Spanish Center's Early Experience With Donation Following Circulatory Death in Heart Transplantation

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Heart transplantation using donation after circulatory death (DCD) has recently re-emerged alongside donation after brain death (DBD). This technique can potentially increase the number of available cardiac grafts. However, its clinical outcomes remain limited. We compared data from patients who received grafts from DCD *versus* DBD between 2012 and 2023. During this period, 131 adult patients underwent isolated heart transplantation. Of these, 25 (19%) were DCD donors. Donation after circulatory death donors were predominantly local (66% *vs.* 42%; $p = 0.027$). Donation after circulatory death graft recipients had fewer ventricular assist devices (12% *vs.* 35%; $p = 0.025$) and were less frequently urgent (12% *vs.* 39%; $p = 0.009$). Donation after circulatory death grafts had shorter myocardial ischemia and extracorporeal circulation times than DBD grafts (70 min [63.5–91] *vs.* 168 [83–219]; $p < 0.001$); (90 min [78–103] *vs.* 120 [96–148], $p < 0.001$). We observed no significant differences in the incidence of primary graft failure (16% *vs.* 22%; $p = 0.526$) or hospital mortality (8% *vs.* 14%; $p = 0.410$) between both groups. In conclusion, cardiac DCD demonstrates hospital outcomes comparable to those of cardiac DBD. Further long-term follow-up of these patients is necessary to determine their rejection, graft vascular disease, and mortality outcomes. *ASAIO Journal* 2026; 72:42–48

Key Words: heart transplantation, donation after circulatory death, normothermic regional perfusion

The population affected by heart failure (HF) is increasing worldwide.[1] Heart transplantation remains the preferred treatment for patients with advanced HF, specifically those classified as New York Heart Association (NYHA) functional class III or IV, who have few other health issues and are resistant to current medical treatments. However, the limited availability of heart grafts restricts the number of patients who can benefit from transplantation.

To address this shortage, transplant teams may consider accepting hearts from brain-dead donors (*i.e.,* donation after brain death, DBD) who are older, have longer cold ischemia times, or are receiving higher doses of inotropic or vasoconstrictive medications. Additionally, other strategies to increase the supply of heart grafts include transplanting hearts from donors with hepatitis C or accepting hearts from donation after circulatory death (DCD).[2–10]

This study aims to analyze the clinical outcomes of heart transplantation with DCD with thoracoabdominal normothermic regional perfusion in our hospital since the beginning of our experience.

Materials and Methods

This retrospective observational study analyzes patients ≥18 years of age who received an orthotopic heart transplant at our center between January 2012 and December 2023. Data from patients who received a heart graft from DBD were compared with data from patients who received a heart graft from DCD.

Donation after circulatory death was performed by thoracoabdominal normothermic regional perfusion (TA-NRP), according to the protocol described by the University of Liège[11] and the national protocol for controlled DCD.[12]

According to this, the donor is intubated, sedated, and mechanically ventilated before being transferred to the operating

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room. The chest and abdomen are disinfected, and 25,000 IU of sodium heparin is administered. Extracorporeal membrane oxygenator (ECMO) veno-arterial (V-A) cannulas are inserted under transesophageal echocardiography (TEE) control, and life support measures are then withdrawn. Circulatory arrest is confirmed by the absence of a pulse wave in the femoral artery. A 5-minute observation period is held before declaring the donor dead. A median sternotomy is performed, and the supra-aortic arterial trunks are clamped to exclude cerebral circulation. Thoracoabdominal normothermic regional perfusion begins using femoral-femoral V-A ECMO. After 20–30 minutes, ECMO is weaned, and the heart is assessed *via* TEE. For transplant acceptance, the heart must have a left ventricle ejection fraction (LVEF) >50%, normal right ventricular size and function, cardiac index >2.5 L/min/m², mean arterial pressure >60 mm Hg, and be arrhythmia-free for 30 minutes. It should be arrested with cardioplegia (Celsior or del Nido) and cooled for transport.

