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### Normothermic Regional Perfusion: Do the Ends Justify the Means







# Outline

# 1.Background2.Technique3.Ethics and Legalities4.Outcomes





"If you want to change the future, you must change what you're doing in the present."



# — Mark Twain



### Death

### Harvard Criteria 1968

- "Irreversible coma" Brain death/death by neurologic criteria
- the characteristics of irreversible coma—a permanently nonfunctioning brain included unreceptivity and unresponsiveness, no movements or spontaneous breathing (apnea) and no brain stem reflexes.

### The Uniform Determination of Death Act (UDDA), the legal standard for death throughout the United States 1981

- Death can be declared, in accordance with accepted medical standards, on one  $\bigcirc$ of two grounds
  - 1. irreversible cessation of circulatory and respiratory functions, or
  - 2. irreversible cessation of all functions of the entire brain, including the brain stem.
- Every state accepted the UDDA, in language or in spirit.



### **Dead Donor Rule**

The dead donor rule is an ethical norm related to deceased organ donation that is often expressed as

- (1) organ donors must be dead before procurement of organs begins; or
- (2) organ procurement itself must not cause the death of the donor.





### **Two Types of Deceased Organ Donors**



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

### Resumption of Cardiac Activity after Withdrawal of Life-Sustaining Measures

S. Dhanani, L. Hornby, A. van Beinum, N.B. Scales, M. Hogue, A. Baker, S. Beed, J.G. Boyd, J.A. Chandler, M. Chassé, F. D'Aragon, C. Dezfulian, C.J. Doig, F. Duska, J.O. Friedrich, D. Gardiner, T. Gofton, D. Harvey, C. Herry, G. Isac, A.H. Kramer, D.J. Kutsogiannis, D.M. Maslove, M. Meade, S. Mehta, L. Munshi, L. Norton, G. Pagliarello, T. Ramsay, K. Rusinova, D. Scales, M. Schmidt, A. Seely, J. Shahin, M. Slessarev, D. So, H. Talbot, W.N.K.A. van Mook, P. Waldauf, M. Weiss, J.T. Wind, and S.D. Shemie, for the Canadian Critical Care Trials Group and the Canadian Donation and Transplantation Research Program

### ABSTRACT

### BACKGROUND

The minimum duration of pulselessness required before organ donation after The authors' full names, academic de circulatory determination of death has not been well studied.

### METHODS

We conducted a prospective observational study of the incidence and timing of KIM IN8, Canada, or at schanani@cheo resumption of cardiac electrical and pulsatile activity in adults who died after .on.ca. planned withdrawal of life-sustaining measures in 20 intensive care units in three "The members of the site research countries. Patients were intended to be monitored for 30 minutes after determination of death. Clinicians at the bedside reported resumption of cardiac activity prospectively. Continuous blood-pressure and electrocardiographic (ECG) wave- This article was updated on January 28, forms were recorded and reviewed retrospectively to confirm bedside observations 2021, at NEJM.org. and to determine whether there were additional instances of resumption of car- N Engl J Mod 2021;384:345-52. diac activity

### RESULTS

A total of 1999 patients were screened, and 631 were included in the study. Clinically reported resumption of cardiac activity, respiratory movement, or both that was confirmed by waveform analysis occurred in 5 patients (1%). Retrospective analysis of ECG and blood-pressure waveforms from 480 patients identified 67 instances (14%) with resumption of cardiac activity after a period of pulselessness, including the 5 reported by bedside clinicians. The longest duration after pulselessness before resumption of cardiac activity was 4 minutes 20 seconds. The last QRS complex coincided with the last arterial pulse in 19% of the patients.

