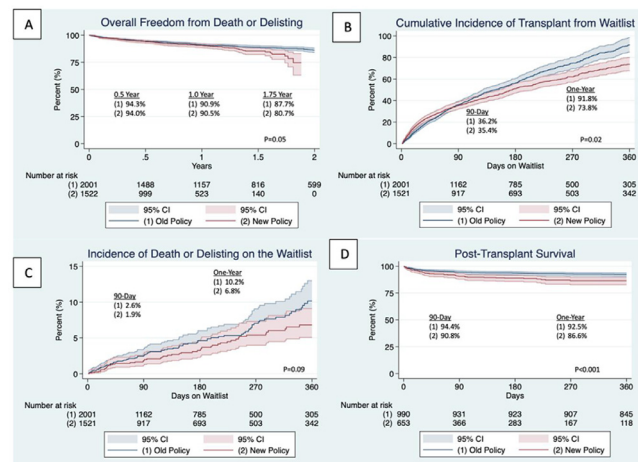


Figure: Comparison of outcomes between allocation policy eras in patients waitlisted with an isolated durable LVAD. A) Overall freedom from death or delisting due to worsening clinical status. B) Cumulative incidence of transplantation from waitlist. C) Cumulative incidence of death or delisting due to worsening clinical status while on the waitlist. D) Post-transplant survival.



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#### Impact of Donation After Circulatory Death Heart Transplantation on Waitlist Outcomes and Transplantation Activity

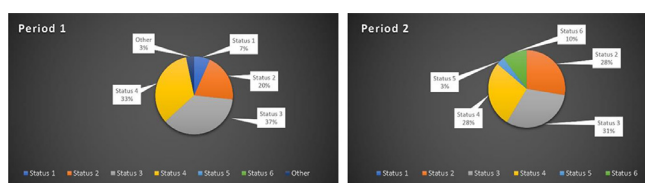
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**Purpose:** To assess the impact of increased availability of donor hearts from donors after circulatory death on waiting list and heart transplantation activity.

**Methods:** We compared changes in waitlist activity and transplant volumes in patients before and after we adopted DCD heart transplantation into our program. Outcomes of patients who were on the waiting list between January and August 2020 (Period 1) were compared to those listed between January and August 2021 (Period 2).

**Results:** Waitlist volumes were 10.6 patients listed per month in Period 1 (N = 85) and 7.5 patients in Period 2 (N = 60). The median waitlist time to transplant decreased from 339 days in Period 1 to 77 days in Period 2 (P = .035). The transplant rate increased from 92 per 100 patient-years in Period 1 to 186 per 100 patient-years in Period 2 (P = .004). No status 5 and 6 recipients were transplanted in Period 1 as opposed to 13% in Period 2 (Figure 1). Waitlist mortality rate, hospital stay post-transplantation, and post-transplant mortality did not differ significantly between the time periods.

**Conclusion:** This single-center retrospective analysis suggests that the use of DCD donor hearts may result in a reduced HTx waitlist time and an increased transplant rate. DCD increases organ availability to recipients in lowers status categories. In addition, transplanting DCD donor hearts can provide comparable short-term post-transplant outcomes to DBD. Figure 1. Transplant activity stratified by recipient status.



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#### Heart Transplant Outcomes with Donation After Cardiac Death: UNOS Registry Analysis

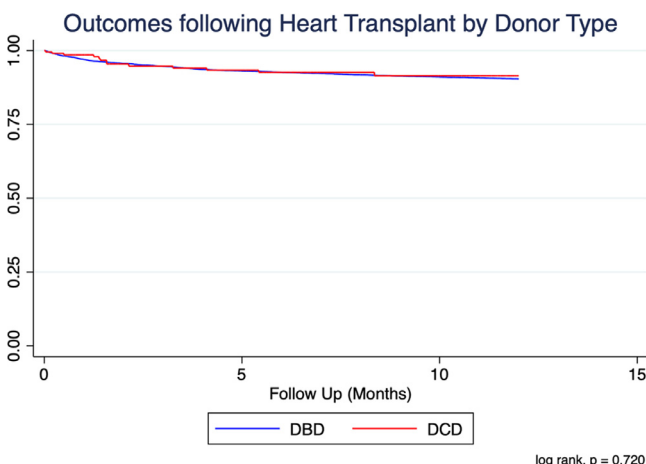
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**Purpose:** Limitations in organ donation have led to approaches to expand the existing donor pool. Donation after cardiac death (DCD) has continued to increase after efforts led by the United Kingdom and Australia. We sought to describe the United States experience.

