Systematic Review

Heart transplantation from donation after circulatory death: a meta-analysis of national registries

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Background: Although it has been widely recognized that heart transplantation (HT) following donation after circulatory death (DCD) can be a successful strategy to expand the donor pool, its clinical outcomes compared to donation after brain death (DBD) are still the subject of intense investigation. We reviewed the clinical characteristics of HT after DCD from the three largest multicenter nationwide registries, highlighting technical aspects, donor and recipient selection, and early outcomes. Moreover, we performed a meta-analysis of survival outcomes of DCD *vs.* DBD using reconstructed individual patient time-to-event data.

Methods: The PubMed, Web of Science, and Scopus databases were searched in January 2024 to identify the most recent reports from three large multicenter nationwide registries (United States, United Kingdom, and Australia) of HT after DCD. Clinical characteristics were summarized using descriptive statistics, and survival curves were reconstructed for DBD using individual patient time-to-event data. The pooled hazard ratio (HR) with confidence interval (CI) was calculated via Cox regression.

Results: A total of 646 DCD HT patients and 7,253 DBD controls were included in this review. In the majority of cases, donors were young males. The mean age of recipients ranged from 48 to 57 years, and the majority were males with idiopathic dilated cardiomyopathy. Up to 40% of patients required postoperative mechanical circulatory support with extracorporeal membrane oxygenation (ECMO). The meta-analysis estimated a pooled 1-year survival of 91.1% (95% CI: 88.6–93.7%) and 90.1% (95% CI: 89.4–90.8%) for DCD and DBD patients, respectively (P=0.91), with a pooled HR of 0.88 (95% CI: 0.65–1.20).

Conclusions: Although the generally more favorable clinical profile of DCD donors and recipients may constitute a potential selection bias, our meta-analysis documented similar early and medium-term survival outcomes for DCD and DBD HT.

Keywords: Heart transplantation (HT); donation after circulatory death (DCD); meta-analysis; registry

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Introduction

The shortage of compatible heart donors has historically represented the most important limitation to heart transplantation (HT), acting as one of the main drivers of waitlist mortality (1-3). To overcome this limitation, several strategies have been implemented over the decades, aiming to increase the recipient's chances of matching a compatible donor, as well as to expand the donor pool. Durable ventricular assist devices (VADs) have been documented as a valid therapy to minimize waitlist mortality by optimizing

the patient's clinical status and successfully bridging patients to HT (4-13). On the other hand, marginal donors (determined by age criteria or prolonged ischemic time) have been safely used to increase HT opportunities, with satisfactory clinical results compared to standard donors (14,15).

Although the first human HT was performed using a heart from a donor donation after circulatory death (DCD), subsequently donors for HT were historically restricted to donation after brain death (DBD). Concomitantly, preclinical studies have observed a reasonable tolerance of myocardial tissue to normothermic ischemia (16-18), paving the way for the systematic use of hearts from DCD. The initial experience, which was limited to isolated reports or case series, demonstrated that the resuscitation of the heart *in situ* via the use of extracorporeal circulation or cardiopulmonary bypass allowed its use as a suitable graft for HT (18-20). Over time, HT from DCD has entered routine practice in several nations and continents, aided by the establishment of national regulatory laws for the determination of circulatory death and the implementation of thoracoabdominal normothermic regional perfusion (TA-NRP) strategies during graft retrieval. To date, three large multicenter nationwide registries (US, UK, and Australia) have been established for the evaluation of clinical outcomes of HT after DCD (21-23), while several other nations are reporting their early experience and preliminary outcomes (24-26).

Although it is now widely accepted that HT after DCD can successfully expand the donor pool and boost HT activities (1,27), its clinical outcomes compared to DBD remain the subject of intense investigation. Several multicenter observational studies have documented similar early- and medium-term survival rates between HT from DCD and DBD (20-23,28), despite concerns about a possible selection bias towards younger and healthier donors in the DCD group (27). Moreover, despite a more preserved preoperative status, DCD recipients manifested a greater risk of acute rejection and hospitalization for rejection than DBD recipients, the long-term implications of which remain unknown (29).

Recently, the outcomes of HT after DCD were evaluated in a multicenter randomized clinical trial including 90 patients assigned to DCD group and 90 patients to the DBD group (30). Risk-adjusted survival at 6 months after HT in the as-treated population documented the non-inferiority of HT after DCD to the standard DBD (94% and 90% in the DCD and DBD groups, respectively). However, a two-fold incidence of primary graft dysfunction was observed in the DCD group (22% *vs.* 10% in the DCD and DBD groups, respectively) (30).

In the present work, we reviewed the donor and recipient characteristics of HT after DCD from three multicenter national registries (US, UK, Australia), as they represent the currently largest DCD HT cohorts with the longest available follow-up and the most established DCD protocols. Moreover, we performed a meta-analysis using reconstructed individual patient time-to-event data (31) to evaluate, on a larger scale, the outcomes of HT after DCD *vs.* DBD.