Myocardial functional warm ischemic time was defined as the time from systolic blood pressure <60 mm Hg to the start of TA-NRP (including 5 min no-touch period).[12]

Data were collected from the donor (age, sex, anthropometric variables, cause of death, need for vasoconstrictors, intensive care unit [ICU] days, donor–recipient sex mismatch, Rh factor, blood group, heart-lung donation, local donation, functional warm myocardial ischemia time in DCD cases) and the recipient (age, sex, anthropometric variables, LVEF, need for inotropes, kidney and liver function, pulmonary vascular resistance [PVR], systolic pulmonary artery pressure [SPAP], NYHA classification, main comorbidities, pretransplant mechanical ventilation, circulatory assistance, previous cardiac surgery, amiodarone treatment, hospitalization status, presence of tumors). Additionally, operative and postoperative variables included urgent transplant status, functional warm myocardial ischemia time, cold myocardial ischemia time, cardiopulmonary bypass (CPB) time, orotracheal intubation time, ICU and hospital stay duration, primary graft failure (PGF) that was defined according to the 2014 International Society of Heart and Lung Transplantation (ISHLT) consensus criteria[13] (all cases involved the left ventricle or both ventricles and were classified at least as moderate or severe severity). Acute hospital rejection was defined as either a clinically suspected rejection episode or a biopsy-confirmed acute rejection (ISHLT > grade 1R) resulting in the administration of intravenous steroids for resolution and, according to the ISHLT criteria,[14] postoperative pacemaker, dialysis, in-hospital death, and type of cardioplegia used. The highest value of high-sensitivity troponin T (hs-TnT) was recorded after transplantation, and the vasoactive inotropic score (VIS) was calculated for the entire population after surgery.

The primary objective of the study was to compare hospital outcomes, mortality, and PGF of heart transplantation from DCD with thoracoabdominal normothermic regional perfusion *versus* those of heart transplantation from DBD. Secondary objectives were the incidence of rejection in the hospital and the first year, the duration of mechanical ventilation, ICU and hospital stays, and survival at 1 year in both groups.

Table 1. Causes of Hospital Death (N = 17)

Primary graft failure	5 (29%)
Infection-sepsis	2 (12%)
Cardiac tamponade	2 (12%)
Mediastinitis	2 (12%)
Stroke	2 (12%)
Acute rejection	1 (6%)
Pulmonary embolism	1 (6%)
Mesenteric ischemia	1 (6%)
Bleeding	1 (6%)

Continuous variables are expressed as mean ± standard deviation (SD) or median and interquartile range (IQR) and analyzed using the Student's t-test or the Mann-Whitney *U* test, as appropriate, and after assessing normality by the Kolmogorov-Smirnov test. Categorical variables are shown as frequencies and percentages, analyzed with the χ^2 test or Fisher's exact test. Post-transplant survival was evaluated using the Kaplan-Meier curve and log-rank test for group comparisons.

We also perform a propensity score matching (PSM) analysis using a 1:1 cardinality matching method without replacement and a caliper of 0.25 SD of the logarithm of the calculated propensity score (PS). Key variables for predicting outcomes were selected based on literature, focusing on preoperative mechanical assistance and ischemic time. The final model included factors such as mechanical circulatory support, total ischemic time, inotropic requirements, NYHA class, sex, age, donor vasoactive needs, and transplant urgency. Model fit was assessed using the standardized mean difference (SMD), where an SMD <0.2 indicated an adequate fit.

Statistical analysis was performed in R 4.2.3 for macOS, using the MatchIt package for cardinality matching, with optimization by HiGHS software.

The study was approved by the medical research ethics committee (Internal code 2024-9-18-HCUVA).

Results

Between January 2012 and December 2023, 131 orthotopic heart transplants were performed in our hospital (median age: 56 years [IQR: 48–62], 76% male). In seven cases (5.3%), there was a sex mismatch between donor and recipient. The median peak level of hs-TnT after transplantation was 1,865 (1,065–2,935) pg/ml, while the median VIS was 24 (13.5–42.5). After transplantation, 27 patients (21%) presented moderate or severe PGF, of which 23 patients (85% of PGF) suffered severe PGF affecting both ventricles and required mechanical support, all of them with venoarterial ECMO and 4 patients (15% of PGF) suffered moderate PGF with only left ventricular involvement. Seventeen patients (13%) died during hospitalization. The main cause of in-hospital death was PGF, with almost 30% of deaths, followed by infections-sepsis (12%), cardiac tamponade (12%), mediastinitis (12%), and stroke (12%) (Table 1). Of the 131 transplants, 25 (19%) were transplanted with DCD. Donors who have experienced circulatory death's number of heart transplants has grown steadily since its introduction in our program in June 2020, going from around 20% of donations in the first years to almost 80% of transplants in 2023 (Figures 1 and 2). In the last 5 years (2019–2023), there were 71 heart transplants, 25 (35%) of which were DCD. Seven patients (9.8%) died in the hospital.

