplantation continues to represent the best evidence-based therapy with symptomatic and prognostic benefit for an increasing number of recipient candidates with end-stage heart failure (HF). This includes an increasing number of HF patients who are being bridged to transplantation with mechanical circulatory support (MCS) systems. The contemporary heart transplant wait-list has consequently become largely populated with more complex and older recipients with a higher degree of immunological sensitization and requiring challenging redo procedures including the removal of in situ implantable MCS devices. In addition to this, the continued shortage of suitable hearts from an increasingly older donor pool with more co-morbidities has placed enormous pressures on transplant centres to accept greater risks in the selection and matching of donors and recipients.

Heart transplantation from distantly procured donation after circulatory death (DCD) hearts was first described by the Sydney group 5 years ago as an important alternative expansion of the donor pool [1]. DCD heart transplantation had occurred prior to this, but in limited numbers and with co-localization of

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PERSONAL VIEWPOINT

AJT

Maintaining the permanence principle for death during in situ normothermic regional perfusion for donation after circulatory death organ recovery: A United Kingdom and Canadian proposal

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Against NRP

ACP American College of Physicians®
Leading Internal Medicine, Improving Lives

Ethics, Determination of Death, and Organ Transplantation in Normothermic Regional Perfusion (NRP) with Controlled Donation after Circulatory Determination of Death (cDCD): American College of Physicians Statement of Concern

Approved by the Board of Regents on April 17, 2021

For NRP

American Journal of TRANSPLANTATION

AST | ASTS

VIEWPOINT

Response to American College of Physician's statement on the ethics of transplant after normothermic regional perfusion

Brendan Parent, Arthur Caplan, Nader Moazami, Robert A. Montgomery

First published: 24 January 2022 | https://doi.org/10.1111/ajt.16947

American Journal of TRANSPLANTATION

AST | ASTS

VIEWPOINT

Applying the ethical framework for donation after circulatory death to thoracic normothermic regional perfusion procedures

Anji E. Wall, Amy Fiedler, Seth Karp, Ashish Shah, Giuliano Testa

First published: 18 January 2022 | https://doi.org/10.1111/ajt.16959

Wall AE et al. Am J Transplant . 2022 Jan 18.

TA-NRP DCD Ethics meets Standards for:

- Informed consent
- Non-maleficence
- Adhere to the dead donor rule
- Irreversibility

UK Pioneering DCD heart transplant

ELSEVIER

The Journal of Heart and Lung Transplantation

SPECIAL FEATURE

Outcome after heart transplantation from donation after circulatory-determined death donors

Simon Messer, MBChB,[a] Aravinda Page, MBBChir,[a] Richard Axell, PhD,[a] Marius Berman, MD,[a] Jules Hernández-Sánchez, PhD,[b,c] Simon Colah, BSc,[a] Barbora Parizkova, MD,[a] Kamen Valchanov, MD,[a] John Dunning, MBChB,[d] Evgeny Pavlushkov, MD, PhD,[a] Sendhil K. Balasubramanian, MBBS,[a] Jayan Parameshwar, MBBS, MD, MPhil,[a] Yasir Abu Omar, MBChB, DPhil,[a] Martin Goddard, BMBCh,[a] Stephen Pettit, MBBS, PhD,[a] Clive Lewis, MBBChir, PhD,[a] Anna Kydd, MBBS, MD,[a] David Jenkins, MBBS, MS,[a] Christopher J. Watson, MBBChir, MD,[d] Catherine Sudarshan, MBBS, MD,[a] Pedro Catarino, BMBCh,[a] Marie Findlay,[a] Ayyaz Ali, MBBS, PhD,[a] Steven Tsui, MBBChir, MD,[a] and Stephen R. Large, MBBS, MS, MBA[a]

From the [a]Department of Transplantation, Papworth Hospital National Health Service Foundation Trust, Papworth Everard, Cambridgeshire, United Kingdom; [b]Papworth Trials Unit Collaboration, Papworth Hospital National Health Service Foundation Trust, Papworth Everard, Cambridgeshire, United Kingdom; [c]Medical Research Council Biostatistics Unit, University of Cambridge, School of Clinical Medicine, Cambridge Institute of Public Health, Cambridge, United Kingdom; and the [d]Department of Surgery, Cambridge University Hospitals National Health Service Foundation Trust and the National Institute for Health Research, Cambridge Biomedical Center, University of Cambridge, Cambridge, United Kingdom.

KEYWORDS:
heart;
transplant;
circulatory death;
normothermic regional perfusion;
direct procurement and perfusion

BACKGROUND: The requirement for heart transplantation is increasing, vastly outgrowing the supply of hearts available from donation after brain death (DBD) donors. Transplanting hearts after donation after circulatory-determined death (DCD) may be a viable additive alternative to DBD donors. This study compared outcomes from the largest single-center experience of DCD heart transplantation against matched DBD heart transplants.
METHODS: DCD hearts were retrieved using normothermic regional perfusion (NRP) or direct procurement and perfusion (DPP). During NRP, perfusion was restored to the arrested heart within the donor with the exclusion of the cerebral circulation, whereas DPP hearts were removed directly. All hearts were maintained on machine perfusion during transportation. A retrospective cohort of DBD heart transplants, matched for donor and recipient characteristics, was used as a comparison group. The primary outcome measure of this study (set by the United Kingdom regulatory body) was 90-day survival.
RESULTS: There were 28 DCD heart transplants performed during the 25-month study period. Survival at 90 days was not significantly different between DCD and matched DBD transplant recipients (DCD, 92%; DBD, 96%; $p = 1.0$). Hospital length of stay, treated rejection episodes, allograft function, and 1-year survival (DCD, 86%; DBD, 88%; $p = 0.98$) were comparable between groups. The method of retrieval (NRP or DPP) was not associated with a difference in outcome.

UK Pioneering DCD heart transplant

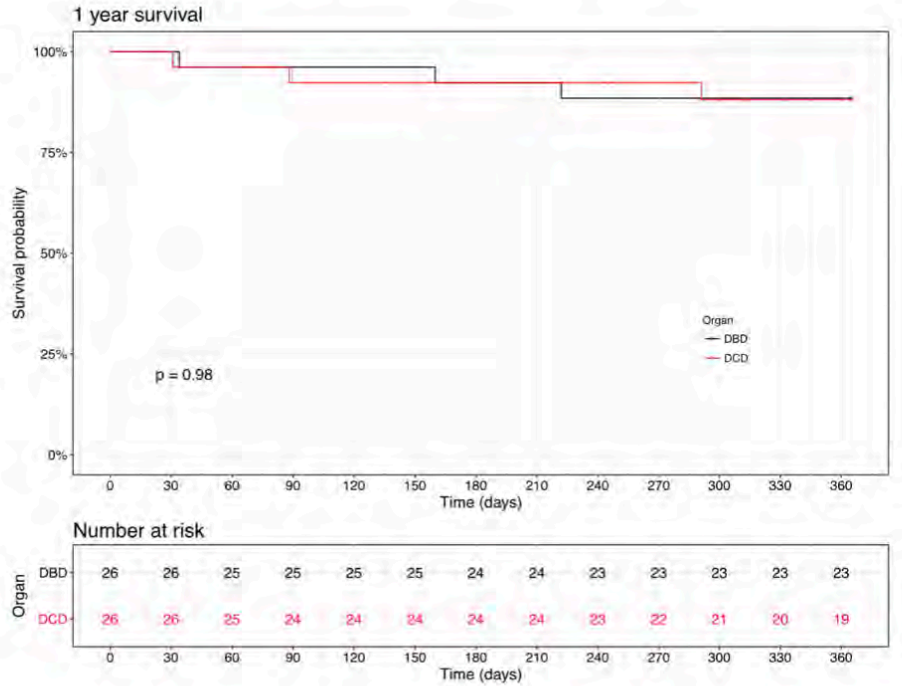


Figure 2 Kaplan-Meier survival of donation after circulatory-determined death (DCD) and donation after brain death (DBD) heart transplantation.

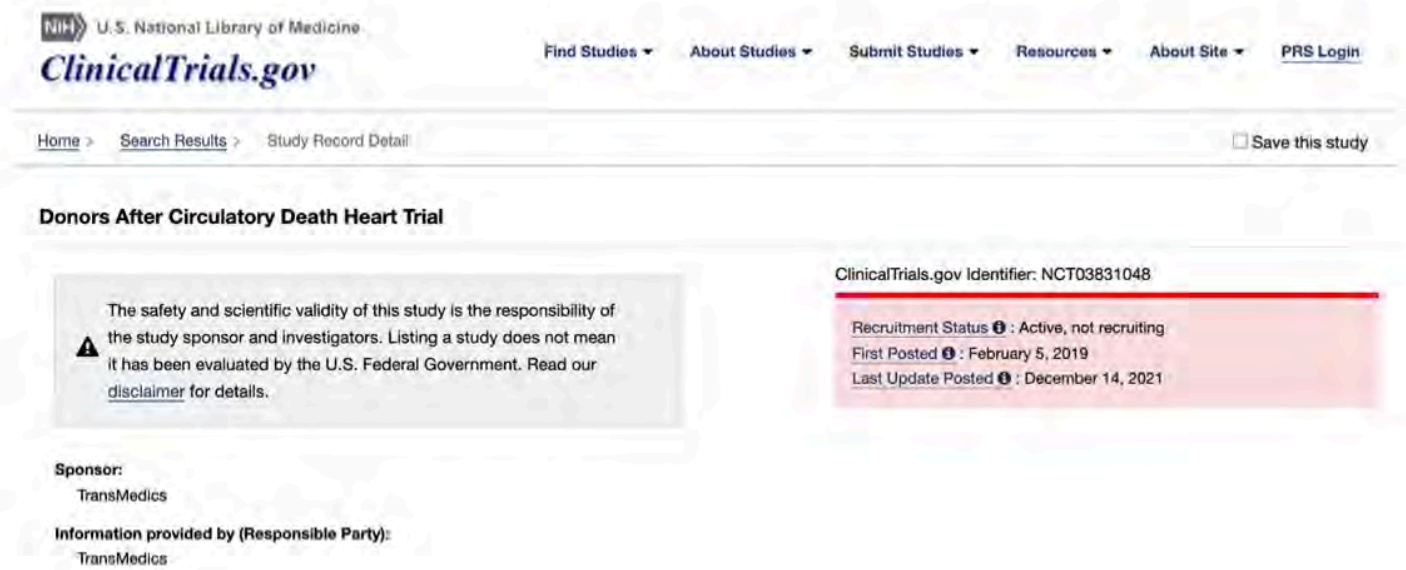
USA DCD resurgence

TransMedics USA DCD trial

NYU NRP with co-location of donor

Vanderbilt Mobile CPB for NRP

- 180 recipients randomized between DCD with direct procurement and OCS ex-situ warm perfusion vs. Standard brain-dead donation pathway



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Donors After Circulatory Death Heart Trial

The safety and scientific validity of this study is the responsibility of the study sponsor and investigators. Listing a study does not mean it has been evaluated by the U.S. Federal Government. Read our disclaimer for details.