Methods

Literature search strategy

A systematic review was conducted according to the PRISMA guidelines (32). This study was registered on the PROSPERO database [580092]. The PubMed, Web of Science, and Scopus databases were searched in January 2024 by two authors (M.P. and V.T.) to identify the most recent reports from three multicenter nationwide registries (US, UK, Australia) of HT after DCD. These cohorts were selected for analysis because they represent the largest registries of DCD HT currently available in countries with well-established DCD protocols and regulatory frameworks, along with extensive experience and the longest available follow-up data. Although DCD HT programs are now being established in other nations, these countries have thus far only reported preliminary outcomes or early case series (24-26). Any eligibility disagreement was resolved by discussion among all authors, followed by consensus. Ethics approval was obtained from each research group. Our institutional Ethics Review Board waived the need for ethics approval for the meta-analysis. The study protocol is available upon request from the corresponding author.

Inclusion criteria

The manuscripts were initially screened based on the title and abstract and then underwent full-text review using the following inclusion criteria: (I) study population composed of patients undergoing HT following DCD; (II) study cohort from the US, UK, and Australian registries of DCD HT; (III) most recent report (at the time of search, in January 2024) from the above-mentioned registries; and (IV) papers written in English published after 1967.

Table 1 Included studies in the review

Study	Year	Cohort period	Country	DCD cases, n	DBD controls, n
Kwon *et al.* (37)	2023	2019–2022	United States	397	6,777
Joshi *et al.* (22)	2023	2014–2022	Australia	74	297
Messer *et al.* (28)	2023	2015–2022	United Kingdom	175	179

DCD, donation after circulatory death; DBD, donation after brain death.

Exclusion criteria

Studies were excluded if they: (I) enrolled DCD HT patients from other cohorts other than the US, UK, and Australian registries; (II) were reviews and meta-analyses; and (III) were case reports or case series with less than five patients.

Data extraction

Two authors (M.P. and V.T.) extracted the following data into a pre-set Excel abstraction form: publication year, cohort period, number of patients (DCD), number of controls (DBD), country, donor characteristics [age, gender, functional warm ischemic time (WIT), asystolic WIT, no-touch time, cold ischemic time, organ care system (OCS) time, TA-NRP time, blood pressure threshold for functional WIT definition, and procurement technique], recipient characteristics [age, gender, etiology of heart failure, preoperative mechanical circulatory support, postoperative extracorporeal membrane oxygenation (ECMO), postoperative VAD, postoperative renal replacement therapy, intensive care unit stay, total hospital stay], survival, and patients at risk.

Quality assessment

The risk of bias was assessed by two reviewers (V.T. and M.P.) using the Appraisal Tool for Cross-Sectional Studies (AXIS) (33). Studies were classified into four quality categories based on the number of positive answers to the 20 questions included in the AXIS tool: "high" (>15 positive answers), "medium" (between 10 and 15), "low" (between 5 and 9), and "very low" (<5) (34).

Statistical analysis

Descriptive statistics

The study characteristics are presented descriptively as mean and standard deviation (SD) or median [interquartile range (IQR)] for continuous variables, depending on the data presented in each included study, and as absolute and relative frequencies in the case of categorical variables.

Meta-analysis

The survival curves and time-to-event data were reconstructed using DigitizeIT software (version 2.5, Braunschweig, Germany) and the algorithm described by Guyot *et al.* (31). The global log-rank test was reported on the plot. The pooled hazard ratios (HRs) were calculated via the Cox regression model using the reconstructed individual patient data along with their confidence interval (CI). A frailty term was included in the model to account for correlation within the data reconstructed in the same study. Survival curves were obtained with the Kaplan-Meier method. Outcomes were presented as pooled proportions for data synthesis. Computations were performed using the R 4.0.1 system with the metaphor and IPDfromKM packages (35,36).

Results

After the removal of duplicates, a total of 133 manuscripts were identified; full-text eligibility was assessed for 49 of them, and finally, three articles were included in this review (22,28,37) (Figure S1), for a total of 646 DCD HT patients compared to 7,253 DBD controls (*Table 1*, *Figure 1*). According to AXIS, the quality was high in all three studies. Quality assessment of each manuscript is provided in Table S1.