### CONCLUSIONS

After withdrawal of life-sustaining measures, transient resumption of at least one cycle of cardiac activity after pulselessness occurred in 14% of patients according to retrospective analysis of waveforms; only 1% of such resumptions were identified at the bedside. These events occurred within 4 minutes 20 seconds after a period of pulselessness. (Funded by the Canadian Institutes for Health Research and others.)



grees, and affiliations are listed in the Appendix. Address reprint requests to Dr Dhanani at Children's Hospital of East ern Ontario, 401 Smyth Rd., Ottawa, ON

groups are listed in the Supplementary Appendix, available at NEJM.org.

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### **Organ Procurement Organizations (OPO)**

Conditions for Coverage Outcomes Measures 2020

- Donation rate measure is the number of organ donors in the OPO's DSA as a percentage of inpatient deaths among patients 75 years old or younger with a primary cause of death that is consistent with organ donation.
- Transplantation rate measure is the number of transplanted organs from an OPO's DSA as a percentage of inpatient deaths among patients 75 years old or younger with a primary cause of death that is consistent with organ donation METHODIST



### **Performance Benchmark**

Tier 1 are the highest performing OPOs in the top 25 percent will be assigned to and automatically recertified for another four years.

Tier 2 OPOs are the next highest performing OPOs, where performance on both measures exceed the median but do not reach Tier 1 and will not automatically be recertified and will have to compete to retain their Donor Service Area (DSA).

Tier 3 OPOs are the lowest performing OPOs that have one or both measures below the median and will be decertified and will not be able to compete for any other open DSA.



### **CMS Benchmark Report 2023**



Tier 2 OPOs: 1 or both measures above the median, but below the top 25% Tier 3 OPOs: 1 or both measures below the median





### **Deceased Donors 2010-2022**



OPTN/SRTR 2022 Annual Data Report

OPTN/SRTR 2022 Annual Data Report

2012 2022 Characteristic N Percent N Percent Mechanism of Death 99 1.2 141 0.9 Drowning Seizure 86 1.1 160 1.1 Drug Intoxication 440 5.4 2485 16.7 Asphyxiation 366 4.5 683 4.6 Cardiovascular 1275 15.7 3055 20.5 Electrical 4 0 5 0 Gunshot Wound 961 766 9.4 6.4 Stab 19 0.2 24 0.2 **Blunt Injury** 1781 21.9 2369 15.9 SIDS 7 0.1 9 0.1 2912 3774 25.3 Stroke 35.8 195 2.4 903 6.1 Natural Causes 2.3 Other/unknown 193 2.4 336

	2	2012	2	022
Characteristic	Ν	Percent	Ν	Percent
DCD status				
DBD	7036	86.4	10127	67.9
DCD	1107	13.6	4778	32.1

OPTN/SRTR 2022 Annual Data Report



### **The Problem with DCD Liver Transplantation**



Skaro AI, Jay CL, Baker TB, Wang E, Pasricha S, Lyuksen. untold story. Surgery. 2009 Oct;146(4):543-53.

Croome KP; Mathur AK. Age B; Yang,L; Taner T; Heimbach J; Rosen Сь, and Long-term Outcomes From a Multicenter Cohort. Transplantation 2022 Jun.

Graft Survival

Complicat	tion	DCD (%)	DBD (%)	P Value
Primary N		1 (2.6)	1 (1.3)	1.000
Vascular	Hepatic artery thrombosis Hepatic artery stenosis Portal vein thrombosis Portal vein stenosis Vena cava thrombosis	5 (13.2) 0 (0.0) 4 (10.5) 0 (0.0) 0 (0.0) 1 (2.6) 0 (0.0)	13 (17.1) 3 (3.9) 5 (6.6) 4 (5.3) 0 (0.0) 0 (0.0)	.786 .550 .478 .299 1.000 .333
Biliary	Biliary leak	7 (18.4)	7 (9.2)	.225
	Biliary necrosis	1 (2.6)	0 (0.0)	.333
	Biliary abscess	0 (0.0)	0 (0.0)	1.000
	Biliary sludge or stones	0 (0.0)	1 (1.3)	1.000
	Anastomotic biliary stricture	3 (7.9)	1 (1.3)	.107
	Ischemic-type diffuse	7 (18.4)	7 (9.2)	.225
	intrahepatic biliary strictures	3 (7.9)	1 (1.3)	.107

Abbreviations: DBD, donation after brain death; DCD, donation after cardiac death

Vanatta JM, Dean AG, Hathaway DK, Nair S, Modanlou KA, Campos L, Nezakatgoo N, Satapathy SK, Eason JD. Liver transplant using donors after cardiac death: a single-center approach providing outcomes comparable to donation after brain death. Exp Clin Transplant. 2013 Apr;11(2):154-63.