In the DCD group, the average myocardial functional warm ischemia time was 14 ± 4.4 minutes, ranging from 5 to 23 minutes, and the reperfusion time was 31.5 ± 23 minutes, ranging between 8 and 55 minutes.

Donation after circulatory death donors when compared with DBD donors were more frequently local donors (67%

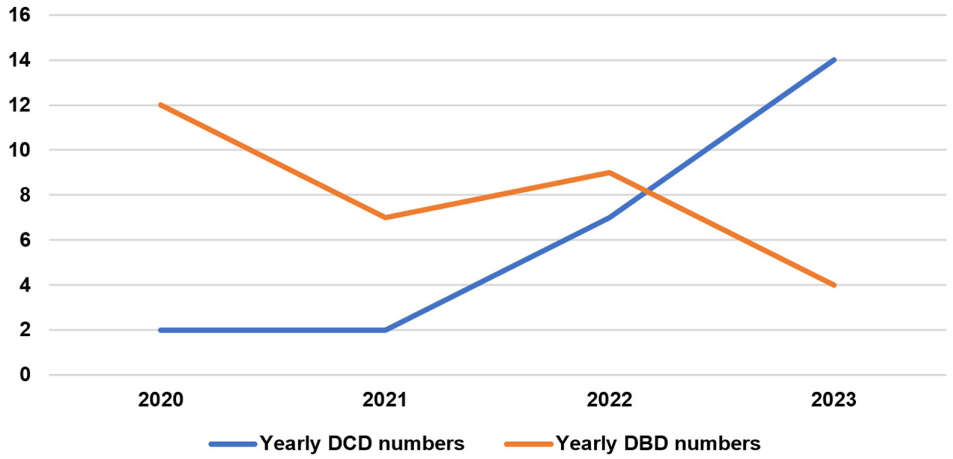

Figure 1. Number of cardiac transplants since 2020 from DCD and DBD. DBD, donation after brain death; DCD, donation after circulatory death.

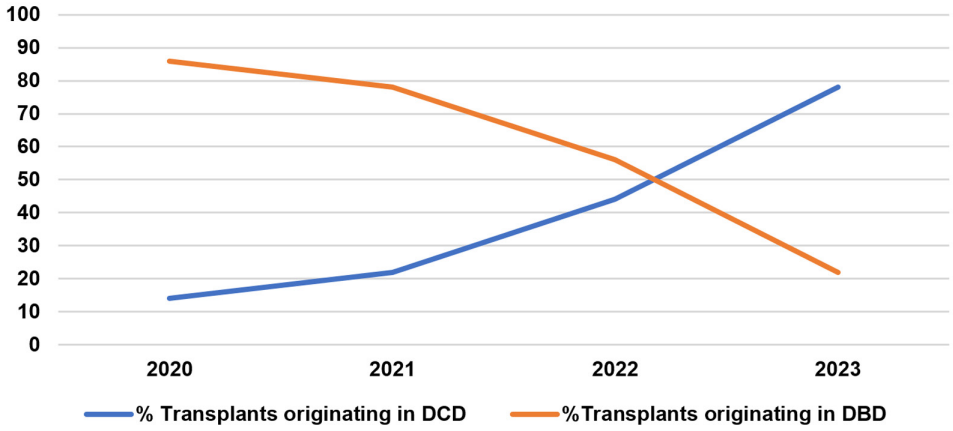

Figure 2. Changes in the percentage of heart transplants since 2020 from DCD and DBD. DBD, donation after brain death; DCD, donation after circulatory death.

vs. 40%; $p = 0.027$), less frequently required vasoconstrictors to maintain hemodynamic status (25% *vs*. 89%; $p < 0.001$), spent longer in intensive care before donation (8 [1–24] *vs*. 2 [1–5.75]; $p = 0.022$), died less from cerebrovascular causes and more from other causes ($p < 0.001$) (Table 2). During this period, two more hearts were considered DCD but were not accepted for transplantation. One heart was rejected due to aortic dissection during arterial cannulation, and the other was not accepted due to irreversible right ventricular failure caused by the donor's acute respiratory distress syndrome.