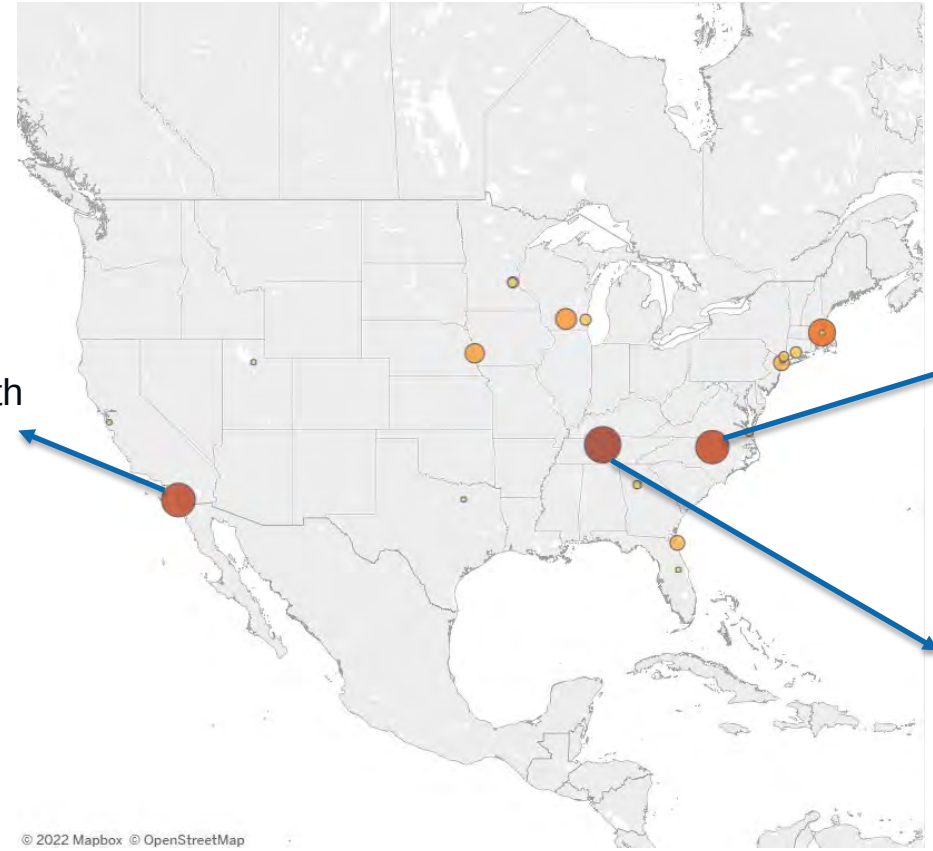
ClinicalTrials.gov Identifier: NCT03831048

Recruitment Status : Active, not recruiting
First Posted : February 5, 2019
Last Update Posted : December 14, 2021

Sponsor:
TransMedics

Information provided by (Responsible Party):
TransMedics

Deceased Donor Heart Transplants by Center
1/1/2021 – 12/31/2021



UC San Diego Health
36 DCD transplants

Duke University Hospital
35 DCD transplants

Vanderbilt Medical Center
42 DCD transplants

NYU early DCD experience with co-location

Early Experience of Donation After Circulatory Death Transplantation Using Normothermic Regional Perfusion in the United States

8 Eligible DCD heart donors (January 2020 – January 2021)

Withdrawal of life-sustaining therapy in OR and cardiac arrest

5 minute no touch period

Normothermic regional perfusion using cardiopulmonary bypass

In situ evaluation of donor allograft

Recipient surgery started

All DCD hearts weaned from bypass without inotropic support and accepted for transplantation

Retrieved heart trans via cold static storage adjoining recipient operating room

8 DCD transplantations: 6 isolated hearts, 1 heart-lung, and 1 heart-kidney

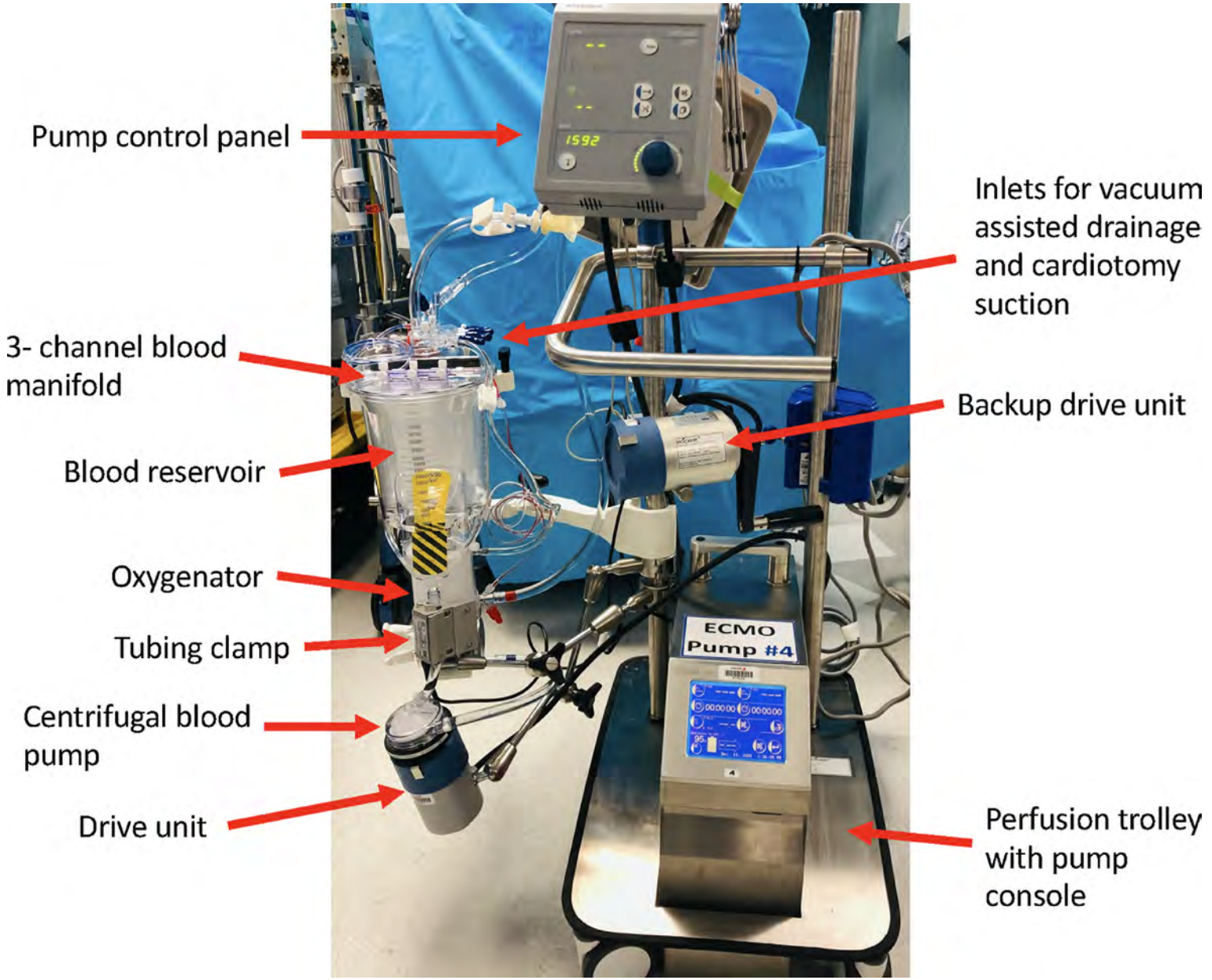
Implications statement: DCD heart transplantation using cardiopulmonary bypass for normothermic regional perfusion allows for in situ cardiac assessment under physiologic conditions, resulting in high organ acceptance rates and excellent immediate graft function, which may substantially expand the donor pool and reduce waitlist time.

Results:
- 100% survival with median follow-up of 304 da
- 1 recipient required VA ECMO for primary lung graft dysfunction
- 7 recipients did not require MCS post-transplar
- Average LVEF prior to hospital discharge: 64%

DCD, donation after circulatory death: OR, operating room: VA ECMO, venoarterial extracorporeal membrane oxygenation: MCS, mechanical circulatory support: LVEF, left ventricular ejection fraction.

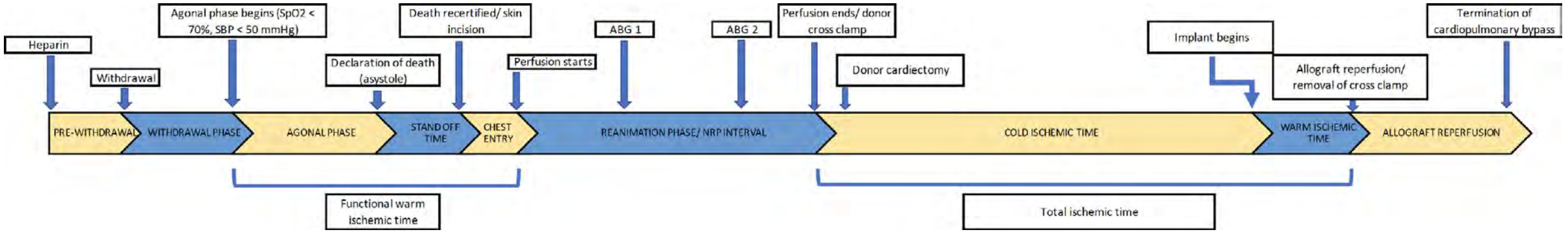
Smith et al. J Thorac Cardiovasc Surg . 2021 Sep 14;S0022-5223(21)01316-7.

VanderBilt data



Hoffman et al Heart Lung transplant. 2021 Nov;40(11):1408-1418

NRP time line



Vanderbilt donors

Table 1 Donor Characteristics

Donor ID[a]	Age (years)	Sex	Ethnicity	BMI (kg/m^2)	Donor distance from transplant center (nautical miles)	Reason for admission	Active hepatitis C[b]	CPR time (minutes)	Pre-donation LVEF (%)	Pre-donation RV function	Other organs procured
1	29	Female	CA	24	219	Injury/trauma	No	0	60	Normal	Liver, kidney
2	25	Male	CA	22	100	Injury/trauma	No	0	55	Normal	Liver, kidney
3	12	Male	CA	27	333	Injury/trauma	No	8	75	Normal	Liver, kidney
4	26	Male	CA	28	160	Injury/trauma	Yes	0	63	Normal	Liver, kidney
5	16	Male	CA	26	470	Suicide	No	0	61	Normal	Liver, kidney
6	33	Female	CA	33	593	Hypoxia	No	20	55	Normal	Liver, kidney
7	28	Male	CA	27	136	Injury/trauma	No	0	60	Normal	Liver, kidney
8	22	Male	CA	24	691	Hypoxia	No	1	70	Normal	Liver, kidney, lung
9	21	Male	CA	22	574	Injury/trauma	No	0	68	Normal	Liver, kidney, lung
10	30	Male	CA	26	250	Injury/trauma	No	15	55	Normal	Liver, kidney
11	23	Male	CA	32	500	Hypoxia	No	0	70	Normal	Kidney
12	19	Female	CA	19	292	Injury/trauma	No	0	55	Normal	Liver, kidney
13	18	Male	CA	28	137	Injury/trauma	No	0	60	Normal	Kidney
14	16	Male	CA	28	612	Injury/trauma	No	0	65	Normal	Liver, kidney, lung
15	34	Male	CA	29	531	Hypoxia	No	13	55	Normal	Liver, kidney

AA, African American; BMI, body mass index; CA, Caucasian American; CPR, cardiopulmonary resuscitation; LVEF, left ventricular ejection fraction; RV, right ventricle.
[a]Donor and recipient ID correspond such that individual donor-recipient pairs are identified
[b]Antibody and nucleic acid amplification test (NAT) positive.

Hoffman et al. Heart Lung Transplant. 2021 Nov;40(11):1408-1418.