Donor characteristics

The donor characteristics, as well as retrieval techniques and times, are summarized in *Table 2* [donor data from Messer *et al.* were reported in two cohorts based on the introduction of the Joint Innovation Fund (JIF) protocol in 2020 (28)]. In

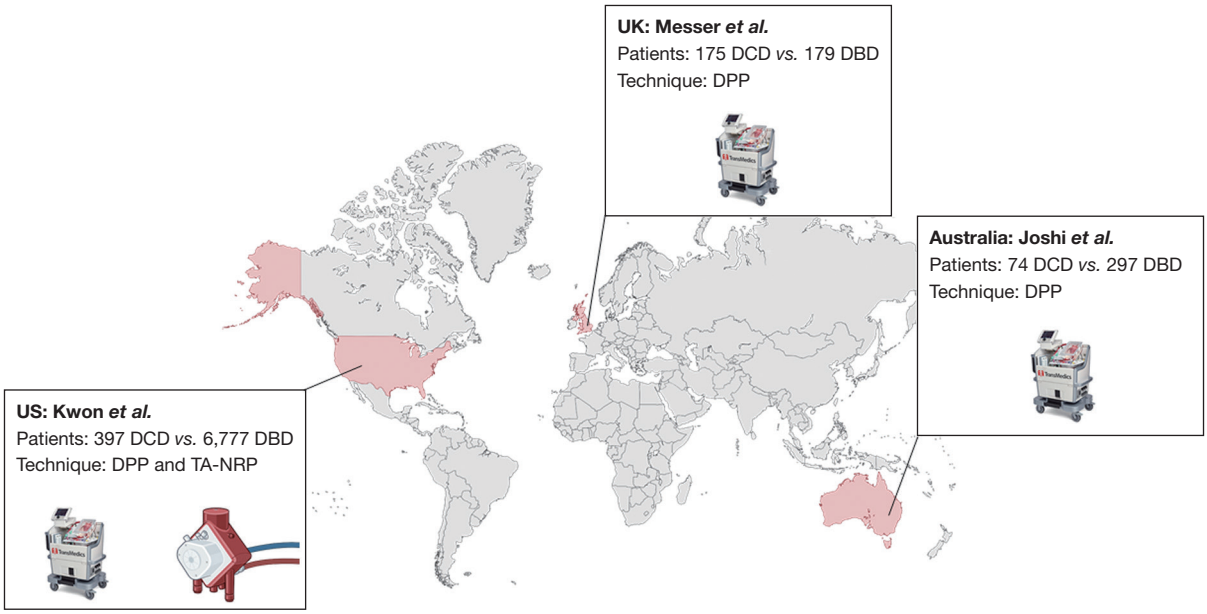

Figure 1 Summary of included studies with main characteristics. DCD, donation after circulatory death; DBD, donation after brain death; DPP, direct procurement and perfusion; TA-NRP, thoracoabdominal normothermic regional perfusion.

Table 2 DCD donor characteristics

Study	Patients, n	Males, n [%]	Age (years)†	BP level for functional WIT definition (mmHg)	No-touch period (min)	Procurement technique	Functional WIT (min)†	Asystolic WIT (min)†	Cold IT (min)†	OCS time (min)†	TA-NRP (min)
Kwon JH	397	348 [88]	28 [23–34]	<80	5	DPP and TA-NRP	–	–	–	–	–
Joshi Y	74	62 [84]	32 [11]	<90	5	DPP	20 [6]	13 [11–14]	36 [10]	282 [57]	–
Messer S (JIF)	50	36 [72]	32 [11]	<50	5	DPP	17 [14–19]	13 [11–14]	13 [9–19]	258 [216–306]	–
Messer S (pre-JIF)	125	104 [83]	34 [11]	<50	5	DPP	15 [13–18]	13 [10–14]	10 [8–13]	242 [200–300]	–

†, data are presented as mean [SD] or median [IQR]. DCD, donation after circulatory death; BP, blood pressure; WIT, warm ischemic time; IT, ischemic time; OCS, organ care system; TA-NRP, thoracoabdominal normothermic regional perfusion; DPP, direct procurement and perfusion; JIF, Joint Innovation Fund; SD, standard deviation; IQR, interquartile range.

the majority of cases, donors were young males. Although the blood pressure threshold for the definition of functional WIT varied across countries, in all cases, the mandatory no-touch period was five minutes long. Graft retrieval was performed using both TA-NRP and direct procurement and perfusion (DPP) in the US, while only DPP was used in the UK and Australia.

Functional WIT ranged from 15 to 20 minutes, whereas asystolic WIT was 13 minutes long. Cold ischemic time varied from 10 to 36 minutes, whereas OCS *ex-vivo* time ranged from 242 to 282 minutes. The donor characteristics of the DBD cohort are reported in Table S2.