Heart transplant recipients with DCD had better NYHA functional class before transplantation than DBD (3 [3–4] *vs*. 4 [3–4]; $p < 0.001$), presented at transplantation with fewer ventricular assist devices (12% *vs*. 35%; $p = 0.025$) and were less frequently urgent transplants (12% *vs*. 40%; $p = 0.009$) than heart transplant recipients with DBD. Of note, all three urgent transplants in the DCD group are alive, though one had a prolonged postoperative hospital stay (Table 3).

Cardiac transplants from DCD had significantly shorter cold myocardial ischemia (70 [63.5–91] *vs*. 168 [83–219]; $p < 0.001$) and CPB (90 [78–103.5] *vs*. 120 [96–148]; $p < 0.001$) times than cardiac transplants from DBD. Cardiac transplants from DCD showed a higher incidence of postoperative renal failure requiring dialysis (12% *vs*. 2%; $p = 0.033$) than transplants performed from DBD. In DCD grafts, del Nido cardioplegia (DNC) was used primarily for myocardial protection (80% *vs*. 13%; $p < 0.001$). There were no differences in the incidence of postoperative ECMO support (0.417), postoperative pacemakers ($p = 0.279$), postoperative VISs ($p = 0.069$), ICU stay ($p = 0.691$), hospital stay ($p = 0.285$), mechanical ventilation time ($p = 0.530$), PGF ($p = 0.526$), acute hospital rejection ($p = 0.933$), or in-hospital mortality ($p = 0.410$) between both groups (Table 4).

At 1 year, there were no significant differences in the incidence of acute rejection between the two groups, with rates of 28% and 32%, respectively ($p = 0.693$). Throughout the follow-up period, mortality rates also showed no differences, with 4.3% in one group compared to 14% in the other ($p = 0.195$) (Table 4)

At 24 months, survival rates were similar between the two populations, as indicated by a log-rank test ($p = 0.968$) (Figure 3).

Propensity Score Analysis

After PSM, 22 matched pairs remained in the study (22 DBD and 22 DCD, *i.e.,* 1:1 distribution). When we analyzed

Table 2. Comparison of Characteristics of Cardiac Donors

Variable	DBD (106)	DCD (25)	*p*
Female donor	19 (18%)	2 (8%)	0.224
Local donation	42 (40%)	16 (67%)	0.027
Donor Rh +	91 (89%)	22 (88%)	0.862
Need for vasoconstrictors	95 (89%)	7 (25%)	<0.001
Donor weight (kg)	84.4 ± 14	80.1 ± 12.5	0.178
Donor age (years)	47 (39–54)	43 (36.5–52.5)	0.652
Donor height(cm)	175 (170–180)	175 (171.5–180)	0.991
Donor BMI (kg/m^2)	27.4 (25.2–29.2)	26.3 (23.6–28.4)	0.269
Donor ICU time (days)	2 (1–5.75)	8 (1–24)	0.022
Heart-lung donation	27 (25%)	5 (20%)	0.567
Donor–recipient sex mismatch	7 (6.6%)	0 (0%)	0.187
Cause of donor death			<0.001
Trauma	40 (38%)	9 (36%)	
Cerebrovascular	60 (57%)	6 (24%)	
Tumoral	2 (2%)	4 (16%)	
Infectious	2 (2%)	0 (0%)	
Others	2 (2%)	6 (24%)	
Donor blood group			0.261
A	45 (42%)	10 (40%)	
B	11 (10%)	0 (0%)	
AB	2 (2%)	0 (0%)	
0	48 (45%)	15 (60%)	

BMI, body mass index; DBD, donation after brain death; DCD, donation after circulatory death; ICU, intensive care unit.