Vanderbilt Procurement process times

Table 3 Donor Allograft Intervals[a]

Allograft ID	Withdrawal phase (minutes)	Agonal phase (minutes)	Stand-off time (minutes)	Chest entry (minutes)	Functional warm ischemia (minutes)	Reanimation period/NRP interval (minutes)	Cold ischemic time (minutes)	Warm ischemic time (minutes)	Allograft reperfusion (minutes)	Total ischemic time (minutes)
1	3	15	5	2	22	59	131	25	57	156
2	3	7	5	2	14	42	108	31	53	139
3	3	21	5	2	28	63	146	23	47	169
4	4	12	3	1	16	56	134	49	43	183
5	3	16	3	2	21	56	166	27	53	193
6	1	15	5	3	23	63	169	27	63	196
7	3	4	5	2	11	50	98	32	166 (108+56)[b]	130
8	1	8	5	2	15	62	175	29	73	204
9	2	9	5	3	17	56	171	54	66	225
10	4	12	5	1	18	48	125	57	68	182
11	1	24	2	2	28	62	177	31	46	208
12	8	11	5	2	18	43	141	34	19	175
13	3	4	5	2	11	56	109	30	146	139
14	8	13	5	4	22	71	161	63	58	224
15	2	21	2	2	25	48	166	51	94	217

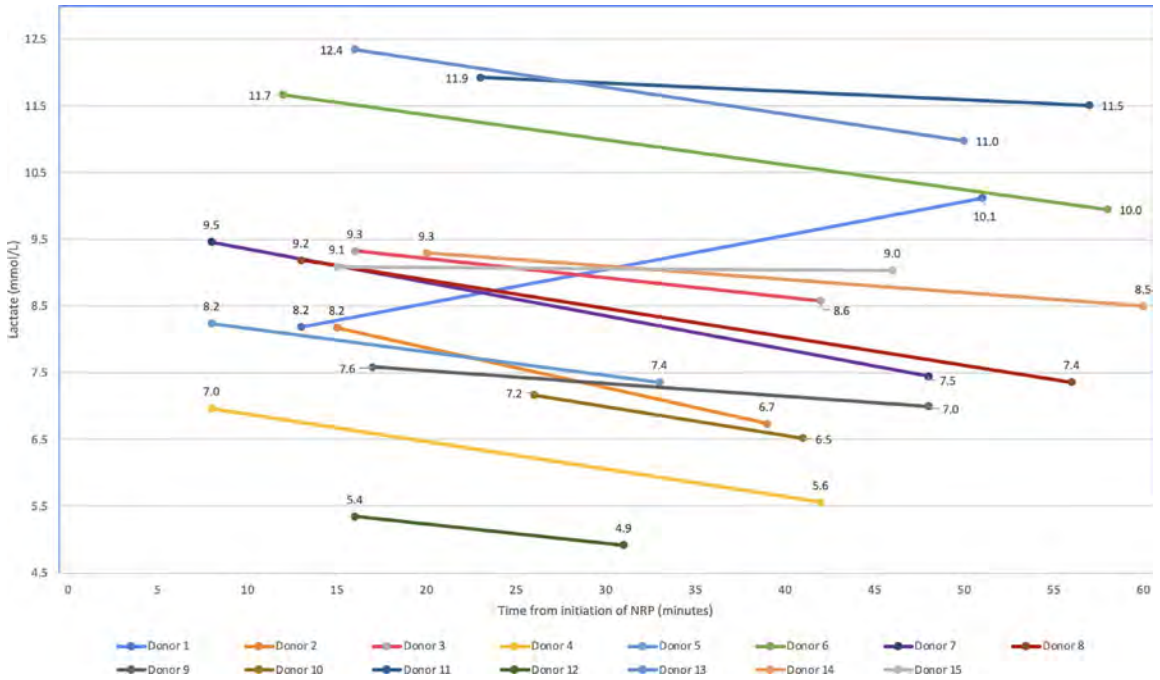
CPB, cardiopulmonary bypass; IABP, intraaortic balloon pump; NRP, normothermic regional perfusion.

[a]Interval definitions- withdrawal phase: time from terminal extubation to saturations <70% or systolic blood pressure <50 mm Hg; agonal phase: period of time from saturations <70% or systolic blood pressure <50 mm Hg to declaration of death; stand-off time: the period of time, determined by individual organ procurement organization, after which sternal incision can begin; chest entry: time from sternal incision to cannulation and systemic reperfusion; functional warm ischemia: summation of "agonal phase" + "stand- off time" + "chest entry;" reanimation period/NRP interval: duration of systemic perfusion prior to donor aortic cross-clamp; cold ischemic time: time from donor aortic cross-clamp to start of recipient allograft implant; warm ischemic time: time from start of recipient allograft implant to removal of recipient aortic cross-clamp; allograft reperfusion interval: time after removal of recipient aortic cross-clamp removal to termination of cardiopulmonary bypass; total ischemic time: includes the sum of cold and warm allograft ischemic times.

[b]Allograft 7 successfully weaned from CPB but required re-initiation of bypass after 152 minutes for further resuscitation and placement of an intra-aortic balloon pump. This recipient spent an additional 56 minutes on CPB.

Hoffman et al. Heart Lung Transplant . 2021 Nov;40(11):1408-1418.

Lactate level trend



Vanderbilt Recipients

Table 2 Recipient Characteristics

Recipient ID[a]	Age (years)	Sex	Ethnicity	BMI (kg/m^2)	PHM ratio[b]	Heart failure etiology	Waitlist status at time of transplant	Time from admission to transplant (days)	Time on waitlist (days)	Preoperative mechanical support	Pulmonary hypertension	Pulmonary vascular resistance (WU)	Chronic kidney disease (stage)[c]
1	19	Female	CA	40	0.91	Chemotherapy	3	0	91	Durable LVAD	No	1.2	None
2	67	Male	CA	26	0.99	Ischemic	6	0	5	None	Yes	1.3	3a
3	64	Female	CA	38	0.96	Ischemic	4	0	1	Durable LVAD	No	0.3	3a
4	46	Male	CA	35	0.84	Idiopathic	4	0	40	Durable LVAD	Yes	1.4	3b
5	69	Male	CA	34	0.9	Ischemic	3	0	9	Durable LVAD	No	2	None
6	42	Male	CA	29	0.89	Familial	4	0	80	Durable LVAD	Yes	1.9	3a
7	56	Male	CA	33	0.84	Idiopathic	6	0	14	None	No	0.8	3a
8	58	Male	CA	24	1.08	Idiopathic	2	12	3	IABP	Yes	1.8	3b
9	58	Male	CA	30	0.91	Ischemic	6	0	37	None	No	2.7	3b
10	58	Male	CA	30	0.99	Ischemic	6	0	4	None	Yes	1.2	3a
11	49	Male	AA	38	0.94	Idiopathic	3	6	18	Durable LVAD	No	2.3	3b
12	68	Female	CA	27	0.98	Idiopathic	4	0	2	None	No	2.8	None
13	67	Male	CA	30	1.12	Idiopathic	6	0	27	None	No	2.5	3b
14	41	Male	AA	27	1.02	Idiopathic	3	0	11	Durable LVAD	No	1	2
15	62	Male	CA	33	0.88	Ischemic	4	0	21	Durable LVAD	No	1	None

AA, African American; BMI, body mass index; CA, Caucasian American; IABP, intraaortic balloon pump; LVAD, left ventricular assist device; PHM, predicted heart mass; PRA, panel reactive antibodies.

[a]Donor and recipient ID correspond such that individual donor- recipient pairs are identified.

[b]Ratio between donor and recipient predicted heart mass.

[c]Chronic kidney disease (CKD) stage definitions by estimated glomerular filtration rate (eGFR): CKD 1-eGFR > 90 ml/min/1.73m^2; CKD 2-eGFR 60 to 89 ml/min/1.73m^2; CKD 3a eGFR 45 to 59 ml/min/1.73m^2; CKD 3b: eGFR 30 to 44 ml/min/1.73m^2; CKD 4-eGFR 15 to 29 ml/min/1.73m^2; CKD 5-eGFR < 15 ml/min/1.73m^2.[26]

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Vanderbilt Transplant Outcomes

Table 4 Transplant Outcomes

Recipient ID	CI 24 hours post-transplant (L/min/m^2)	Inotrope score 24 post-transplant	PGD within 24 hours post-transplant	Post-transplant mechanical support	Biventricular function on post-transplant day 7 TTE (LVEF %/RV function)	First biopsy results (AMR/ACR)	ICU length of stay (days)	Hospital length of stay (days)	Alive at 30 days	Readmission within 30 days	Other adverse outcomes
1	3.3	4	None	None	60%/mild RV dysfunction	0/2R	9	20	Yes	Yes- COVID	AKI requiring CRRT
2	3.2	8	None	None	65%/mild RV dysfunction	0/0	3	15	Yes	No	
3	2.1	14	PGD-LV: mild	None	60%/normal RV function	0/0	7	29	Yes	No	
4	4	7	None	None	55%/normal RV function	0/0	10	29	Yes	No	AKI requiring CRRT
5	2.1	21	PGD-LV: mild	None	60%/mild RV dysfunction	0/1R	16	57	Yes	Yes- AMS	
6	3	15	PGD-LV: mild	None	60%/normal RV function	0/0	7	15	Yes	No	
7	3.3	32	PGD-LV: moderate	IABP	55%/normal RV function	0/1R	21	36	Yes	No	AKI requiring CRRT and HD at discharge, tracheostomy placement, stroke
8	4.9	19	PGD-LV: mild	None	65%/normal RV function	0/0	6	17	Yes	No	Stroke
9	4.4	19	PGD-LV: mild	None	65%/normal RV function	0/1R	8	16	Yes	No	
10	4.6	5	None	None	65%/normal RV function	0/0	5	9	Yes	No	
11	2.8	9	None	None	65%/normal RV function	0/0	10	16	Yes	Yes- volume overload	
12	3.1	8	None	None	60%/normal RV function	0/1R	4	10	Yes	No	
13	2.4	25	PGD-LV: moderate	IABP	55%/normal RV function	0/0	26	32	Yes	No	
14	3.4	17	PGD-LV: mild	None	65%/normal RV function	0/0	4	22	Yes	No	
15	3.7	11	PGD-LV: moderate	IABP	60%/moderate RV dysfunction	0/0	6	12	Yes	No	

ACR, acute cellular rejection; AKI, acute kidney injury; AMR, antibody mediated rejection; AMS, altered mental status; CI, cardiac index; BMI, body mass index; CRRT, continuous renal replacement therapy; DBD, donation after brain death; DCD, donation after circulatory death; ECMO, extracorporeal membrane oxygenation; HD, hemodialysis; IABP, intraaortic balloon pump; ICU, intensive care unit; LVEF, left ventricular ejection fraction; PGD: primary graft dysfunction; PGD-LV, left- ventricle primary graft dysfunction; TTE, transthoracic echocardiogram.

Hoffman et al. Heart Lung Transplant. 2021 Nov;40(11):1408-1418.

UCSD DCD Heart History

Heart DCD OCS TransMedics trial Activated September 19, 2020	2 heart DCD transplants in DCD Trial, prior to trial closing.
Heart DCD CAP Trial Activated January 6, 2020	Completed 11 transplants via OCS TransMedics CAP Trial
Heart Normothermic Regional Perfusion May 2021	To date 34 NRP DCD hearts transplanted

UCSD DCD Team

- Dr. Victor Pretorius, Surgical Director of Heart Transplant
- Dr. Mark Kearns, Assistant Professor of Clinical Surgery
- Yan Gernhofer, NP- Cardiac Surgery NP
- Brandon Jackson, Lead of Transplant Recovery and Normothermic Perfusion
- Ken Hudson, Transplant Recovery Specialist
- UCSD Perfusion group

UCSD NRP experience first 10 months

- Donor Age 29 (15-44)
- Longest fWIT 90 min
- CPB cannulation time

  2-5 min

  average 3 min
- Time on CPB 67 min (43-117 min)

NRP DCD #	Date	OPO	Donor Age	Sex	COD	FWIT	Time On Pump
1	5/6/21	CASD	37	Male	Peds versus auto	35	105
2	5/24/21	CADN	15	male	GSW	15	53
3	5/25/21	TXSB	32	Male	GSW	24	69
4	6/1/21	CADN	28	male	Hanging	29	77
5	5/31/21	CADN	20	male	trauma	37	53
6	6/13/21	CAOP	27	male	gsw	29	47
7	7/2/21	AZOB	41	male	overdose	24	50
8	7/4/21	TXSA	37	male	MVA	20	48
9	7/11/21	AZOB	27	male	head trauma	22	
10	7/28/21	TXSB	24	male	hanging	66	51
11	8/11	NMOP	28	male	CA	37	62
12	8/20	NMOP	34	female	head trauma	32	
13	8/25	AZOB	19	male	head trauma	58	67
14	9/11	MWOB	35	male	hanging	36	56
15	9/16	AZOB	32	female	MVC	16	72
16	9-18	AZOB	18	male	CVA	23	72
17	9-27-21	TXGC	39	male	hanging	53	68
18	10-9-21	OKOP	37	male	overdose	19	51
19	10-10-21	nvlv	24	male	head trauma	90	59
20	10-11-21	AZOB	32	male	anoxia	26	35
21	10-25-21	CASD	38	male	anoxia	21	58
22	11/5/21	CASD	23	male	CVA	63	43
23	11-10-21	CaSD	43	male	anoxia	15	118
24	12-12-21	CAOP	22	male	overdose		
25	12-30-21	Casd	**30**	male	head trauma	20	91
26	2/12/21	CORS	23	male	GSW head trauma		
27	2/13/22	CASD	19	male	head trauma	20	96
28	2/15/22	CASD					
29	2/16/22	TXSB	25	male	head trauma	55	57
30	2/19/22	TXGC					
31	2/19/22	TXGC	24	male	anoxia	22	68
32	2/22/22	CORS	44	male	head trauma	12	68
33	2/22/22	AZOB	32	male	anoxia	23	117

