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Primary Graft Dysfunction in Donor After Brain Death versus Normothermic Regional Perfusion Heart Transplants

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Purpose: Primary graft dysfunction (PGD) is a leading cause of death within 30 days of heart transplant. Advancements in organ procurement in donors after circulatory death (DCD) including normothermic regional perfusion (NRP) have led to increased utilization in recent years. The purpose of this study was to assess incidence of PGD in a modern cohort of heart transplants who received donors after brain death (DBD) versus DCD allografts procured using NRP. Risk factors for PGD were also assessed.

Methods: This was a retrospective cohort analysis of adult, heart-only transplants at a single center from 1/1/21-6/30/23. Modified ISHLT 2014 Consensus Criteria were used; moderate and severe PGD were defined by need for intra-aortic balloon pump and/or extracorporeal membrane oxygenation post-transplant. Risk factors were assessed in univariate analyses and multivariable logistic regression.

Results: 172 patients met inclusion criteria; 100 DBD, 72 NRP. The DBD arm had higher rates of inotrope dependence and mechanical circulatory support (MCS) pre-transplant, while the NRP arm had longer total ischemic time and MCS duration. Other baseline characteristics were similar. Incidence of PGD was non-significantly higher in the NRP arm (22% vs 13%, p=0.11). In the multivariable model, NRP was associated with significantly higher risk of PGD (OR 2.66, p=0.03). PGD patients had longer ICU stays, post-transplant inotrope duration, and higher rates of renal replacement therapy. Post-transplant mortality and cardiac function were not significantly different (Table 1).

Conclusion: After adjustment for demographics and clinical characteristics, NRP was associated with higher risk of PGD compared to DBD. While index hospitalization resource utilization was increased for PGD patients, midterm outcomes were not different. Further studies are warranted to understand characteristics of NRP that may be associated with increased PGD risk, as well as the clinical significance of PGD post-NRP.

Table 1. Primary and Secondary Outcomes in DBD vs NRP and PGD vs Non-PGD arms

Outcomes: DBD vs NRP	Total (N=172)	DBD (N=100)	NRP (N=72)	P-value
Incidence Primary Graft Dysfunction, n (%)	29 (16.9)	13 (13)	16 (22.2)	0.11
Moderate PGD	23 (13.4)	11 (11)	12 (16.7)	0.28
Severe PGD	6 (3.5)	2 (2)	4 (5.6)	0.21
Secondary Outcomes				
Duration MCS post-transplant, days, median (IQR)				
IABP	2 (2-3)	2 (2-3)	2 (2-3)	0.48
ECMO	1.5 (1-4)	2.5 (1-4)	1.5 (1-3.5)	0.74
Vasoplegia Inotrope Score (VIS)*	16.5 (10.9-24.5)	16.4 (10.6-24.2)	16.8 (11.2-24.7)	0.98
Inotrope Score**	15.6 (10.3-22.5)	15.8 (8.8-22.2)	15.4 (11-22.6)	0.96
Mortality				
30-day	2 (1.2)	1 (1)	1 (1.4)	0.89
1 year	5 (2.9)	2 (2)	3 (4.2)	0.38
3 year	10 (5.8)	5 (5)	5 (6.9)	0.34
LVEF, %, median (IQR)				
30-day	65 (60-71)	65 (60-72)	64 (60-69)	0.41
1-year	62 (57-67)	62 (57-67)	61 (56-67)	0.53
Hospital length of stay, days, median (IQR)	15 (13-22)	15 (12.3-24)	15 (13-20.8)	0.42
ICU length of stay, days, median (IQR)	5 (4-8)	5 (4-8)	5 (4-7)	0.17
Days on inotrope post, median (IQR)	6 (5-8)	6 (5-8)	6 (5-9)	0.63
Days intubated post, median (IQR)	2 (2-3)	2 (2-3)	2 (2-3)	0.89
Days requiring pacing, median (IQR)	3 (1-6)	3 (2-8)	2 (0-5)	0.13
Post-op Renal Failure requiring RRT, n (%)	20 (11.6)	14 (14)	6 (8.3)	0.25
Outcomes: PGD vs Non-PGD	**Total (N=172)**	**PGD (N=29)**	**Non-PGD (N=143)**	**P-value**
Vasoplegia Inotrope Score (VIS)*	16.5 (10.9-24.5)	26.7 (15.4-39.2)	15.4 (9.9-21.6)	0.001
Inotrope Score**	15.6 (10.3-22.5)	21.9 (16.6-36.9)	14.8 (9.1-21.5)	0.001
Mortality				
30-day	2 (1.2)	1 (3.4)	1 (0.7)	0.31
1 year	5 (2.9)	1 (3.4)	4 (2.8)	0.85
3 year	10 (5.8)	1 (3.4)	9 (6.3)	0.55
LVEF, %, median (IQR)				
30-day	65 (60-71)	66 (62-72.5)	64.5 (60-71)	0.25
1-year	62 (57-67)	60 (54-65)	62 (57-67)	0.15
Hospital length of stay, days, median (IQR)	15 (13-22)	20 (12.5-34)	15 (13-21)	0.13
ICU length of stay, days, median (IQR)	5 (4-8)	7 (6-13.5)	5 (4-7)	0.03
Days on inotrope post, median (IQR)	6 (5-8)	8 (6-11)	6 (5-7)	0.02
Days intubated post, median (IQR)	2 (2-3)	4 (3-4.5)	2 (2-2)	0.18
Days requiring pacing, median (IQR)	3 (1-6)	3 (2-5.8)	3 (1-6)	0.49
Post-op Renal Failure requiring RRT, n (%)	20 (11.6)	8 (27.6)	12 (8.4)	0.003