Recipient characteristics and early outcomes

The recipient characteristics are summarized in *Table 3* [data from Messer *et al.* were reported in two cohorts based on the introduction of the JIF protocol in 2020 (28)]. The mean age of recipients ranged from 48 to 57 years, and the majority of patients were male. The most common etiology

Table 3 DCD recipient characteristics

Study	Patients, n	Males, n [%]	Age (years)†	Etiology of heart failure, n [%]							Preoperative LVAD/ECMO, n [%]
				Idiopathic DCM	Ischemic	RCM	Myocarditis	HCM	CHD	Other	
Kwon JH	397	309 [78]	57 [44–64]	218 [55]	112 [28]	19 [5]	–	20 [5]	11 [3]	17 [4]	158 [40]
Joshi Y	74	62 [84]	53 [13]	39 [53]	20 [27]	7 [9]	4 [5]	0	0	4 [5]	32 [43]
Messer S (JIF)	50	41 [82]	48 [38–58]	29 [58]	5 [10]	1 [2]	–	6 [12]	5 [10]	4 [8]	16 [32]
Messer S (pre-JIF)	125	100 [80]	52 [40–59]	65 [52]	22 [18]	4 [3]	–	12 [10]	4 [3]	18 [14]	37 [30]

†, data are presented as mean [SD] or median [IQR]. DCD, donation after circulatory death; DCM, dilated cardiomyopathy; RCM, restrictive cardiomyopathy; HCM, hypertrophic cardiomyopathy; CHD, congenital heart disease; LVAD, left ventricular assist device; ECMO, extracorporeal membrane oxygenation; JIF, Joint Innovation Fund; SD, standard deviation; IQR, interquartile range.

Table 4 Early postoperative outcomes after DCD heart transplantation

Study	Patients, n	ECMO, n [%]	LVAD, n [%]	Stroke, n [%]	Renal replacement therapy, n [%]	ICU stay (days), median [IQR]	Total hospital stay (days), median [IQR]
Kwon JH	397	–	–	–	–	–	–
Joshi Y	74	12 [16]	0	2 [3]	23 [31]	6 [4–10]	20 [11–31]
Messer S (JIF)	50	20 [40]	2 [4]	–	29 [58]	9 [7–19]	29 [22–44]
Messer S (pre-JIF)	125	21 [17]	5 [4]	–	63 [50]	7 [4–14]	24 [19–34]

DCD, donation after circulatory death; ECMO, extracorporeal membrane oxygenation; LVAD, left ventricular assist device; ICU, intensive care unit; IQR, interquartile range; JIF, Joint Innovation Fund.

of heart failure was idiopathic dilated cardiomyopathy, followed by ischemic cardiomyopathy. Notably, a significant proportion of patients was supported with mechanical devices [either ECMO or left VAD (LVAD)], ranging from 30% to 43%. The recipient characteristics of the DBD cohort are reported in Table S3.

Early outcomes after DCD HT are reported in *Table 4*. The mean or median intensive care unit stay ranged from 6 to 9 days, and total hospital stay from 20 to 29 days. A considerable proportion of patients required postoperative renal replacement therapy (31% to 58%) and mechanical circulatory support [with up to 40% requiring ECMO in the report by Messer *et al.* (28)].

Meta-analysis

Available Kaplan-Meier curves and time-to-event data from the selected studies were reconstructed, and a pooled survival curve was generated (*Figure 2*). The meta-analysis estimated pooled survival rates at 6 months, 1 year, and 2 years of follow-up of 92.5% (95% CI: 90.3–94.8%), 91.1% (95% CI: 88.6–93.7%), and 87.8% (95% CI: 82.8–93.1%) for DCD patients and 92.7% (95% CI: 92.1–93.3%), 90.1% (95% CI: 89.4–90.8%), and 88.8% (95% CI: 87.3–90.4%) for DBD controls (P=0.91). The pooled HR was 0.88 (95% CI: 0.65–1.20), indicating similar survival outcomes for DCD and DBD patients (*Figure 2*).

Discussion

The use of DCD heart grafts has been documented as an effective strategy to increase the donor pool and expand HT activity (1,19). To date, several countries have incorporated DCD programs into their routine HT practice, whereas others are now approaching this technique (24-26,38). Although several studies and registries have shown promising early and medium-term outcomes of DCD HT (23,37), debate remains regarding the potential selection bias of DCD donors and recipients (27), as well as an apparent increased risk of early rejection or graft dysfunction (29). In the present work, we aimed to provide a comprehensive and up-to-date review of DCD HT results from three large multicenter nationwide registries (US, UK, and Australia), including a total of 646 DCD patients