Table 3. Comparison of Characteristics of Cardiac Recipients

Variable	DBD (106)	DCD (25)	*p*
Recipient age	56 (47.75–63)	55 (47.5–61)	0.758
Female recipient	24 (23%)	8 (32%)	0.327
IV inotropics	43 (41%)	9 (36%)	0.675
Renal failure	31 (29%)	5 (20%)	0.352
Bilirrubin >2 mg/dl	14 (13%)	4 (16%)	0.729
Baseline bilirrubin	0.860 (0.6–1.5)	0.8 (0.65–1.1)	0.882
Baseline creatinine	1.2 (0.91–1.47)	1.1 (0.87–1.4)	0.618
SGOT	25 (20–36)	24 (20–30.5)	0.599
SGPT	24 (16.5–32)	21 (16.5–28.5)	0.337
LVEF (%)	24.5 (18–30)	21 (15–29)	0.566
PVR (U Wood)	1.75 (1.25–2.4)	1.55 (0.74–2.2)	0.148
SPAP (mm Hg)	40.5 ± 11.8	40.3 ± 13.5	0.956
MPAP (mm Hg)	27 ± 8.2	28 ± 9.5	0.524
Recipient NYHA	4 (3–4)	3 (3–4)	<0.001
Recipient weight (kg)	77.6 ± 13.7	74.8 ± 16.2	0.386
Recipient BMI (kg/m^2)	27 ± 4	26 ± 4.6	0.301
Recipient height (cm)	168 (162–175)	170 (163–175)	0.963
Diabetes mellitus	36 (34%)	5 (21%)	0.211
COPD	3 (3%)	1 (4%)	0.760
High blood pressure	40 (38%)	9 (36%)	0.872
Smoking	5 (5%)	4 (16%)	0.141
Hyperuricemia	76 (74%)	13 (54%)	0.059
Hypercholesterolemia	45 (42%)	6 (24%)	0.089
Hypertriglyceridemia	30 (28%)	4 (16%)	0.207
Peripheral vascular disease	12 (11%)	3 (12%)	0.924
Pre-transplant mechanical ventilation	11 (10%)	0 (0%)	0.092
Pre-transplant circulatory assistance	37 (35%)	3 (12%)	0.025
Previous cardiac surgery	23 (22%)	5 (20%)	0.835
Recipient amiodarone treatment	21 (22%)	5 (20%)	0.820
Non-hospitalized recipient	61 (58%)	19 (76%)	0.335
Tumor previous to transplant	5 (5%)	1 (4%)	0.877

BMI, body mass index; COPD, chronic obstructive pulmonary disease; DBD, donation after brain death; DCD, donation after circulatory death; IV, intravenous; LVEF, left ventricle ejection fraction; MPAP, Presión Arteria Pulmonar Media; NYHA, New York Heart Association; PVR, pulmonary vascular resistance; SGOT, glutamic oxaloacetic transaminase; SGPT, glutamate pyruvate transaminase; SPAP, systolic pulmonary artery pressure.

the characteristics of donors from both groups and compared them with the characteristics of donors in the complete study series, we found that the difference in local donations between the two groups was not significant: DBD donors were 15 (68%) compared with DCD donors at 16 (72%), with a p value of 0.65. Additionally, the cause of death of the donors was also not statistically significant ($p = 0.120$), when compared with the complete study series. However, the length of stay in the ICU remained higher in the DBD donors (DBD donors averaging 3.6 days ± 3.4 *vs.* DCD

Table 4. Comparison of Operative and Postoperative Variables of Cardiac Transplants

Variable	DBD (106)	DCD (25)	*p*
Urgent transplant	42 (40%)	3 (12%)	0.009
Cold myocardial ischemic time (min)	168 (83–219)	70 (63.5–91)	<0.001
CPB time (min)	120 (96–148)	90 (78–103.5)	<0.001
Orotracheal intubation time (hours)	4 (4–12)	4 (4–7.5)	0.530
ICU time (days)	8 (6–12)	7 (6–13)	0.691
Postoperative hs-TnT peak (pg/ml)	1899 (1090–3154)	1662 (1014–2655)	0.265
Postoperative VIS	24 (8.5–45)	22 (16–37)	0.964
Hospital time (days)	19 (16–26)	23 (16–29)	0.285
PGF	23 (22%)	4 (16%)	0.526
Postoperative ECMO support	20 (19%)	3 (12%)	0.417
Noradrenaline need after transplant (hours)	40 (18–20)	40 (9–70)	0.060
Postoperative pacemaker	5 (7.4%)	0 (0%)	0.279
Postoperative dialysis	2 (2%)	3 (12%)	0.033
In-hospital death	15 (14%)	2 (8%)	0.410
Follow-up death	13 (14%)	1 (4.3%)	0.195
Del Nido cardioplegia	14 (13%)	20 (80%)	<0.001
Hospital acute rejection	22 (21%)	5 (20%)	0.933
First-year acute rejection	34 (32%)	7 (28%)	0.693