**Methods:** 5153 heart transplant (HT) recipients were identified in the UNOS Registry between 1/2019 and 6/2021, of which 229 were DCD recipients. HT recipients were grouped by DCD status or donation after brain death (DBD). Comparisons between groups were assessed using standard statistical methods, survival analysis was censored at 12-months via the Kaplan-Meier method. Multivariate Cox proportional hazard regression analysis (adjusted for age, sex, diabetes, race, ischemic time, dialysis, life support, waiting time & HLA mismatch) were performed.

**Results:** Recipients of DCD donors were of lower UNOS status (p<0.001), increased VAD use (p=0.01), and less dialysis (p=0.011). Additionally, DCD donor recipients had longer wait times (46.0 vs 30.0d, p=0.007), longer ischemic times (p<0.001) but younger donors (29.8 vs 23.4y, p<0.001). There was no difference in 1-month or 1-year survival by donor type (p=0.720). Unadjusted analysis demonstrated HR 0.91 (0.52-1.57) and following adjustment HR 0.88 (0.48-1.61).

**Conclusion:** Short-term survival of DCD donors is similar to DBD donors in this UNOS Registry analysis. DCD donor use has potential to expand the donor pool. Further study is warranted to assess longer term outcomes as well as best strategies for donation.



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#### Results of Heart Transplants from Donation After Circulatory Death (DCD) Donors Using Thoraco-Abdominal Normothermic Regional Perfusion (TA-NRP) Compared to Donation After Brain Death (DBD)

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**Purpose:** In the U.S., heart transplantation from donation after circulatory death (DCD) is increasing. We present our institutional experience of DCD transplantation by using a thoracoabdominal-normothermic regional perfusion (TA-NRP) protocol and compare the results to a cohort concomitantly transplanted, from standard brain death (DBD) donation.

**Methods:** For TA-NRP protocol, suitable local DCD donors were transferred to our institution and co-located with the recipient in proximate operating rooms. Standard DCD procurement involved resuscitation of the donor on cardiopulmonary bypass after declaration of death and assessment for suitability by echocardiogram and hemodynamic data. Heart transplant from DBD was performed per standard protocol. Immunosuppression and management followed the same standardized protocol for all recipients.

**Results:** Between January 2020 and October 2021, we performed 10 DCD transplantations with TA-NRP protocol (7 isolated heart, 2 heart-lung and 1 heart-kidney). The median age was 54 years (44-72), and 70% were male. One heart-lung transplant recipient required VA ECMO post-op, for 3 days. During the same period, 70 patients received heart transplant from a DBD donor (71.4% isolated heart, 7.1% heart-lung, 21.4% heart-kidney). The median age was 56 years (24-77) -  $p=0.916$ , 84% were male  $p=0.27$ . At mean follow-up of 397.6 days (DCD recipients) and 305.9 days (DBD recipients), there were no significant differences in acute cellular, antibody mediated rejection, cardiac allograft vasculopathy, heart graft function, and survival. Compared to DBD recipients, DCD recipients received transplant at lower listed statuses.

**Conclusion:** Short-term results suggest that transplant outcomes from DCD TA-NRP are comparable to recipients from DBD. Expanding heart transplantation by using DCD is a viable option for lower-status listed patients and wide adoption should be considered.

| UNOS Listing Status | # of DCD recipients | # of DBD recipients |
|---------------------|---------------------|---------------------|
| 6                   | 1                   | -                   |
| 5                   | 2                   | 2                   |
| 4                   | 6                   | 5                   |
| 3                   | 1                   | 10                  |
| 2                   | -                   | 49                  |
| 1                   | -                   | 4                   |

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#### Outcomes of Mechanical Circulatory Support for Severe Primary Graft Dysfunction After DBD versus DCD Heart Transplantation

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**Purpose:** Severe primary graft dysfunction (PGD) is defined by need for mechanical circulatory support (MCS) after heart transplantation. Severe PGD is associated with increased short-term mortality but reported outcomes vary widely. The mechanism of PGD may differ for hearts donated after brainstem-determined death (DBD) and circulatory-determined death (DCD). The purpose of this study was to determine whether there are differences in PGD outcomes between DBD and DCD heart transplants.

**Methods:** We undertook a retrospective, observational study of all heart transplants performed at our institution since the onset of the DCD heart transplant programme (May 2015 to June 2021). Baseline donor and recipient characteristics were recorded. Outcome measures included duration of MCS, length of intensive care (ICU) stay, total length of hospital stay (LOS) and 90-day mortality.