NORMAL





### FIGURE 1.

Classification of patterns of ischemic cholangiopathy. A, Normal cholangiogram. B. Diffuse necrosis-severe abnormalities of the entire biliary tree seen shortly after transplant. C, Multifocal progressive-mild to moderate stenosis of the second-order and peripheral ducts that progressively worsen over time. D. Confluence dominantstrictures and casts confined to the biliary confluence that geographically never expand beyond the confluence. E, Minor form-mild radiologic abnormalities consistent with ischemic cholangiopathy that ultimately resolve, never going on to develop more extensive strictures.

isplantation using donors after cardiac death: the

### ...pathy Following DCD Liver Transplantation: Distinct Clinical Courses



### **Discarded Donor Livers 2010-2021**



FIGURE 2. Discard and utilization of SCD, ECD, and DCD donors between 2010 and 2021. A, Transplanted livers by donor type from 2010 to 2021. B, Discarded livers by donor type between 2010 and 2021. C, Discard rate by donor type between 2010 and 2021. DCD, donation after circulatory death; ECD, expanded criteria donor; SCD, standard criteria donor.

Torabi J; Todd R, van Leeuwen L, Bekki Y, Holzner M; Moon J; Schiano T; Florman SS, Akhtar MZ. A Decade of Liver Transplantation in the United States: Drivers of Discard and Underutilization. Transplantation Direct 10(6):p e1605, June 2024



### **Clinical Need**



OPTN/SRTR 2021 Annual Data Report



Fig. 4. Map of the 56 continental DSAs shaded by percentage of missed opportunities for donation after cardiac death liver recover

- DCD organs are one of the most immediate ways to increase the pool of transplantable organs
- The organs are there, but they are not being used.

Cannon RM, Nassel AF, Walker JT, Sheikh SS, Orandi BJ, Lynch RJ, Shah MB, Goldberg DS, Locke JE. Lost potential and missed opportunities for DCD liver transplantation in the United States. Am J Surg. 2022 Sep;224(3):990-998.







### **Normothermic Regional Perfusion (NRP)**

A recovery technology that makes increasing DCD utilization feasible and with good outcomes.

Post-mortem in situ oxygenated perfusion to the organs intended for transplantation after the patient has been declared deceased and a notouch period has been observed

- A-NRP: Abdominal cavity only
- TA-NRP: thoracic and abdominal cavity



### **Process and Technique**

### **Conventional DCD**



Process: Cannulation, occlusion of blood vessels to the head, initiation of perfusion with warm, oxygenated blood, organ evaluation and intervention, cold perfusion and crossclamp





### TA-NRP vs. A-NRP







### **American College of Physicians Statement**

The American College of Physicians (ACP) issued a statement of concern about the use of controlled donation after circulatory determination of death involving normothermic regional perfusion.

The ACP concludes that the use of DCD protocols involving NRP should be halted until these ethical concerns have been addressed and rejected.

American College of Physicians. 2021. 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. Accessed July 17, 2024. https://assets.acponline.org/acp\_policy/policies/ethics\_determination\_of\_death\_and\_organ\_transplantation\_in\_nrp\_2021.pdf.





### **ACP Statement 2021**

Four concerns:

- (1) in NRP death does not take its natural course, but that brain death is instead induced by preventing reperfusion of the brain.
- (2) the criterion for determination of circulatory death is violated and that the donor is successfully resuscitated.
- (3) that the practice is unjust because it disproportionally affects a stigmatized part of the population, namely people with substance abuse.
- (4) that lack of transparency in the practice could damage the trust in health care and clinical research.