DBD=donor after brain death; NRP=normothermic regional perfusion; PGD=primary graft dysfunction; IABP=intra-aortic balloon pump; ECMO=extracorporeal membrane oxygenation; LVEF=left ventricular ejection fraction; ICU=intensive care unit; RRT=renal replacement therapy; IQR=interquartile range

*Vasoplegia Inotrope Score=Dopamine + Dobutamine + (100*Epinephrine) + (10*Milrinone) + (10000*Vasopressin) + (100*Norepinephrine); highest dose within 24 hours post-transplant in mcg/kg/min (units/kg/min for vasopressin)

**Inotrope score=Dopamine + Dobutamine (Milrinone*15) + (Epinephrine*100) + (Norepinephrine*100); highest dose within 24 hours post-transplant in mcg/kg/min

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Early Graft Dysfunction Requiring VA-ECMO Following Donation After Circulatory Death (DCD) Heart Transplantation Impact on Short- and Long-Term Survival

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Purpose: Clinical DCD heart transplantation (HTx) was established in the UK in 2015 and now accounts for more than 30% of UK HTx. Early graft dysfunction (EGD) post-transplant requiring veno-arterial extra-corporeal membrane oxygenation (VA-ECMO) support is more common in DCD heart recipients. There is paucity of data on the impact of early graft dysfunction requiring (VA-ECMO) on recipient survival in DCD HTx.

Methods: This is a single-centre retrospective study of consecutive DCD HTx performed between February 2015 and July 2024. Multi-organ transplants were excluded. The recipients were divided in two groups according to those with and without EGD post-transplant. Donor and recipient characteristics, duration of ICU and hospital stays were compared using logistic regression. Post-transplant survival was assessed with Kaplan-Meier analysis and compared with log-rank test.

Results: There were DCD HTx of which 27 (21.1%) developed EGD and required VA-ECMO support. Baseline characteristics are summarized in Table1. EGD post-transplant was associated with longer ICU stay (5 vs 18.5 days, p < 0.001) and hospital stay (20 vs 42 days, p < 0.001). Survival free of re-transplantation was significantly worse in the EGD group at 90 days (74.1% vs 99% ys, p < 0.001). However, long-term conditional survival of recipients who survived the first 90 days post-transplant was similar (Figure1).

Conclusion: In this study, DCD heart recipients who developed EGD requiring VA-ECMO after HTx had longer ICU and hospital stays and lower survival. However, EGD recipients who survived the first 90 days post-transplant, their long-term survival was comparable to those without EGD. Further studies are needed to identify modifiable risk factor for the development of EGD following DCD HTx to improve outcomes.

Table 1: Baseline donor and recipient characteristics

	No EGD post-transplant (n=101)	EGD post-transplant (n=27)	P
Donor characteristics			
Thoracoabdominal normothermic regional perfusion, n	21 (20.8)	2 (7.4)	0.158
Age, years	35.7 ± 9.8	34.9 ± 9.8	0.72
Female sex, n	23 (22.8)	2 (7.4)	0.101
BMI, kg/m2	25.3 (22.4 – 28.7)	26.9 (22.9 – 29.8)	0.414
Cause of death, n			0.598
*Hypoxic brain injury	28 (27.7)	11 (40.7)	
*Intracranial bleed	36 (35.6)	8 (29.6)	
*Trauma	34 (33.7)	8 (29.6)	
*Brain tumour	3 (3)	0 (0)	
FWIT, min	24 (21 – 29)	25 (23 – 31)	0.326
Ex-situ perfusion time, min	245.1 ± 62.7	278.7 ± 77.7	**0.023**
Implant time, min	44 (37 – 53)	55 (47 – 62)	**<0.001**
CPB time, min	151 (125 – 201)	263 (188 – 315)	**<0.001**
Recipient characteristics			
Age, years	53.7 (45 - 61.2)	54.1 (48.2 - 59.4)	0.733
Female sex, n	23 (22.8)	7 (25.9)	0.731
BMI, kg/m2	26 ± 4.3	26.3 ± 4.8	0.705
Recipient primary disease (%) *Ischaemic CM *Dilated CM *Hypertrophic CM *Other	20 (19.8) 54 (53.5) 16 (15.8) 11 (10.9)	8 (29.6) 11 (40.7) 7 (25.9) 1 (3.7)	0.269
Diabetes, n	17 (16.8)	4 (14.8)	1
Previous sternotomy, n	40 (39.6)	15 (55.6)	0.137
RA pressure, mmHg	9 (6 - 14)	8 (6 - 13)	0.616
PVR, Wood units	2 (1.39 - 2.82)	2.28 (1.71 - 2.84)	0.336
TPG, mmHg	7.8 ± 3.1	8 ± 3.3	0.741
Inotropes, n	37 (36.6)	8 (29.6)	0.498
Temporary MCS, n	9 (8.9)	5 (18.5)	0.155
Durable LVAD, n	19 (18.8)	6 (22.2)	0.691
Gender mismatch, n	26 (25.7)	7 (25.9)	0.318
Weight mismatch, %	0 (-10.3 - 22.4)	3.3 (-9.1 - 29.9)	0.557
Predicted heart mass mismatch, %	2.3 (-5.3 - 16.8)	9.8 (-3.4 - 24.8)	0.13

Figure 1: long-term survival free of re-transplantation in EGD vs no EGD groups (top) and long-term survival conditional to surviving first 90 days post-transplant (bottom)