**Results:** 280 heart transplants were performed during the study period, including 192 DBD and 88 DCD heart transplants. The overall incidence of severe PGD was 11.8% (n=33). These patients were initially supported with VA ECMO (n=28, 84.9%) or CentriMag RVAD (n=5, 15.1%), of which 6 patients (18.2%) were later converted from ECMO to CentriMag RVAD/BiVAD. The incidence of PGD was similar for DBD (n=21, 10.9%) and DCD (n=12, 13.6%) heart transplants ( $p=0.541$ ). There were no significant differences in baseline characteristics between DBD and DCD groups. There were no significant differences in outcomes between DBD and DCD groups, including median duration (in days) of MCS (5 vs 6,  $p=0.679$ ), ICU stay (22 vs 20.5,  $p=0.881$ ) or total LOS (46 vs 48.5,  $p=0.454$ ). 90-day mortality was 57.1% in the DBD group and 33.3% in the DCD group ( $p=0.188$ ).

**Conclusion:** In one of the world's largest cohorts of DCD heart transplantation, we have not seen a significant difference in PGD incidence or outcomes between DBD and DCD heart transplant patients. The potential lower 90-day mortality in the DCD group may suggest that the natural history of PGD after DCD heart transplantation is more favourable compared with PGD seen after DBD heart transplantation.

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#### Preliminary Development of the Lung Transplant Frailty Index

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**Purpose:** Existing measures of frailty developed in community dwelling older adults may misclassify frailty in lung transplant candidates. We aimed to develop a novel frailty index for lung transplantation with improved performance characteristics compared to existing measures.

**Methods:** In a three-center cohort study of lung transplant candidates, we measured the Short Physical Performance Battery (SPPB) and Fried Frailty Phenotype (FFP) measures; body composition by bioelectrical impedance; and serum biomarkers associated with frailty (hemoglobin, albumin, and C-reactive protein). We evaluated individual variable domains to identify those associated with the criterion of candidate delisting for becoming too ill or death. Next, we built composite multidimensional models by testing

Table. Comparing candidate Lung Transplant Frailty Index measures to the Short Physical Performance Battery and Fried Frailty Phenotype

|                            | SPPB*                | FFP*                 | LT-FI 1              | LT-FI 2              |
|----------------------------|----------------------|----------------------|----------------------|----------------------|
| OR for death/delisting     | 1.61<br>(0.87, 2.99) | 1.78<br>(0.95, 3.32) | 2.72<br>(1.57, 4.73) | 2.83<br>(1.45, 5.54) |
| AUC for death/delisting    | 0.54<br>(0.48, 0.60) | 0.56<br>(0.49, 0.64) | 0.62<br>(0.56, 0.69) | 0.63<br>(0.55, 0.71) |
| Sensitivity                | 0.82                 | 0.72                 | 0.59                 | 0.60                 |
| Specificity                | 0.27                 | 0.41                 | 0.65                 | 0.65                 |
| % died/delisted, not frail | 10.2                 | 8.2                  | 7.2                  | 7.0                  |
| % died/delisted, frail     | 15.5                 | 13.8                 | 17.5                 | 17.4                 |
| Model Components           |                      |                      |                      |                      |
| Low activity               |                      | x                    |                      |                      |
| Weight loss                |                      | x                    |                      |                      |
| Fatigue                    |                      | x                    |                      |                      |
| Chair stands               | x                    |                      |                      |                      |
| Gait speed                 | x                    | x                    | x                    | x                    |
| Balance                    | x                    |                      | x                    | x                    |
| Grip strength              |                      | x                    | x                    | x                    |
| % body fat**               |                      |                      | x                    | x                    |
| Skeletal muscle mass**     |                      |                      | x                    | x                    |
| Albumin                    |                      |                      | x                    | x                    |
| C-reactive protein         |                      |                      |                      | x                    |

\*SPPB frailty defined as score of  $\leq 9$ ; \*FFP frailty defined as score of  $\geq 3$ . For LT-FI models, cutpoints for model components calculated by Youden, Balance, and Distance to Perfect methods; when methods yielded different results, cut-point preferentially selected based on specificity. \*\*% body fat and skeletal muscle mass quantified by bioelectrical impedance. Hemoglobin and albumin measured by clinical laboratory. C-reactive protein measured by MSD as part of a research multiplex. OR = Odds Ratio; AUC = Area Under the Curve; SPPB = Short Physical Performance Battery; FFP = Fried Frailty Phenotype; LT-FI = Lung Transplant Frailty Index