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Early outcomes for liver transplant utilizing thoracoabdominal normothermic regional perfusion for donation after circulatory death: a multi-center experience

Table 2: Recipient Characterisatics and Transplant Course

Recipient	Etiology of Liver Disease	Age	Sex	Lab MELD	Listed MELD	Prior Abdominal Surgery (Y/N)	Re-Transplant (Y/N)	CIT (m)	PNF (Y/N)	Peak AST (U/L)	Peak ALT (U/L)	Peak Lactate (mmol/L)	ICU LOS (days)	Hospital LOS (days)	Length of Follow Up (days)	Transplant Related Complications and Readmissions
1	HCV, HCC	60	M	10	27	N	N	511	N	2239	2131	7.8	1	5	237	Anastomotic biliary stricture requirinng readmission, ERCP and stent
2	HCV, Alcohol, HCC	59	M	7	27	N	N	500	N	3420	1735	5.2	7	10	229	Readmission for abdominal pain, normal allograft function, no intervention
3	A1AT, NASH	51	M	24	33	N	N	500	N	286	139	3.5	1	17	230	N
4	NASH	42	M	21	19	N	N	470	N	3220	1960	4.9	5	9	196	N
5	Alcohol	69	M	22	22	N	N	210	N	317	494	0.9	2	7	189	N
6	Intrahepatic cholangiocarcinoma (RESTORE Trial)	59	M	8	7	Left Liver Lobectomy	N	342*	No	6298	2072	3.4	2	7	127	N
7	NASH/hemochromatosis	66	F	27	27	Y	N	288	No	1170	920	1.7	1	4	122	N
8	Alcohol	50	M	26	26	N	N	226	No	318	155	1.8	1	5	120	Anastomotic and non-anastomotic biliary stricture requiring outpatient ERCP and stent
9	Alcohol	67	M	24	24	N	N	200	N	720	421	1	3	7	97	N
10	Alcohol	66	M	19	17	N	N	218	N	431	350	2	1	9	93	N
11	HCV, HCC	59	M	19	22	N	N	296	N	1412	1580	1.8	2	7	67	N
12	Alcohol	52	M	18	21	N	N	205	N	814	783	5.5	1	5	35	N

* Allograft #6 was additionally placed on an ex vivo normothermic perfusion pump prior to implantation

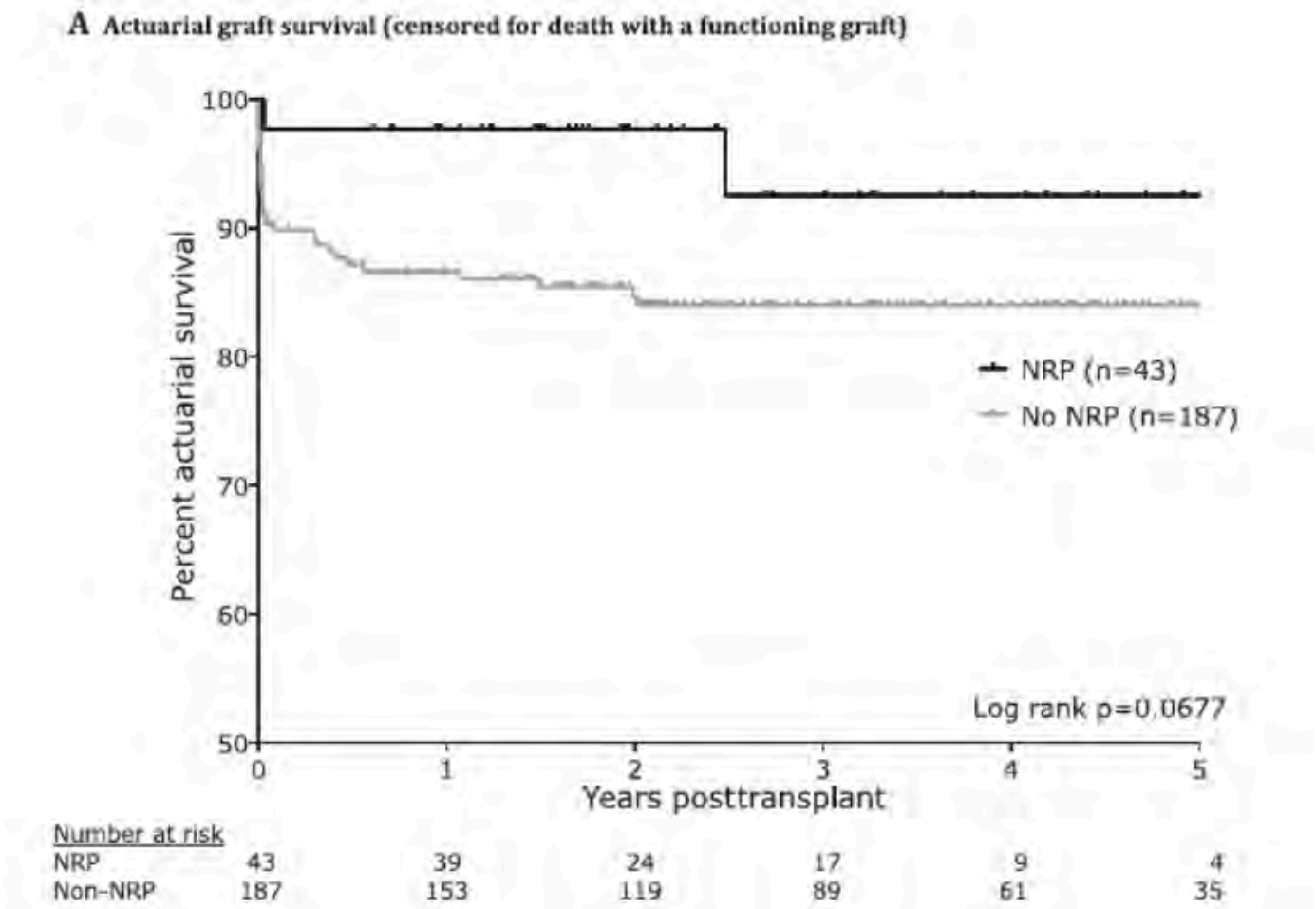
Kidney graft outcome

Graft outcomes	NRP Kidney transplants (N=865)	Non NRP kidney transplants (N=1437)
12-month graft failure N(%)	57 (7%)	118 (8.5%)
Delayed Graft Function* N(%)	**238 (30.3%)**	**640 (48.4%)**
Primary non-function N(%)	40 (4.8%)	61 (4.4%)
1 yr serum creatinine (mg/dl) Mean (SD)^	**1.5 (0.7)**	**1.8 (0.9)**

*. P<0.001 / ^ - p<0.001

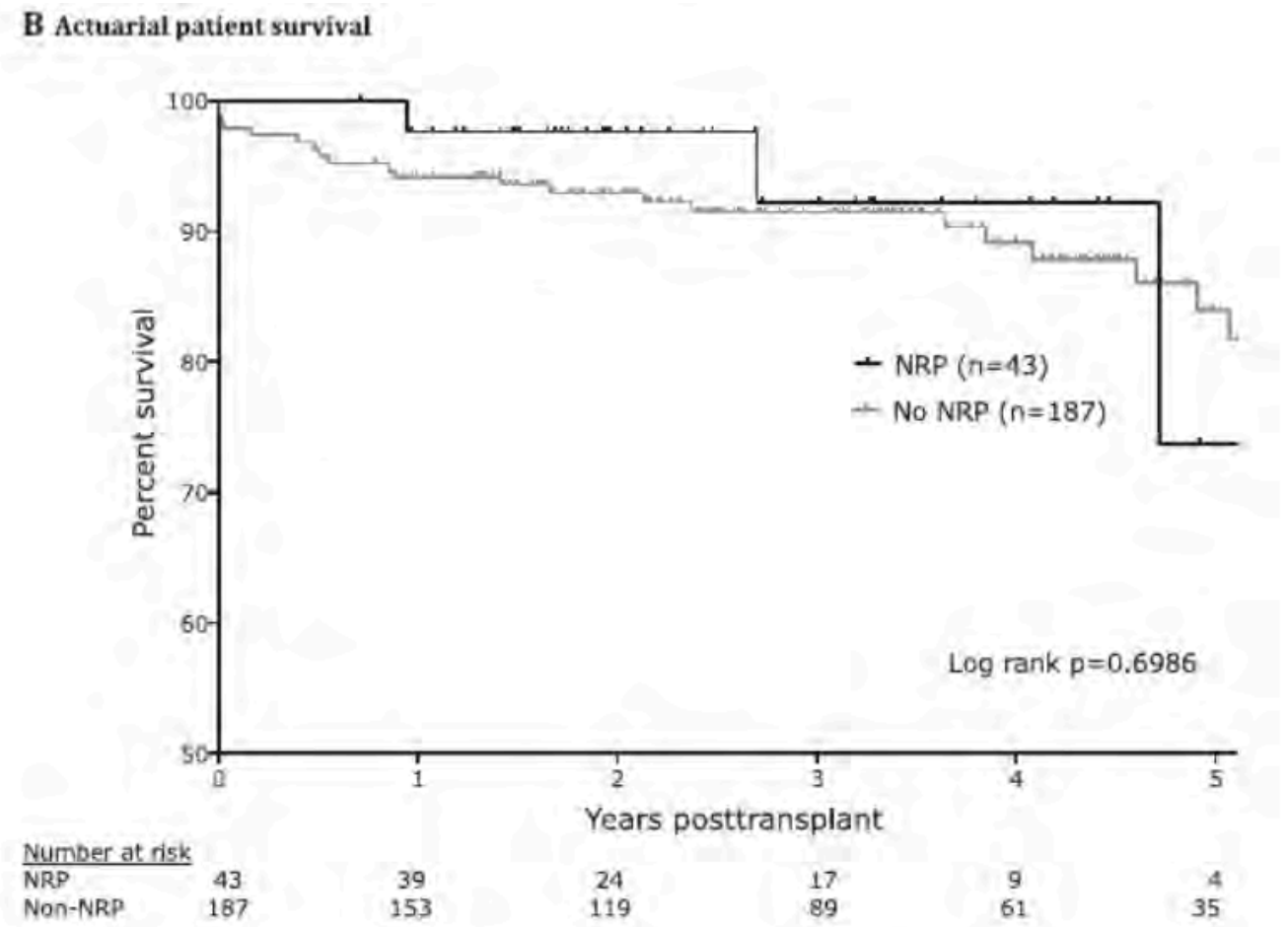
Padilla M et al. Am J Transplant 2021

NRP vs non-NRP for DCD liver outcomes



Watson et al
Am J Transplant. 2019;19:1745–1758.