### **Irreversible Versus Permanent**

Irreversible cessation of circulation means that, once it ceases, it ceases in perpetuity because it will not restart itself spontaneously (autoresuscitation) and it is impossible to restart it with available technology, i.e., it "cannot return."

Permanent cessation means that once it ceases, it ceases in perpetuity because autoresuscitation will not occur and no medical intervention will be performed to attempt to reestablish it, i.e., it "will not return."





### **Declaring Death**

Guidelines generally authorize physicians, or designated providers, to declare death once circulation and respiration have ceased permanently and does not require them to await or prove its irreversible cessation.

Permanent cessation has been the time-honored accepted medical practice for the circulatory-respiratory determination of death in settings outside of organ donation.



### **Pronouncing Death**

State death statutes, are based on the UDDA, which uses the term "irreversible" to describe the cessation of circulation and respiration.

- Strict construal of the term could conclude that the DCD donor had not satisfied the legal standard at the time of death declaration.
- The UDDA does not define "irreversible" so less strict construal is plausible.





### **The Organism as a Whole Integrated Entity**

The cessation of svet brain functi

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It is not the intentional exclusion of circulation to the brain that is the cause of the patient's death rather it is underlying disease or condition that led to the decision to withdraw life-sustaining therapies that is the underlying reason for choosing death by circulatory cessation to the entire body.

donor no longer the whole integrated organism.



# the cessation of ion the ral vital work of

### **Collateral Circulation**



<sup>-</sup>IGURE 1. A, Potential <u>collateral circulations</u> A to D that could theoretically restore flow and/or perfusion to the brain. B, Proposed solution of flow diversion away from the brain by occluding the descending <u>thoracic aorta</u> and draining the <u>aortic arch</u> arteries to atmosphere either by inserting a large bore <u>cannula</u> into the <u>ascending aorta</u> or draining the arch arteries individually. Any potential collateral flow to the brain should be preferentially diverted to the low resistance large bore subclavian vessels open to atmospheric pressure

Manara A, Shemie SD, Large S, Healey A, Baker A, Badiwala M, Berman M, Butler AJ, Chaudhury P, Dark J, Forsythe J, Freed DH, Gardiner D, Harvey D, Hornby L, MacLean J, Messer S, Oniscu GS, Simpson C, Teitelbaum J, Torrance S, Wilson LC, Watson CJE. Maintaining the permanence principle for death during in situ normothermic regional perfusion for donation after circulatorydeath organ recovery: A United Kingdom and Canadian proposal, American Journal of Transplantation, Volume 20 (8); 2020, 2017-2025





### **Brain Perfusion**







Download: Download high-res image (586KB) Download: Download full-size image

Figure 3. Transcranial Doppler of donation after circulatory death case 2 performed in the operating room setting. (A) Patient 2: baseline, pre-extubation left carotid artery siphon insonated via the transorbital window at a depth of 56 mm with anterograde blood flow; (B) Patient 2: baseline, pre-extubation right carotid artery siphon insonated via the transorbital window at a depth of 56 mm with anterograde blood flow; (C) Patient 2: baseline, pre-extubation basilar artery insonated via the transforaminal (foramen magnum) window at a depth of 86 mm with nonperfusing isolated systolic spikes/biphasic oscillating flow; (D) Patient 2: postdeclaration of death, there was no anterograde flow, nor isolated spikes/biphasic oscillating flow detected in the posterior circulation (depth 86 mm shown). Similarly, there was no anterograde flow, nor isolated spikes/biphasic oscillating detected in either anterior circulation temporal or orbital windows

points during the experiment. The BPU value at AS + 5 was defined as biological zero and subtracted from all other values. Values are mean 95% CI. AW, after weaning; BPU, blood perfusion unit; CI, confidence interval; ICP, intracranial pressure.