DBD, donation after brain death; DCD, donation after circulatory death; CPB, cardiopulmonary bypass; ECMO, extracorporeal membrane oxygenator; hs-TnT, high-sensitivity troponin T; ICU, intensive care unit; PGF, primary graft failure; VIS, vasoactive inotropic score.

donors averaging 12.8 days ± 2.7, $p = 0.007$) (Table PSM1, Supplemental Digital Content, https://links.lww.com/ASAIO/B511).

When analyzing the characteristics of cardiac recipients in both the DBD and DCD groups using this PSM, we observed that the NYHA functional level of recipients before transplantation no longer shows statistical significance. Specifically, the functional levels were similar in both groups (DBD: 4 [3–4] *vs.* DCD: 4 [3–4], $p = 1.000$). Additionally, the requirement for pretransplant circulatory assistance also lost statistical significance in the PSM analysis (DBD: 3 [14%] *vs.* DCD: 5 [23%], $p = 0.370$) (Table PSM2, Supplemental Digital Content, https://links.lww.com/ASAIO/B512).

Finally, when we analyzed the operative and postoperative variables of the heart transplants in both groups (DBD and DCD) in the PSM, we found that the incidence of urgent transplantation in both groups has no statistical significance (DBD 4 [18%] *vs.* DCD 3 [14%]; $p = 0.68$), as well as the cold myocardial ischemia time (DBD 107.5 ± 56 min *vs.* DCD 100.1 ± 60 min; $p = 0.430$), nor the need for postoperative dialysis between both groups in the PSM (DBD 1 [14.5%] *vs.* DCD 2 [9%]; $p = 0.500$). However, the CPB time between both groups in the PSM does maintain statistical significance (DBD 112.5 ± 35 min *vs.* DCD 94 ± 18 min; $p = 0.035$) (Table PSM3, Supplemental Digital Content, https://links.lww.com/ASAIO/B513).

Discussion

Our results indicate that there are no significant differences in PGF or in-hospital mortality between transplant patients who received their grafts from DCD and those who received grafts from DBD. Therefore, we can affirm that DCD is a safe and effective method of organ donation. Although other studies[7,8,15] have reported a higher incidence of moderate to severe PGF in patients receiving grafts from cardiac DCD, this increased incidence did not impact survival rates in those studies.

We also did not find any significant differences in secondary events between the two groups regarding the duration of mechanical ventilation, ICU stay, or hospital stay.

Previous American studies based on the United Network for Organ Sharing (UNOS) database[10,16] indicate a higher incidence of acute rejection requiring treatment before hospital discharge in patients who received grafts from DCD compared to those from DBD. However, our results do not support this finding, as we did not observe a higher incidence of rejection during the hospital stay or in the first year following transplantation.

We found a higher incidence of postoperative dialysis among patients who received transplants from DCD grafts. While this finding should be approached with caution due to the small sample size and the fact that this result is not confirmed in our PSM analysis, it aligns with observations made by other researchers.[9] This increased incidence of post-transplant renal failure is thought to be linked to a temporary dysfunction of the right ventricle, which occurs during the warm ischemia period of the graft.[17] Maybe more specific monitoring methods for right ventricular function, like the pulmonary artery pulsatility index (PAPi),[18] could help predict right ventricular dysfunction and prevent renal failure in DCD transplant cases.