NRP vs non-NRP for DCD liver outcomes



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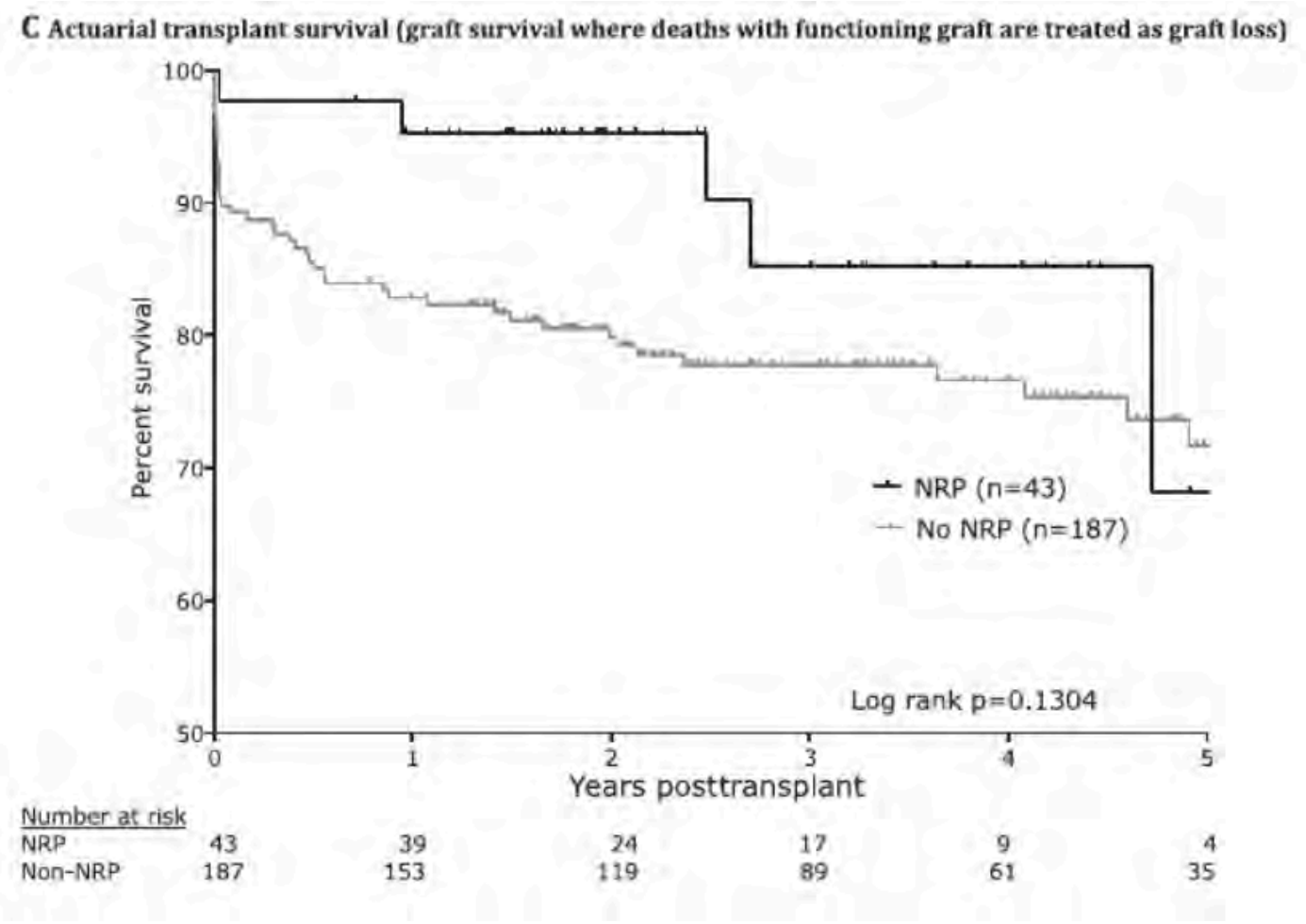
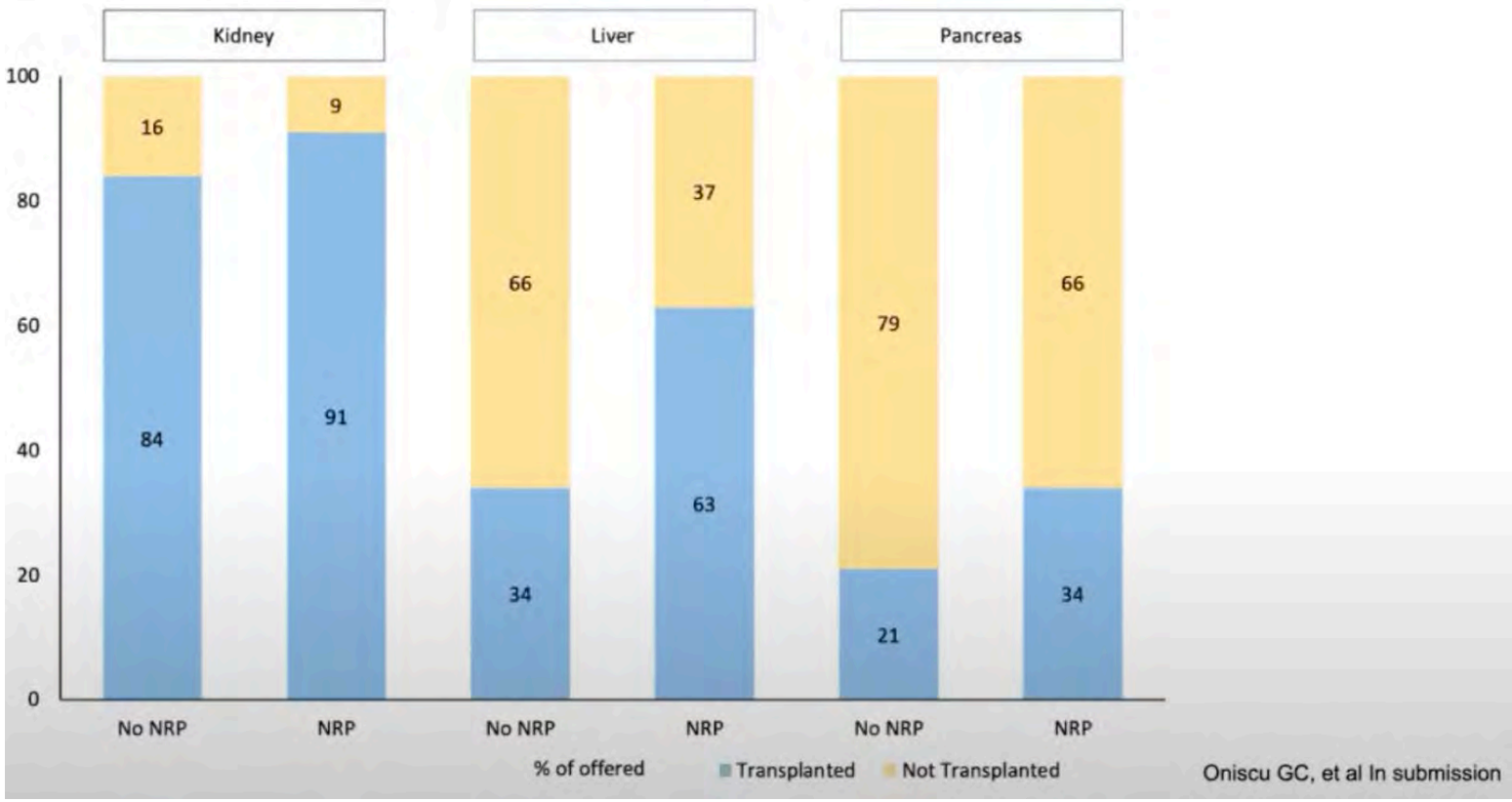
NRP vs non-NRP for DCD liver outcomes

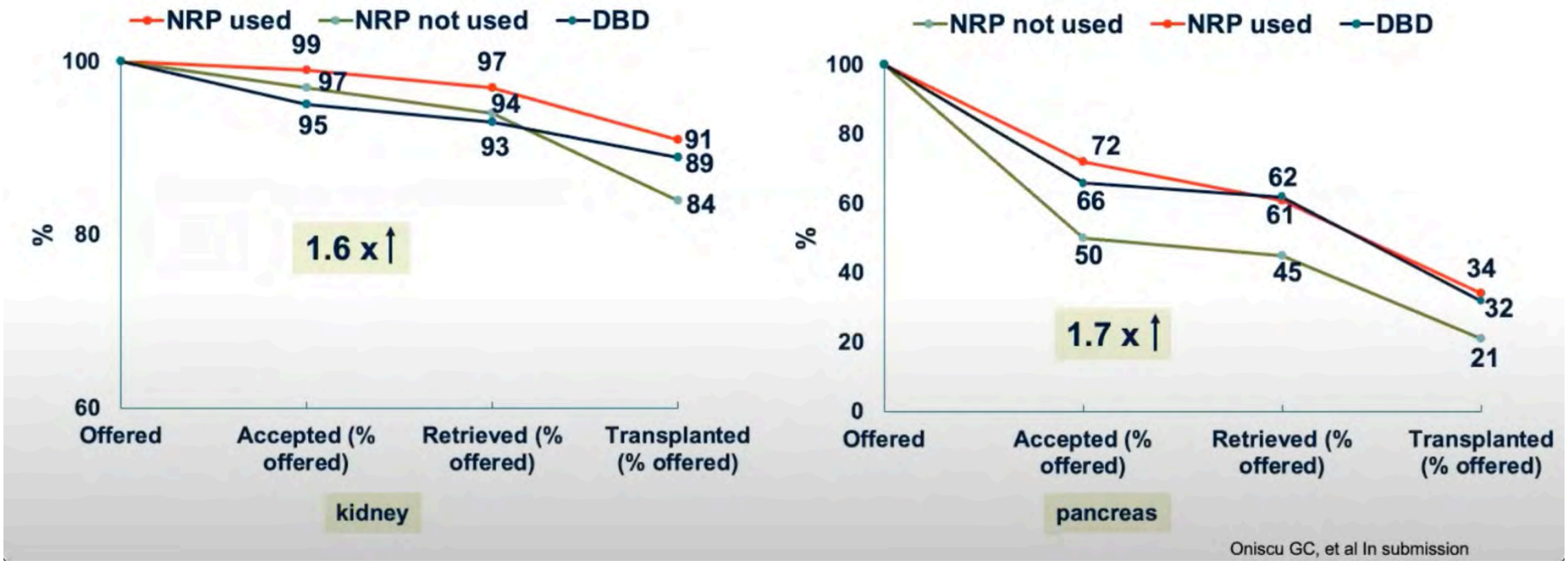


Watson et al
Am J Transplant. 2019;19:1745–1758.