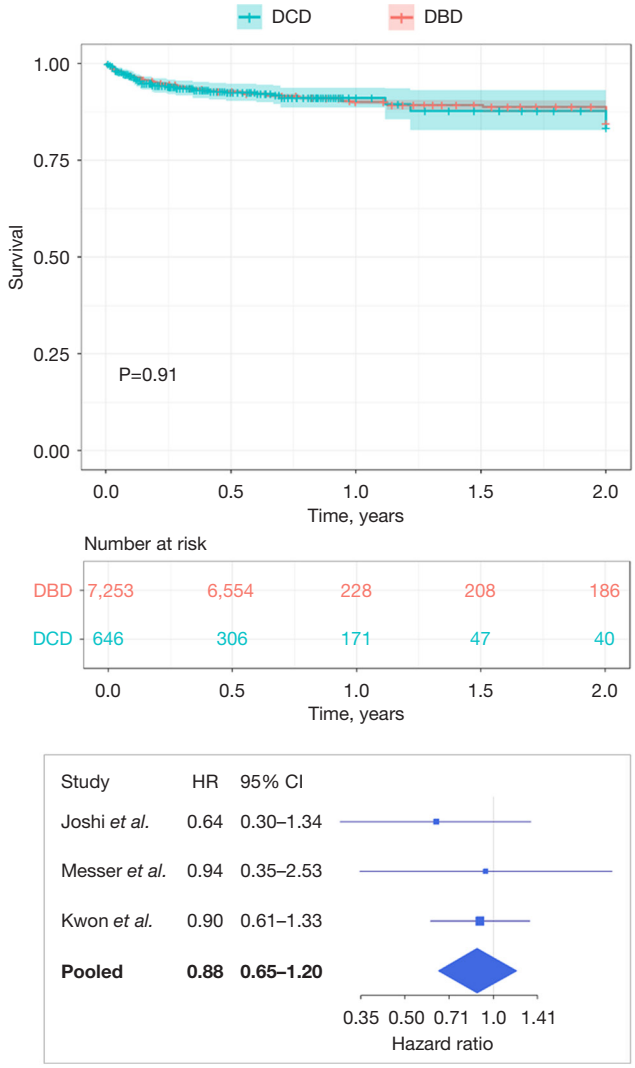

Figure 2 Pooled survival curves of DCD and DBD HT with estimated HR. DCD, donation after circulatory death; DBD, donation after brain death; HR, hazard ratio; CI, confidence interval; HT, heart transplantation.

compared to 7,253 DBD controls (*Figure 1*). Furthermore, by performing a meta-analysis using reconstructed individual patient time-to-event data, we observed a similar survival rate between DCD and DBD HT.

DCD has been introduced for those potential donors not meeting the clinical criteria for brain death required under the conventional DBD harvesting protocol (18). In the presence of severe brain injury without meaningful recovery potential, ethical and legal questions have historically been raised against organ donation, making DCD transplantation a practice that is not currently available in every country. Additionally, in the specific case of DCD HT, concerns regarding myocardial tolerability to warm ischemia and potential graft injury have contributed to this hesitancy. However, DCD HT has entered routine clinical practice in Australia, the UK, and the US, proving its benefit in dramatically increasing the donor pool (18,37), and encouraging other countries to pursue this strategy, even in the presence of stricter stand-off periods for circulatory death determination (25,26).

To meet ethical and legal requirements for DCD HT, a rigorous protocol for donor selection and pre-conditioning is mandatory (26,39). This requirement has the potential to introduce a selection bias for DCD heart donors with respect to conventional DBD donors. From our review of the most recent nationwide registries of DCD HT, we observed that the DCD donor demographics tend to show a generally more favorable profile than conventional DBD donors (*Table 2*). In particular, the mean or median donor age was as low as 28 years (in the US registry), which was significantly lower than that of their contemporary DBD control cohort (32 years) (37). Moreover, both the US and UK DCD donor cohorts displayed a lower percentage of female individuals compared to their DBD controls (12.3% *vs.* 28.5% and 28% *vs.* 46% in the US and UK registries, respectively). It is known that female donors may increase the risk of undersized predicted heart mass in female-to-male donations (40,41), which can escalate the mortality risk by 17% following HT (40). In addition, Kwon and colleagues reported a significantly lower rate of diabetes and hypertension in DCD compared to DBD donors (23,37), which may suggest a lower comorbidity status for DCD donors, possibly impacting graft quality. Despite the use of propensity matching analysis (23,37) and randomized-controlled patient recruitment (30) in some studies comparing DCD *vs.* DBD HT outcomes, it is important to recognize that a concrete risk of donor selection bias is present in the DCD HT routine practice, which should not be underestimated when evaluating its outcomes.

Similar considerations should be made for DCD recipient selection. From our review, the DCD recipient demographics aligned with those of conventional DBD recipients, with a mean or median age ranging from 48 to 57 years and the majority of patients being male (*Table 3*). Moreover, the etiology of heart failure was comparable between DCD and DBD recipients based on the analysis of the UK and US registries (28,37). However, a significant difference emerged regarding the hemodynamic status of recipients. Specifically, Kwon *et al.* observed a higher need

for preoperative mechanical circulatory support in the DBD cohort (66.2% *vs.* 50.6% in DCD recipients), as well as a higher incidence of dialysis, mechanical ventilation, and hospitalization (37). This translated into a more severe listing status for DBD recipients in both the US (status 1 and 2 in 57.1% *vs.* 20.9% in DBD and DCD recipients, respectively) (23) and the UK registries (urgent and super urgent status in 76% *vs.* 58% in DBD and DCD recipients, respectively) (28). Interestingly, a similar trend of less compromised listing status was found also in pediatric DCD recipients by Laurence *et al.* (42). Collectively, these data indicate that DCD HT may represent a more protected clinical setting than conventional DBD HT, with more selected donors and recipients. We hypothesize that this potential selection bias may be intrinsically linked to the more rigid characteristics of the DCD protocols and the relative novelty of the technique itself.