Dalsgaard FF, Moeslund N, Zhang ZL, Pedersen M, Qerama E, Beniczky S, Ryhammer P, Ilkjær LB, Erasmus M, Eiskjær H. Clamping of the Aortic Arch Vessels During Normothermic Regional Perfusion After Circulatory Death Prevents the Return of Brain Activity in a Porcine Model. Transplantation 106(9): 1763-1769, 2022

Frontera JA, Lewis A, James L, Melmed K, Parent B, Raz E, Hussain ST, Smith DE, Moazami N. Thoracoabdominal normothermic regional perfusion in donation after circulatory death does not restore brain blood flow, The Journal of Heart and Lung Transplantation, Volume 42 (9), 2023, 1161-1165.







### **Outcomes**

### 14 Za – IC

IAD										
		NRF	·	Non-N	RP		Risk Ratio		Risk Ratio	
	Study or Subgroup	Events	Total	Events	Total	Weight	IV, Random, 95% C		IV, Random, 95% Cl	
	DeGoeij 2022	2	20	7	49	19.5%	0.70 [0.16, 3.08]	1		
	Gauray 2022	4	646	34	164	32.9%	0.28 [0.10, 0.76	1		ue
	Mohkem 2022	1	68	24	200	37.0%	0.12 [0.05, 0.29	1		
EAL	Montani 2022		00	5	54	10.170	0.17 [0.02, 1.54	1		0
PNF	Total (95% Cl)		702		505	100.0%	0.23 [0.11, 0.49]	1	•	4
HAT	Total events	13		68			220			2
	Heterogeneity: Tau <sup>2</sup> =	= 0.20; Ch	1= 4.5	1, df = 3 (	P = 0.2	(1); I <sup>2</sup> = 3	3%	0.0	1 0.1 1 10 100	1
	lest for overall effect	Z= 3.78	(P = 0.0	1002)					Favours NRP Favours Non-NRP	
11									<	1
Re-t	2b – PNF								<.	1
Grat		NIDE		Non N	00		Dials Datia		Disk Datis	1
Deti	Study or Subgroup	- NRP	Total	Non-N	Total	Moight	N Pandom 05% C		KISK Kallo	4
Pau	DeCoeii 2022	Events	20	Events	1014	A 100	0.70 0.02 19.70	1	IV, Raildoni, 95% Ci	1
Abbre	Gauray 2022	0	69	6	164	5.0%	0.18 0.01 3.18	i —		У
throm	Hessheimer 2022	16	545	15	258	86.8%	0.50 [0.25, 1.01]	1		
Obser	Mohkam 2022	1	68	0	34	4.1%	1.52 [0.06, 36.40	i		
<sup>a</sup> Adju										;
of dea	Total (95% CI)		702		505	100.0%	0.51 [0.27, 0.97]	1	-	t
labora	Total events	17	2-10	22	<b>D</b> = 0.7	01:17 - 01	×	L		
postm	Test for overall effect	7 - 2.05	P = 1.0	5, ui = 5 ( M)	F = 0.7	9), 1 = 0	20	0.01	0.1 1 10 100	
<sup>b</sup> Risk	restion overall ellect	2 - 2.05	(F = 0.0	(4)					Favours NRP Favours Non-NRP	m
Cox n										
<sup>c</sup> Inclu	2c – Recipien	it Dea	th							
<sup>d</sup> Not							Hazard Ratio		Hazard Ratio	
Bold i	Study or Subgroup	log[Ha	zard Ra	atio]	SE \	Neight	IV, Random, 95% Cl		IV, Random, 95% Cl	
	DeGoeij 2022		-1.0	724 1.0	703	2.3%	0.34 [0.04, 2.79]			
	Gaurav 2022		-0.3	933 0.6	581	8.6%	0.67 [0.23, 2.01]			
	Hessheimer 2022		-0.7	061 0.1	754	87.3%	0.49 [0.35, 0.70]			
	Mohkam 2022		-1.3	093 1.2	323	1.8%	0.27 [0.02, 3.02]	-		
Hessheime	Tetel (OEV, CD)					100.0%	0.50 10.25 0.601		•	A. López-Andujar R. A
	Total (95% CI)	0.00.01		7 46 0	-	100.0%	0.50 [0.36, 0.69]		<b>~</b>	
nerrera IVI	Test for overall affect	= 0.00; CI	/P = 0.0	0001	(r <sup>2</sup> = 0.	.00); F=1	0.76	0.01	0.1 1 10 100	J, Jimenez C, Lopez-
Tomé S, Va	restion overall effect	L L = 4.20	(F ¥ U.	0001)					Favours NRP Favours non-NRP	) J, López D, Blanco G