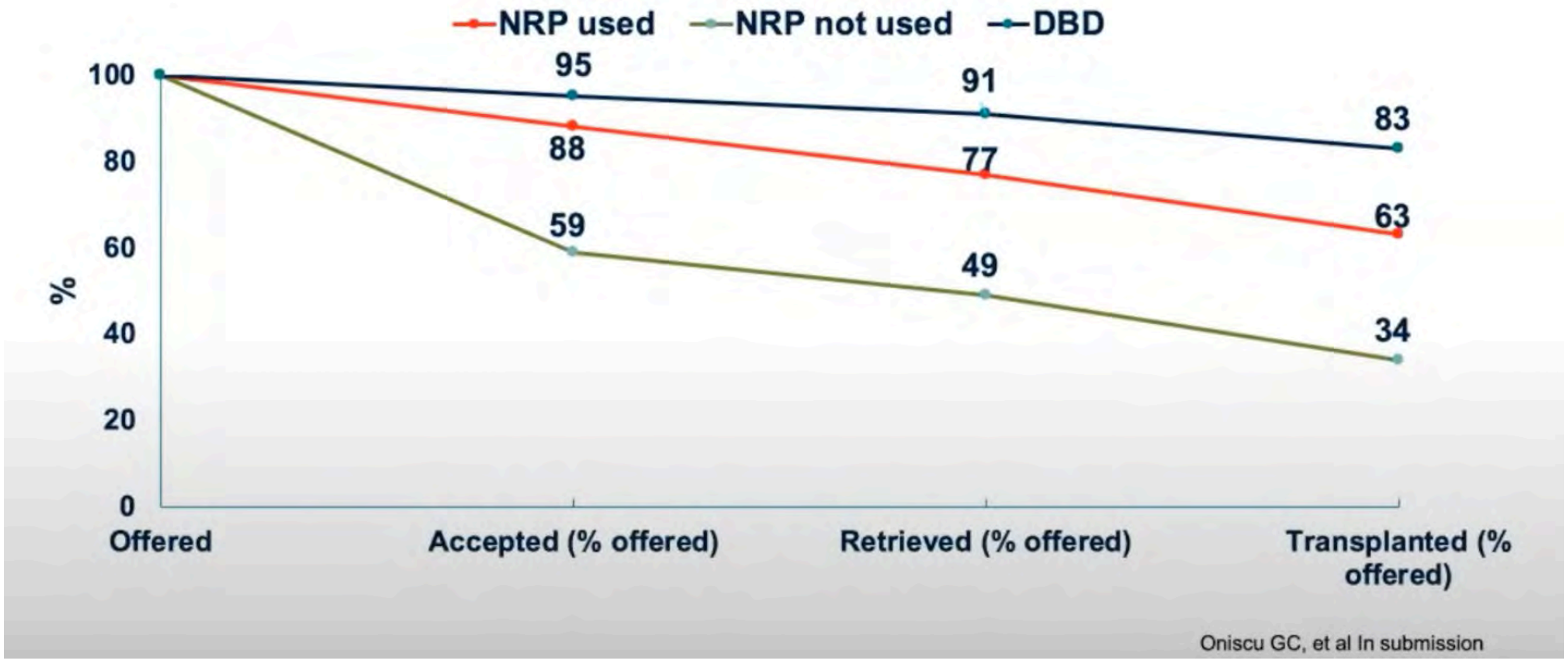
Organ Utilization with NRP



NRP increases Kidney and Pancreas utilization



NRP increases Liver graft utilization



UK experience @ 5 years

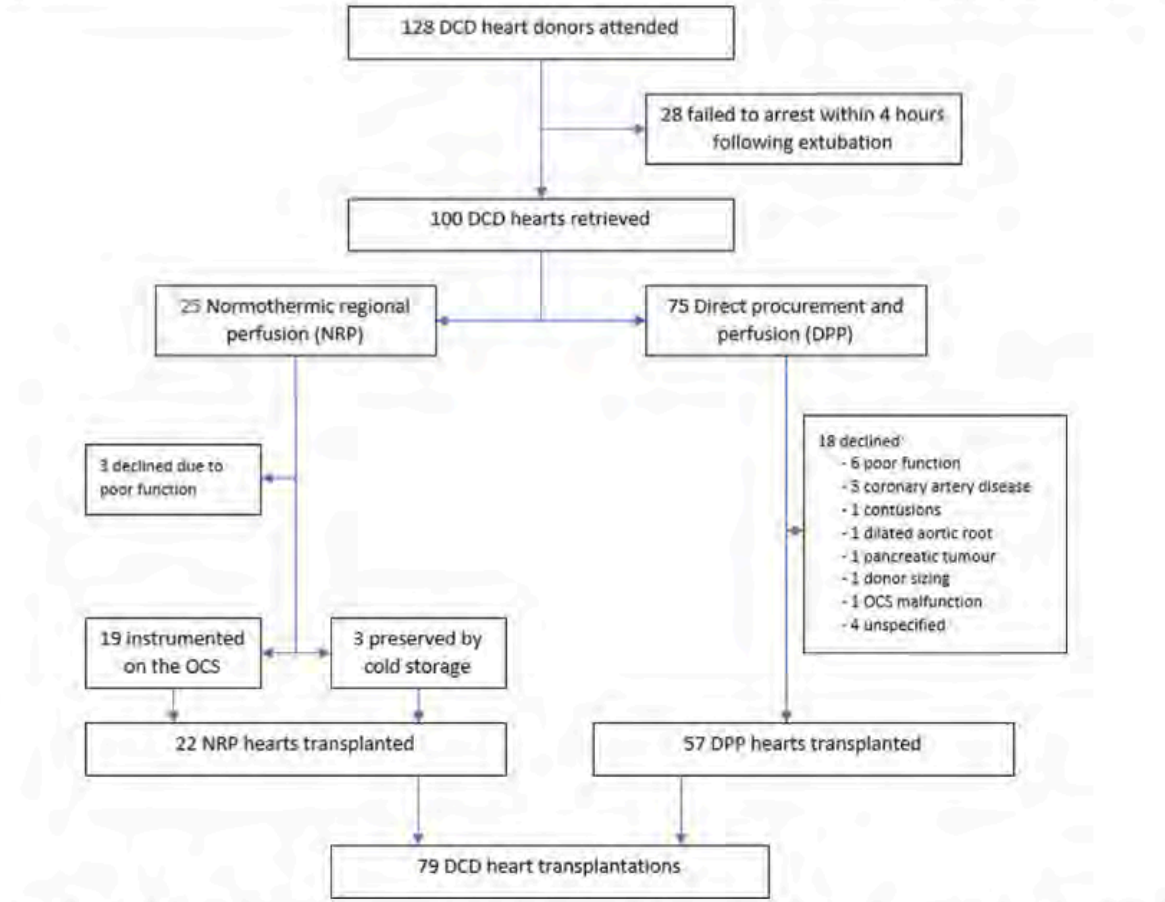
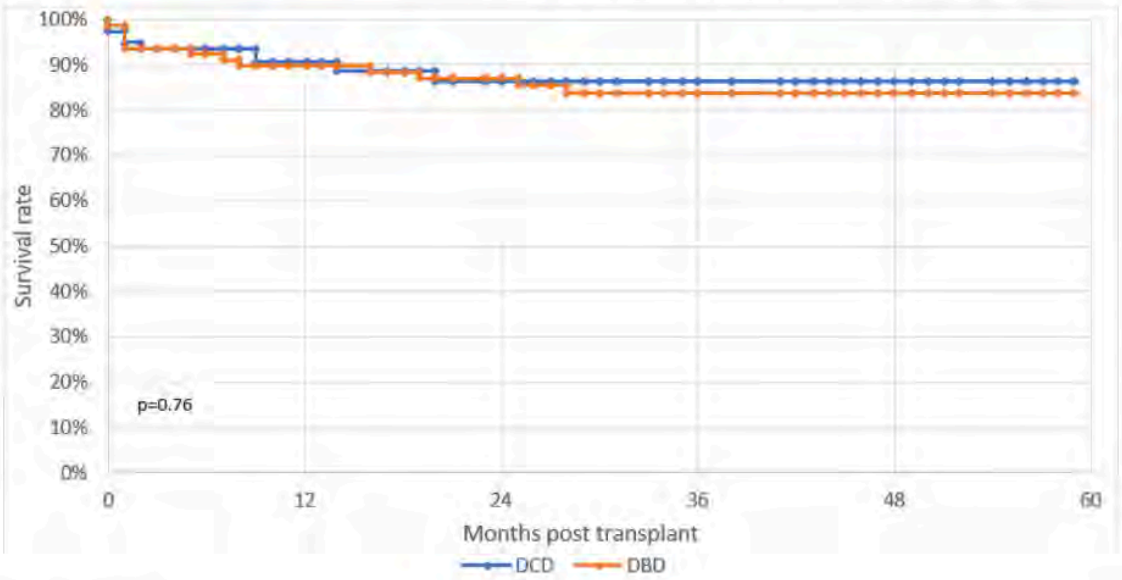


Figure 1 DCD donors, retrieval, and utilization over the first 5 years. DCD, donation after circulatory-determined death; DPP, direct procurement and perfusion; NRP, normothermic regional perfusion; OCS, Organ Care System.

Messer et al
The Journal of Heart and Lung Transplantation, Vol 39, No 12, December 2020

DCD vs DBD outcomes at 5 years in UK



Number at risk

time [months]	*0*	*3*	*6*	*12*	*24*	*36*	*48*	*60*
DCD	79	70	67	53	36	23	14	1
DBD	79	74	72	65	59	44	36	25

DBD, donation after brain death; DCD, donation after circulatory-determined death

Figure 3 Kaplan–Meier survival after transplantation between DCD and DBD. DBD, donation after brain death; DCD, donation after circulatory-determined death

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NRP vs DPP

Number at risk

time [months]	0	3	6	12	18	24	30	36	42	48	54
DPP	57	48	45	32	22	20	11	10	8	4	1
NRP	19	19	19	19	16	15	12	12	11	9	6

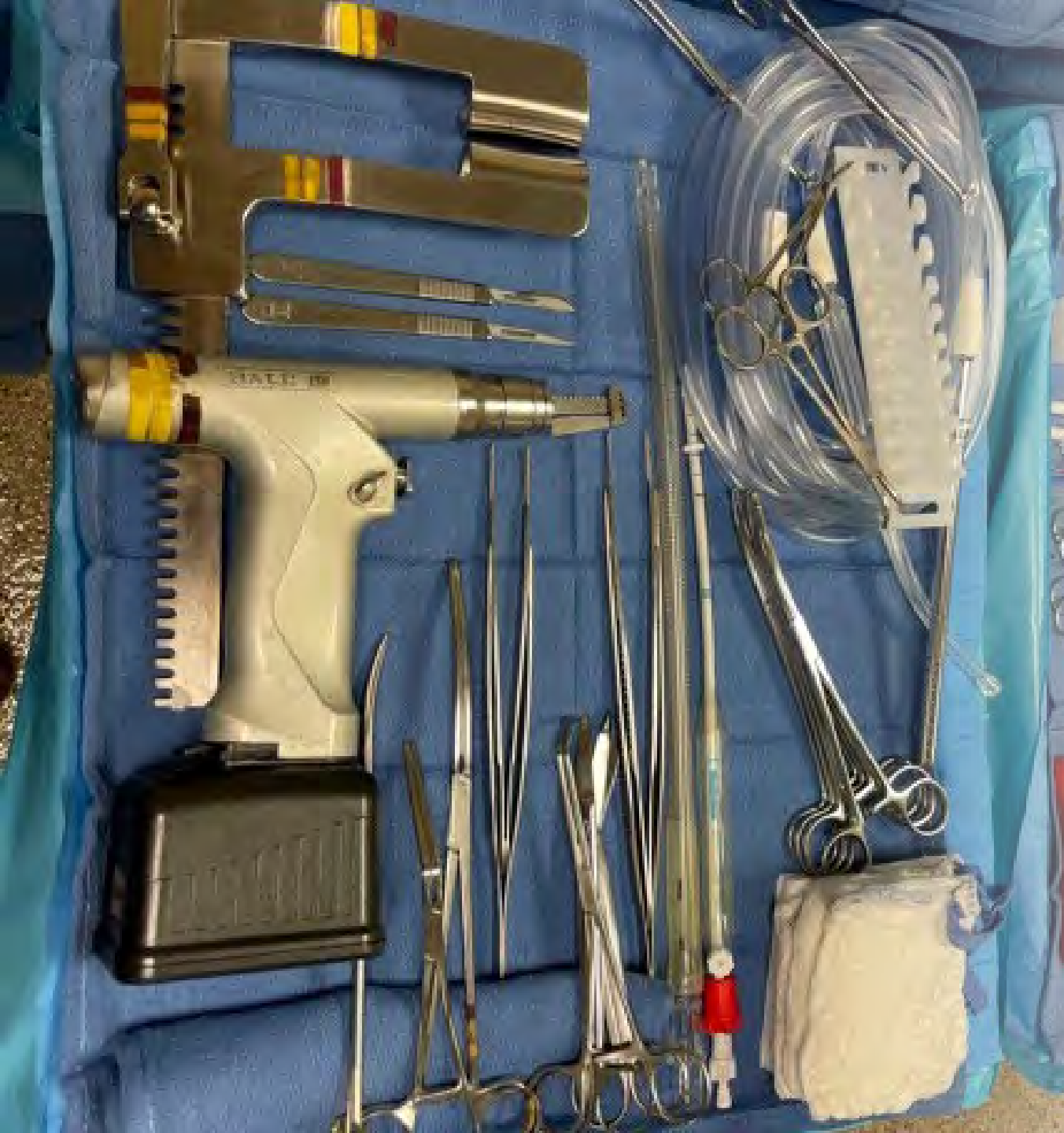
DPP, direct procurement and perfusion; NRP, normothermic regional perfusion

Figure 4 Kaplan–Meier survival after transplantation between DPP and NRP. DPP, direct procurement and perfusion; NRP, normothermic regional perfusion.