Harvesting protocols and techniques in DCD HT currently vary significantly worldwide. Although the analyzed studies in our review shared a similar five-minute duration of the mandatory no-touch period (*Table 2*), the blood pressure thresholds for the definition of functional WIT differed across registries, influencing the comparison of harvesting times. However, the most significant difference was in the adopted technique for graft reperfusion. According to the Australian and UK regulations, DCD heart procurement is performed by DPP only, whereas in the US registry, TA-NRP was also utilized. During DPP, after the declaration of circulatory death, a rapid sternotomy is performed and a cold cardioplegia flush is administered to the heart. Subsequently, the graft is harvested and cannulated for OCS *ex-vivo* perfusion. Following evaluation, a second flush of cold cardioplegia is administered, and the graft is removed from the OCS and prepared for implantation (19,22). Conversely, TA-NRP entails *in-situ* warm reperfusion of the heart through a standard cardiopulmonary bypass (with simultaneous clamping of supra-aortic vessels), which is initiated rapidly after the declaration of circulatory death. After weaning from cardiopulmonary bypass, the graft is evaluated, and a cold cardioplegia flush is used to arrest the heart, which is then harvested and prepared for implantation (24). Although Ran and colleagues observed similar 1-year post-transplant survival between DCD hearts procured with DPP and TA-NRP (43), pre-clinical studies have highlighted that reperfusion temperature and location (*in-situ vs. ex-vivo*) could impact graft recovery potential and myocardial damage (44). Apart from the obvious differences in terms of exposition to different temperatures and the use of *ex-vivo* technologies in the TA-NRP *vs.* DPP techniques, it is also important to highlight the distinctly different biological setting where the graft evaluation is performed (*in-situ* when using TA-NRP, and during OCS after DPP). Further experimental and clinical studies are needed to better evaluate the functional, tissue-level, and molecular implications of DCD graft procurement techniques, as well as the subsequent clinical outcomes, to help standardize DCD HT protocols and increase the acceptance of TA-NRP.

The susceptibility of the myocardium to warm ischemia has long been considered the most significant concern during DCD HT (16,17,20). The functional WIT, defined as the period of time from marginal blood pressure level impacting coronary perfusion to warm reperfusion (during TA-NRP) or cold cardioplegia administration (during DPP), describes the amount of time in which the ventricular myocardium may accumulate irreversible cell loss and functional deterioration. As part of the functional WIT, the asystolic WIT is the period which coronary perfusion is absent, and the risk of myocardial injury is at its peak. The asystolic WIT is primarily driven by the mandatory no-touch period, as required by the national law. In the present report, we observed very similar asystolic WIT and functional WIT (ranging from a median of 15 to 20 minutes) across the included studies. However, it is important to highlight that recent reports have shown the possibility of a successful use of DCD heart graft with asystolic WIT exceeding 30 minutes, making DCD HT a viable possibility even in countries with longer no-touch periods required by law (25,26).

Keeping in mind the above-mentioned risk of donor and recipient selection bias, our meta-analysis, which included 646 DCD patients compared to 7,253 DBD controls, demonstrated a comparable survival probability for DCD and DBD patients (P=0.91). DCD recipients displayed an outstanding 91.1% (95% CI: 88.6–93.7%) 1-year survival rate, consistent with modern standards of HT (7). However, our work highlighted a notable rate of early postoperative need for ECMO support, reaching as high as 40% (28), as well as the requirement for renal replacement therapy, ranging from 31% to 58% of patients (*Table 4*). Some authors have documented a potentially increased risk of early graft rejection and or dysfunction after DCD HT. Kwon and colleagues reported a 4.6% higher risk of acute rejection before discharge in DCD compared to DBD HT recipients, even after propensity matching for possible

confounding factors (23). Similarly, Schroder *et al.* observed double the rate of early left or right severe ventricular dysfunction in DCD recipients in their randomized controlled trial comparing DCD and DBD HT (22% *vs.* 10% at 30 days in the as-treated DCD and DBD cohorts, respectively) (30). Similar trends were also documented in pediatric DCD HT recipients by Laurence *et al.*, with a 33.3% rate of endomyocardial biopsy-confirmed early rejection rate in DCD patients (*vs.* 0% in DBD controls, though not statistically different given the small sample size) (42). Although this potentially higher risk of early graft rejection and or dysfunction does not appear to significantly impact the early survival of DCD HT recipients, its long-term effects on graft function, chronic rejection risk, and overall prognosis remain to be determined.