perfusion | FIGURE 2 | Summary of primary outcomes for NRP vs. non-NRP for cDCD. (A) ischemic cholangiopathy, (B) primary non-function, (C) recipient death.

### 3A – IC

	CDCD N	IRP	DBD	)		Risk Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	IV, Random, 95% CI	
DeGoeij 2022	2	20	5	81	67.4%	1.62 [0.34, 7.75]	
Fernandez-delaVarga 2022	0	22	0	51		Not estimable	
Minambres 2019	0	16	0	29		Not estimable	
Rodriguez 2022	0	39	1	78	16.3%	0.66 [0.03, 15.80]	
Rodríguez-Sanjuán 2019	0	11	0	51		Not estimable	
Ruiz 2021	0	100	0	200		Not estimable	
Savier 2020	1	50	0	100	16.3%	5.94 [0.25, 143.27]	
Total (95% CI)		258		590	100.0%	1.73 [0.48, 6.24]	
Total events	3		6				
Heterogeneity: Tau <sup>2</sup> = 0.00; Cl	ni <sup>z</sup> = 0.94	df = 2	(P = 0.63)	); <b> </b> <sup>2</sup> = 0	%		ţ
Test for overall effect: Z = 0.83	(P = 0.40)	))					1

### 3B – PNF

Study or Subgroup	CDCD N	IRP Total	DBD	) Total	Moight	Risk Ratio	
study of Subgroup	Evenus	TUtal	Evenus	Total	weight	iv, Rahuom, 95% Ci	
DeGoeij 2022	0	20	0	81		Not estimable	
Fernandez-delaVarga 2022	1	22	0	51	17.7%	6.78 [0.29, 160.31]	
Minambres 2019	2	16	0	29	19.7%	8.82 [0.45, 173.28]	
Rodriguez 2022	0	39	3	78	20.1%	0.28 [0.01, 5.33]	-
Rodríguez-Sanjuán 2019	1	11	1	51	23.3%	4.64 [0.31, 68.58]	
Ruiz 2021	0	100	2	200	19.1%	0.40 [0.02, 8.21]	
Total (95% CI)		208		490	100.0%	2.00 [0.48, 8.37]	
Total events	4		6				
Heterogeneity: Tau <sup>2</sup> = 0.40; Cł	$hi^2 = 4.70$	df = 4	(P = 0.32)	); I <sup>2</sup> = 1	5%		5
Test for overall effect: Z = 0.95	(P = 0.34	-)					0.0

### 3C – Recipient Death

					Hazard Ratio	
	Study or Subgroup	log[Hazard Ratio]	SE	Weight	IV, Random, 95% Cl	
	DeGoeij 2022	-0.7667	1.0529	9.0%	0.46 [0.06, 3.66]	
	Minambres 2019	1.1374	1.0004	9.9%	3.12 [0.44, 22.16]	
	Ruiz 2021	-0.9092	0.5466	27.9%	0.40 [0.14, 1.18]	
	Viguera 2021	-0.1673	0.3405	53.2%	0.85 [0.43, 1.65]	
t						
Ν	Total (95% CI)			100.0%	0.74 [0.39, 1.41]	
-17	Heterogeneity: Tau <sup>2</sup> =	0.09; Chi <sup>2</sup> = 3.65, df	= 3 (P =	0.30); F=	18%	0.01
ì.	Test for overall effect:	Z = 0.91 (P = 0.36)				Eav
· /						1 614

comes and risk factors FIGURE 3 | Summary of primary outcomes for cDCD with NRP vs DBD. (A) ischemic cholagniopathy, (B) primary non-function, (C) recipient death.