Messer et al
The Journal of Heart and Lung Transplantation, Vol 39, No 12, December 2020

NRP DCD Heart Pre-Recovery Needs

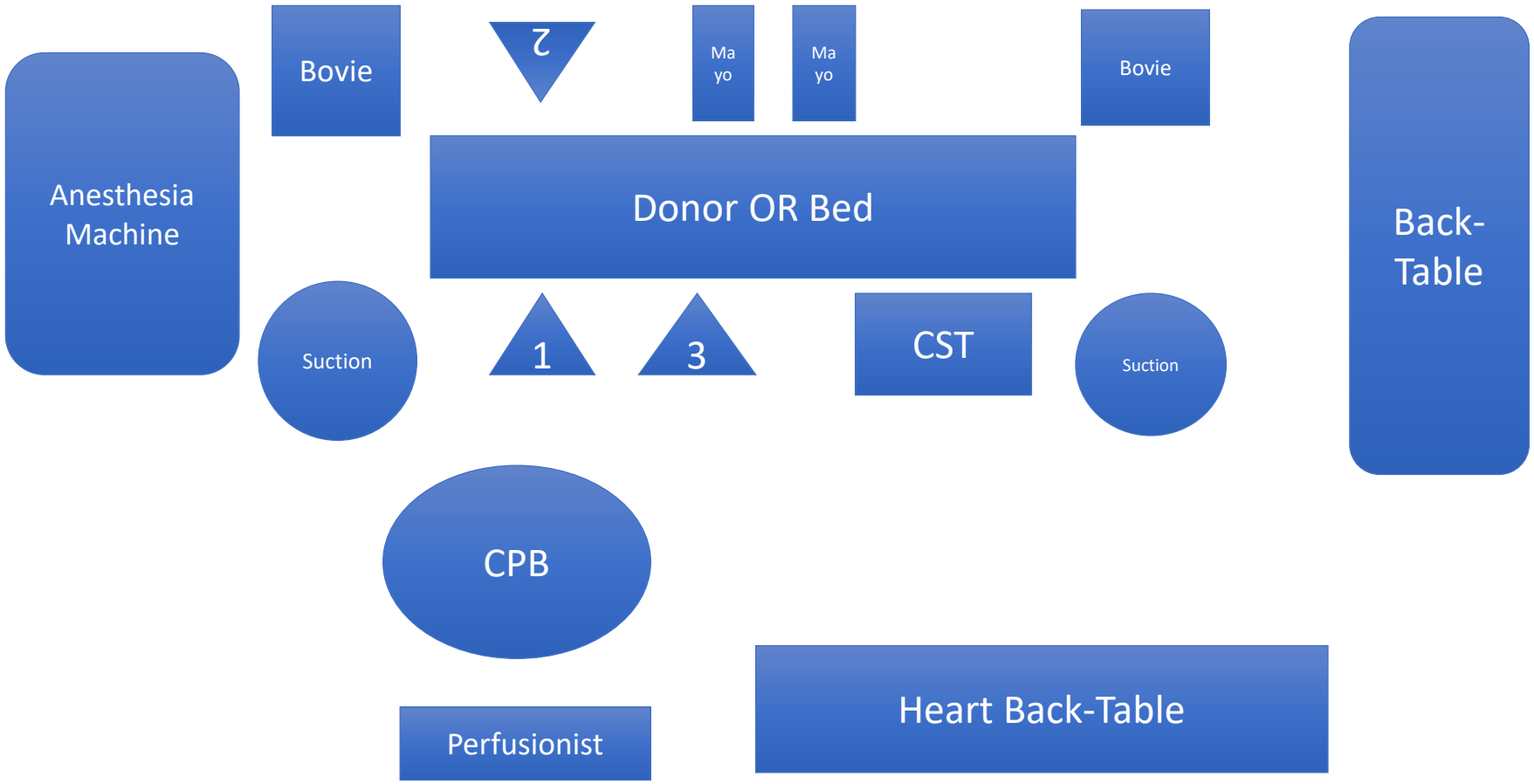
- Prior to arrival to hospital UCSD is willing to speak to all recovery surgeons or implanting physicians to go over protocol
- Pre-recovery huddle with all team members prior to extubation
- 50,000 units of heparin given before extubation
    - Half life ~ 45 mins post IV push
    - Due to the extended WIT wait period a larger dose is given to avoid need for re-dosing
    - Bypass filter and oxygenator clotting prevention
- Q 1 minute vital signs and direct communication with member of UCSD transplant team
- Femoral Line to be placed by ICU team as part of DCD donor care



NRP OR Needs

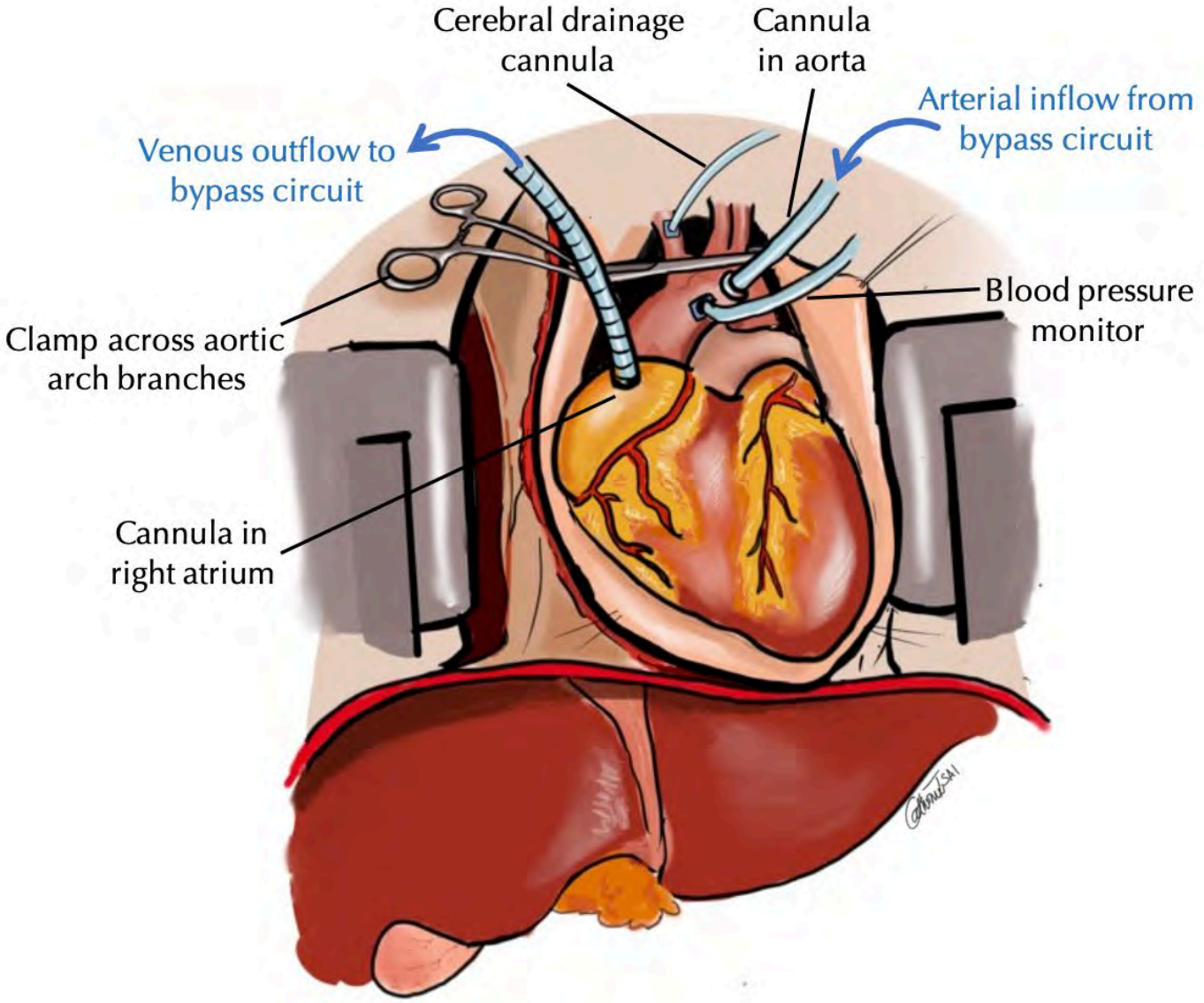
- 1 mayo stand draped
- 1 a-line setup
- 1 sterile extension tubing for a-line
- 1 laryngoscope handle
- Bronch/video laryngoscope if available
- Mac 4 and mac 3
- 7.0 to 7.5 ET tube
- Stylet
- Standard Procurement Instruments