Limitations

Our study has several limitations. Firstly, conducting a meta-analysis of observational registries inherently presents challenges. Although we selected the largest and most comprehensive registries of DCD HT for our analysis, the results may not be generalizable to other countries with different DCD procurement techniques and protocols. As discussed, significant technical differences, such as graft reperfusion techniques, and varying definitions of ischemic times across registries, could have influenced the outcomes and their interpretation. Additionally, the reconstruction of Kaplan-Meier curves using individual patient data in the pooled analysis does not account for patient-specific characteristics or potential confounding factors that may affect the outcomes.

A risk of bias assessment was not conducted due to the limited number of studies (n=3) included in the meta-analysis. With only three studies, the variability in population characteristics and methodologies could lead to significant heterogeneity, making it challenging to apply standard risk of bias tools effectively. Additionally, the small number of included studies limited our ability to perform subgroup analyses or sensitivity analyses. Although each study was carefully reviewed for methodological rigor and quality assessment using AXIS, the lack of a formal risk of bias assessment may introduce some uncertainty in the interpretation of the results.

Conclusions

HT from DCD represents one of the most promising strategies to overcome the historical shortage of compatible donors and substantially expand the donor pool. However, several open questions remain about DCD HT, limiting its worldwide adoption. In the present work, we reviewed the clinical and technical characteristics and outcomes of HT after DCD from the largest multicenter nationwide registries currently available (US, UK, and Australia). Our analysis revealed a generally more favorable profile of DCD donors than conventional DBD donors, as well as a more elective clinical status of DCD recipients. Although the more protected clinical setting of DCD HT may be intrinsically related to the relative novelty of DCD protocols, it is important not to underestimate this potential selection bias in evaluating DCD HT outcomes. Moreover, we performed a meta-analysis using reconstructed individual patient time-to-event data, including a total of 646 DCD patients compared to 7,253 DBD controls, which demonstrated similar early and medium-term survival outcomes for DCD and DBD recipients. Despite the significant need for postoperative mechanical circulatory support and the apparent increased risk of early graft rejection and dysfunction, DCD recipients displayed an impressive 91.1% (95% CI: 88.6–93.7%) 1-year pooled survival rate. Further investigations are needed to optimize DCD HT candidate selection and retrieval techniques, as well as to determine the long-term functional and tissue-level effects of DCD on graft performance, in order to increase the acceptance of DCD as an effective strategy to boost HT activity.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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Supplementary

Appendix 1

Methods

The PubMed, Web of Science, and Scopus databases were searched in January 2024, by two authors (M.P. and V.T.), using the following search string:
((“Heart Transplantation”[MeSH] OR “heart transplant”[tiab] OR “cardiac transplant”[tiab])
AND (“Circulatory Death”[MeSH] OR “Donation after Circulatory Death”[tiab] OR “DCD”[tiab])
AND (“Australia”[MeSH] OR “United Kingdom”[MeSH] OR “United States”[MeSH] OR Australia[tiab] OR “United Kingdom”[tiab] OR “UK”[tiab] OR “United States”[tiab] OR “US”[tiab]))