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### Outcomes

Variable	TA-NRP Heart DCD	DBD	SRR Heart DCD	SRR Non-Heart DCD	p Value
Total, N (%)	219 (0.6)	27820 (71.1)	436 (1.1)	10,630 (27.2)	
Donor factor					
Donor age, y, median (IQR)	28.0 (21.5-34.0)	38.0 (28.0-50.0)	30.0 (24.0-35.2)	43.0 (32.0-53.0)	< 0.001
Agonal to clamp, min, median (IQR)	83.0 (69.0–125.0)	NA (NA-NA)	21.0 (18.0-24.0)	23.0 (18.0-30.0)	< 0.001
Donor peak serum creatinine, mg/dL, median (IQR)	1.3 (1.1–1.6)	1.5 (1.1–2.1)	1.3 (1.1–1.6)	1.2 (1.0–1.7)	< 0.001
Donor hypertension, n (%)					< 0.001
No	200 (91.7)	19,933 (72.9)	375 (86.0)	7,105 (67.5)	
Yes, 0–5 y	16 (7.3)	3,549 (13.0)	46 (10.6)	1,547 (14.7)	
Yes, 6–10 y	0 (0.0)	1,267 (4.6)	4 (0.9)	606 (5.8)	
Yes, >10 y	0 (0.0)	1,486 (5.4)	9 (2.1)	685 (6.5)	
Yes, unknown duration	2 (0.9)	1,106 (4.0)	2 (0.5)	582 (5.5)	
Donor diabetes, n (%)					< 0.001
No	217 (99.5)	25,181 (92.0)	428 (98.2)	9,617 (91.3)	
Yes, 0-5 y	0 (0.0)	951 (3.5)	7 (1.6)	424 (4.0)	
Yes, 6–10 y	0 (0.0)	437 (1.6)	0 (0.0)	154 (1.5)	
Yes, >10 y	1 (0.5)	521 (1.9)	1 (0.2)	208 (2.0)	
Yes, unknown duration	0 (0,0)	286 (1.0)	0 (0,0)	136 (1.3)	
Cold ischemic time, h, median (IQR)	18.3 (14.4–23.2)	17.2 (11.8–22.9)	17.8 (12.8–22.2)	20.0 (15.7–24.5)	<0.001
Recipient factor					
Recipient age, y, median (IQR)	44.2 (34.7-56.7)	54.3 (41.7-63.8)	49.1 (37.8-58.8)	57.7 (47.7-65.4)	< 0.001
Dialysis before transplant, n (%)					< 0.001
No	26 (12.9)	4,092 (15.4)	51 (11.9)	1,239 (12.3)	
Yes	175 (87.1)	22,527 (84.6)	379 (88.1)	8,845 (87.7)	
cPRA, median (IQR)	0.0 (0.0-53.5)	0.0 (0.0-41.7)	0.0 (0.0-67.2)	0.0 (0.0-36.9)	0.001
HLA-MM, n (%)					0.001
0	7 (3.2)	1,190 (4.3)	16 (3.7)	517 (4.9)	
1	0 (0.0)	301 (1.1)	6 (1.4)	116 (1.1)	
2	9 (4.1)	1,292 (4.7)	21 (4.8)	507 (4.8)	
3	37 (16.9)	3,904 (14.1)	67 (15.4)	1,487 (14.0)	
4	70 (32.0)	7,533 (27.2)	136 (31.3)	2,996 (28.2)	
5	70 (32.0)	9,092 (32.8)	142 (32.6)	3,501 (33.0)	
6	26 (11.9)	4,427 (16.0)	47 (10.8)	1,499 (14.1)	
Recipient pretransplant dialysis time, y, median (IQR)	4.6 (2.6-7.0)	3.9 (1.9-6.2)	4.3 (2.2-6.4)	4.0 (2.1-6.0)	0.002
Outcomes					
Post-transplant hospital length of stay, d, median (IQR)	4.0 (3.0-5.0)	5.0 (4.0-7.0)	5.0 (4.0-7.0)	5.0 (4.0-7.0)	0.014
Delayed graft function, n (%)					< 0.001
No	171 (85.1)	19,981 (75.0)	249 (57.9)	5,767 (57.3)	
Yes	30 (14.9)	6,663 (25.0)	181 (42.1)	4,301 (42.7)	
Recipient serum creatinine at discharge, mg/dL, median	2.0 (1.3-4.7)	2.9 (1.5–5.7)	5.6 (2.9-8.5)	5.6 (3.2-8.1)	<0.001