NRP Heart Donor OR Recovery Setup



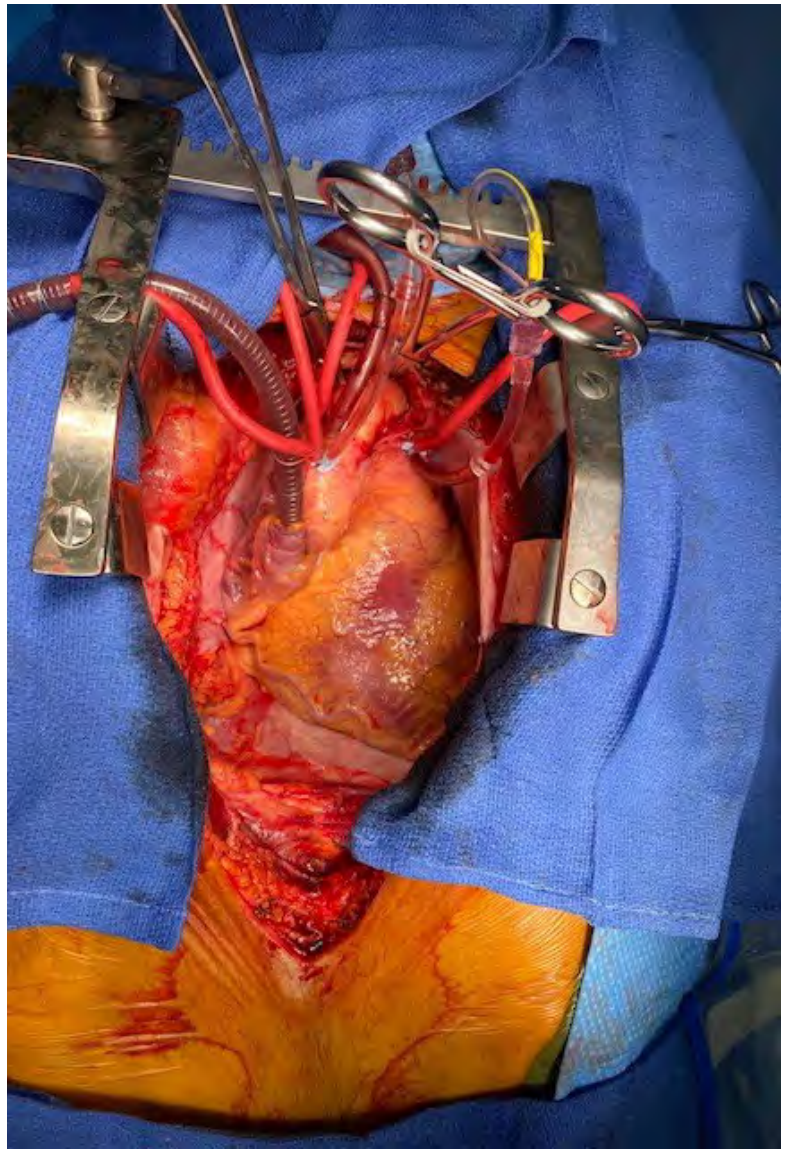
NRP Steps

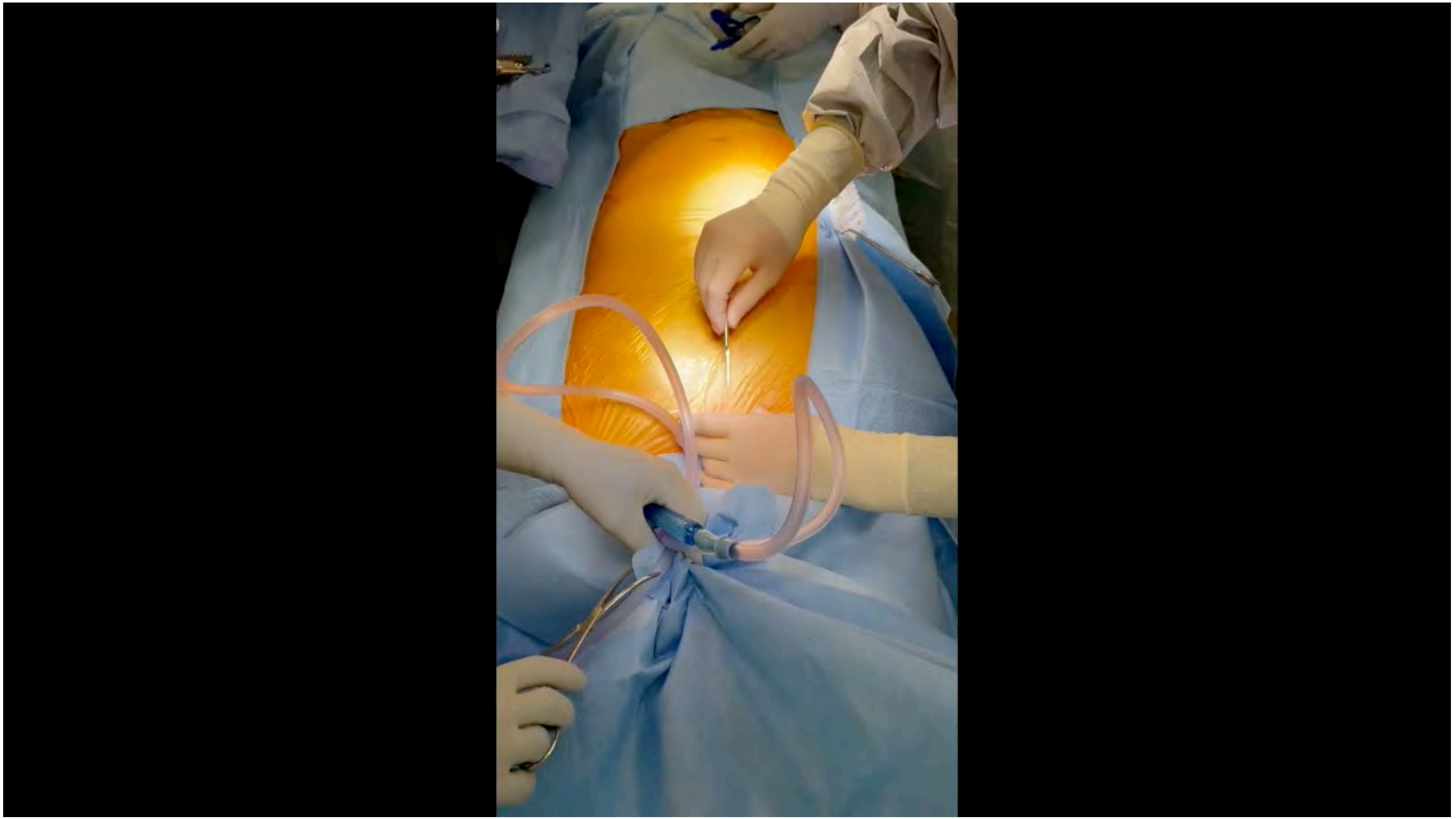
- Chest Emergently open
- Head vessels exposed and clamped
- Venous cannula placed in right atrium, blood drained into pump
- Aortic Cannula placed in aorta
- Cardio-pulmonary Bypass initiated
- Average time from incision to CPB, 3 min

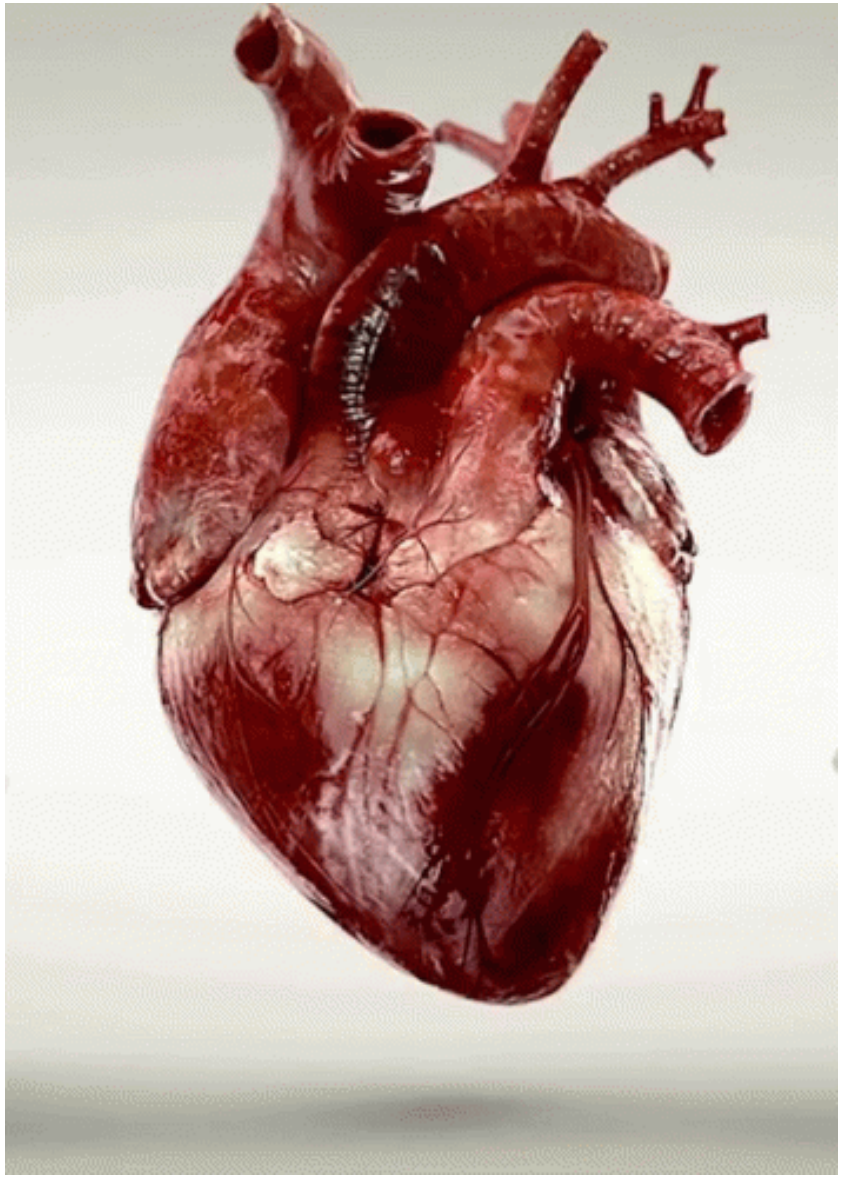


Head Vessels

- All 3 head vessels (brachiocephalic, left common carotid, and left subclavian) are cleanly dissected and identified.
- Vascular clamp is placed over all three head vessels prior to any cannulation of CBP.
- Clamping all 3 head vessels occludes flow to the brain
- Result in loss of upper limb blood pressure monitoring







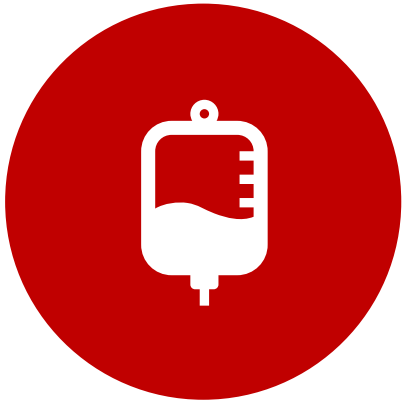
How do you assess the heart and other organ suitability for transplant?

- Ability to wean off bypass
- Visual inspection
- Palpation
- Arterial and intra cardiac pressures
- Central venous saturation
- Lactate trend
- Echo seldom needed

How do organs get stored and transported after NRP procurement?

COLD STATIC STORAGE

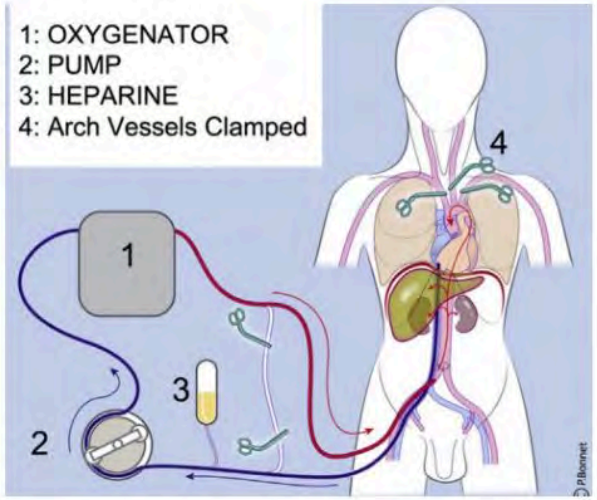
COLD PERFUSION SYSTEM

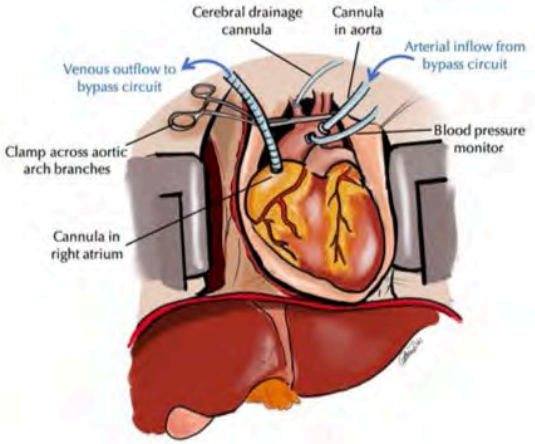


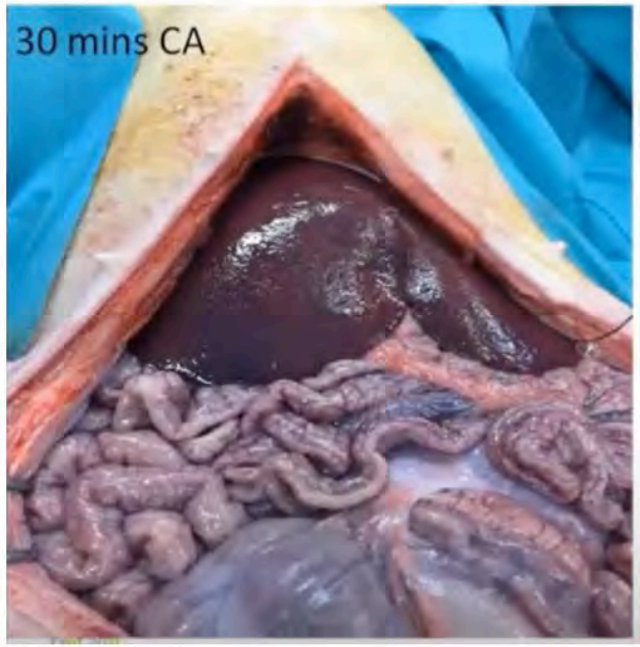
WARM PERFUSION SYSTEM

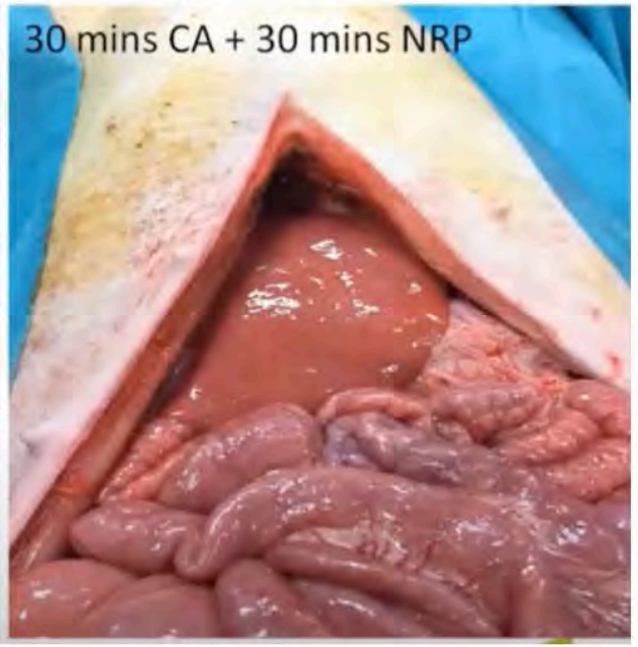
NRP Summary

Restore	Restore flow of oxygenated blood following death due to cardiac arrest
Reverse	Reverse warm ischemic injury of thoraco-abdominal organs after circulatory death
Increase	Increase organ donation by 30-40% cost effective medicine (bang for $)









Thank You!

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