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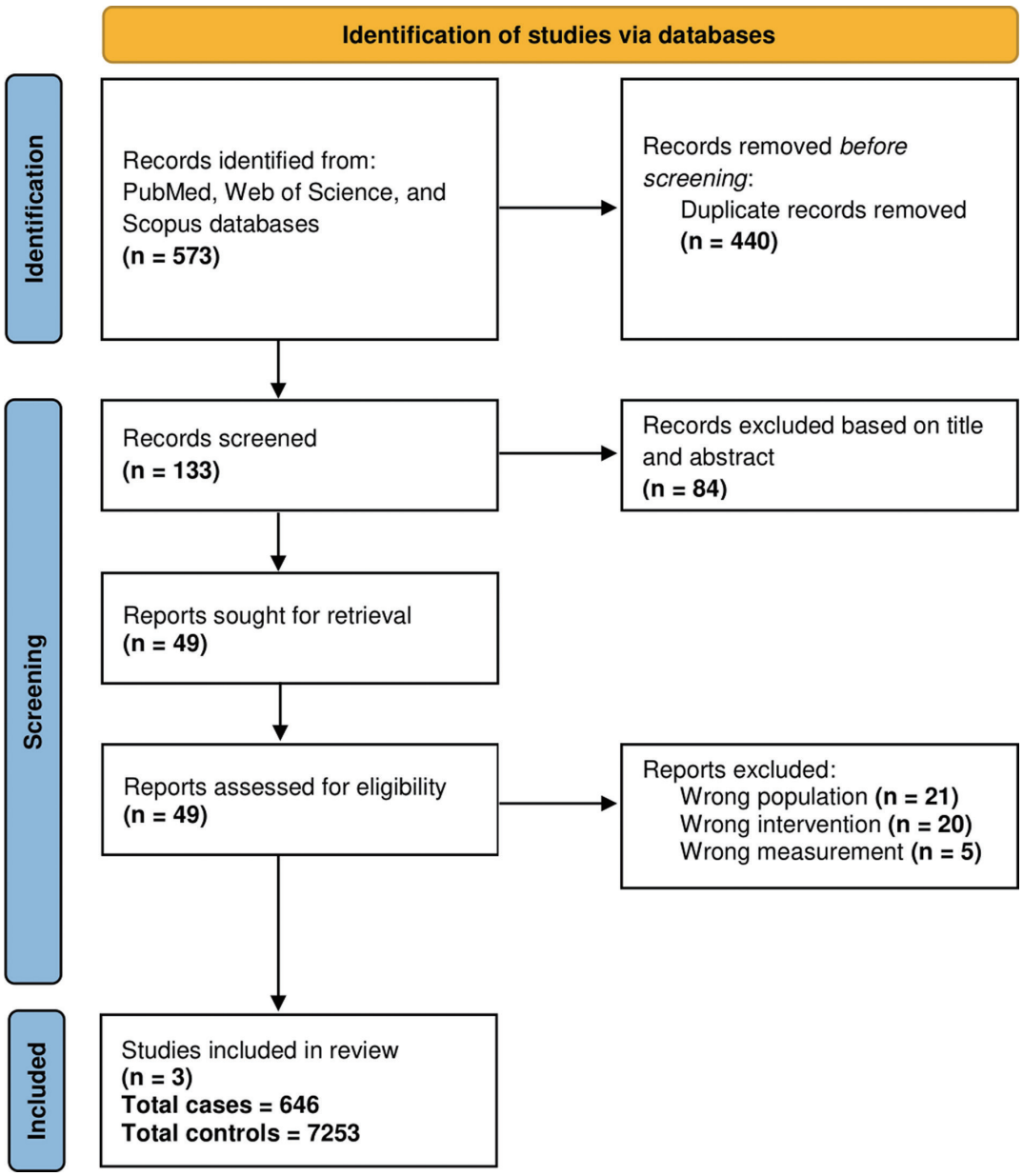

Figure S1 PRISMA 2020 flow diagram for new systematic reviews.

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Table S1 Results of quality assessment using AXIS tool for each study included in the meta-analysis

Study	1. Aims clear?	2. Study design appropriate?	3. Sample size?	4. Target population clearly defined?	5. Sample represents reference population.?	6. Selected representative subjects?	7. Non-responders?	8. Appropriate risk factors-outcomes?	9. Measurements trialed/published previously?	10. Transparence in statistical analysis?	11. Repeatable methods?	12. Data adequately described?	13. Concerns about non-response bias?	14. Information about non-responders?	15. Internally consistent?	16. Results for all analyses in methods?	17. Discussions justified by the results?	18. Limitations discussed?	19. Funding/ conflicts of interest?	20. Ethical approval?
Kwon *et al.*	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Joshi *et al.*	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	0
Messer *et al.*	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0

AXIS, Appraisal Tool for Cross-Sectional Studies.

Table S2 DBD donor characteristics

Study	Patients, n	Males, n [%]	Age (years), mean [SD]/median [IQR]	Cold IT (min), median [IQR]
Kwon JH	6,777	4,844 [71]	32 [25–50]	204 [174–240]
Joshi Y	297	–	–	–
Messer S	179	97 [54]	34 [13]	–

DBD, donation after brain death; SD, standard deviation; IQR, interquartile range; IT, ischemic time.

Table S3 DBD recipient characteristics

Study	Patients, n	Males, n [%]	Age (years), median [IQR]	Etiology of heart failure, n [%]							Preoperative LVAD/ECMO, n [%]
				Idiopathic DCM	Ischemic	RCM	Myocarditis	HCM	CHD	Other	
Kwon JH	6,777	4,944 [73]	57 [46–64]	3,824 [56]	1,883 [28]	298 [4]	–	248 [4]	230 [3]	294 [4]	4,488 [66]
Joshi Y	297	–	–	–	–	–	–	–	–	–	–
Messer S	179	104 [58]	46 [31–56]	101 [56]	29 [16]	8 [4]	–	13 [7]	16 [9]	12 [7]	59 [33]

DBD, donation after brain death; IQR, interquartile range; DCM, dilated cardiomyopathy; RCM, restrictive cardiomyopathy; HCM, hypertrophic cardiomyopathy; CHD, congenital heart disease; LVAD, left ventricular assist device; ECMO, extracorporeal membrane oxygenation.

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