cPRA, calculated pand reactive antibody; DBD, donation after brain death; DCD, donation after cardiac death; HLA-MM, human leukocyte antigen mismatch; IQR, interquartile range; NA, not available; SRR, super rapid recovery; TA-NRP, thoracoabdominal normothermic regional perfusion.

Merani S, Urban M, Westphal SG, Dong J, Miles CD, Maskin A, Hoffman A, Langnas AN. Improved Early Post-Transplant Outcomes and Organ Use in Kidney Transplant Using Normothermic Regional Perfusion for Donation after Circulatory Death: National Experience in the US. Journal of the American College of Surgeons 238(1):p 107-118, 2024.



### **Benefits**

- Improves organ utilization through increased viability
- Reduction in DGF and graft failure for kidneys
- Reduction in biliary complications (IC) and graft failure for livers
- Utilization of medically complex organs, e.g., steatotic livers, high Kidney Donor Profile Index kidneys, elderly donors) from DCD donors
- Multi-organ perfusion at significantly less cost (\$5000-9000 vs. \$100000-275000, individually)



FIGURE 2. Utilization rates of livers (A), kidneys (B), and pancreas (C) were compared between DCD with and without TA-NRP. The utilization rate of liver and pancreas in DCD with TA-NRP donors was significantly higher compared with that in DCD without TA-NRP donors and similar to that of DBD (P < 0.001 in both; 70.6% vs 24.4% vs 80.3% and 8.8% vs 0.8% vs 10.2%, respectively). The utilization rate of kidney was also higher in DCD with TA-NRP donors (P=0.06, 78.7% in DBD, 78.2% in DCD without TA-NRP, and 94.1% in DCD with TA-NRP). DBD, donation after brain death; DCD, donation after circulatory death; KT, kidney transplantation; LT, liver transplantation; PT, pancreas transplantation; TA-NRP, thoracoabdominal-normothermic regional perfusion.

Bekki Y, Croome, KP, Myers B; Sasak K, Tomiyama K. Normothermic Regional Perfusion Can Improve Both Utilization and Outcomes in DCD Liver, Kidney, and Pancreas Transplantation. Transplantation Direct 9(3):p e1450, March 2023.





### **The Decapitation Gambit**



Suppose a subject underwent surgical decapitation with care taken to attach both the head and decapitated body portions to life-support systems: a ventilator for the body portion and ECMO machine for the head portion

In which part does the person reside? It would generally be agreed that the person resides in the head-brain portion as the body portion maintained on a ventilator, whose beating heart generates circulation and allows visceral organ functioning, lacks awareness, movement, sensation, breathing, and all other brain functions.



### A (Potential) Guiding Principle for DCD Donors

Protecting these patients from harm while honoring their views about whether and how to donate their organs for the benefit of others should take priority over the indeterminate questions about whether or how they are dead.



# Thank you



## Questions?