On the other hand, patients who received a heart graft from DCD experienced shorter cold myocardial ischemia and CPB times compared to those who received a graft from DBD (although cold myocardial ischemia is not confirmed in the PSM analysis). These differences can be attributed to circulatory death donations being primarily local, significantly reducing these times. Additionally, the use of DNC for donor hearts in circulatory death donation simplifies graft protection. A single dose of DNC can provide up to 90 minutes of myocardial protection, allowing the graft to be implanted without the need for additional doses of cardioplegia.[19,20]

Our results indicate that heart transplants from DCD have accounted for over 40% of transplants performed since 2020. According to the XXXV official report of the Spanish Heart Transplant registry for the year 2023,[20] heart transplants from DCD represented an average of 18% of total transplants in Spain.

In 2023, nearly 80% of heart transplants at our hospital were performed using organs from DCD, a figure significantly higher than the Spanish average (18%)[21] and the American average

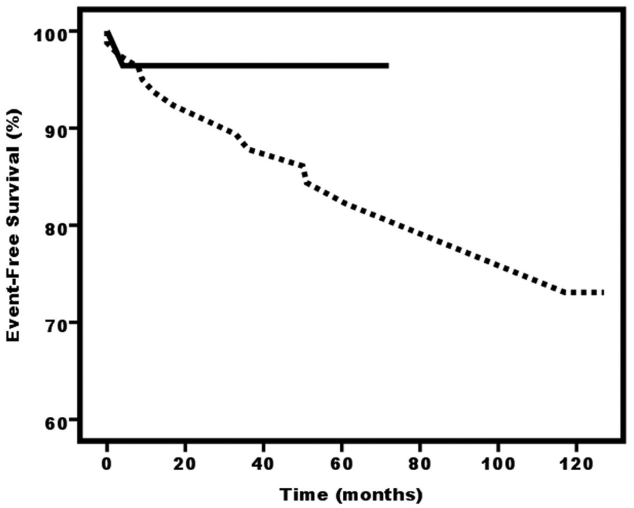

Figure 3. Survival curves comparing the DCD and DBD groups. DBD, donation after brain death; DCD, donation after circulatory death.

(13%).[22] While this percentage may decrease shortly as more cardiac transplant centers adopt the practice of using DCD, this approach is expected to ultimately increase the availability of cardiac grafts. This increase will benefit patients with HF who are refractory to medical treatment and are on the transplant waiting list.[23]

Our study found that two-thirds of cardiac donors from DCD were local cases. This prevalence may be attributed to the fact that this technique is still emerging and requires significant logistical effort at both personnel and technical levels. Unlike studies conducted in the United States, our analysis revealed no significant differences in factors such as sex, age, weight, or height between the donors of both groups.[7,9,10,16,22,23]

Additionally, we observed no significant demographic differences between the recipients of the two groups, nor did we find any discrepancies regarding donor–recipient sex mismatch.

This study shares our initial experience with organ DCD, utilizing normothermic thoracoabdominal regional perfusion in heart transplantation. This technique aims to enhance the preservation of heart grafts, which are in limited supply. However, it is not the only method being explored. Other approaches for improving heart graft preservation include *ex-vivo* perfusion,[24] controlled temperature storage, cold perfusion, and beating heart transplantation.[25]

Limitations

Our study has several limitations. Its retrospective design and single-center focus may restrict generalizability. While the National Transplant Organization advocates for a national cardiac donation protocol for DCD using regional thoracoabdominal normothermic perfusion,[12] variations can occur between groups. The small number of recipients and clinical outcomes may limit statistical power. Nonetheless, this study represents one of the largest national series of cardiac transplants from DCD to date. The higher circulatory support needs and urgent transplants in the DBD cohort could skew comparisons. However, this does not undermine the viability of DCD-normothermic regional perfusion donors for heart transplants. Differences in comparison periods should be considered, and clinical follow-up for heart transplant recipients from DCD donations remains limited due to its recent incorporation into routines. Ultimately, we could not provide values that would allow for a more comprehensive description of the donor population during DCD, such as the highest lactate level or the lowest pH level.

Conclusions

Cardiac DCD using normothermic thoracoabdominal regional perfusion shows clinical outcomes comparable to those from DBD, making it a safe and effective method. This approach could increase the availability of cardiac grafts, helping to reduce waiting lists for heart transplants. However, longer follow-up is needed to evaluate outcomes related to graft rejection, graft vascular disease, and mortality.

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