Featured Article

A critical evaluation of donor heart offer acceptance in the United Kingdom

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Background: In the United Kingdom (UK), the adoption of donation after circulatory determination of death (DCD) has boosted transplantation rates by 20%. However, about 100 patients per year on the waitlist still do not receive a transplant due to low transplantation rates. Current reports review rates of utilisation after offer acceptance but fail to report the offer acceptance rate and the reasons for offer declines. We have therefore analysed the reasons why heart offers were declined over the past 16 years.

Methods: A retrospective analysis was conducted on the primary reasons for the decline of heart offers between 1st January 2008 and 31st December 2022. Reasons were obtained directly from the National Health Service Blood and Transplant Registry and categorised into five groups: 'donor-related', 'organ-related', 'recipient-related', 'logistical' and 'other'. These categories were then analysed.

Results: During this period, 2,673 heart offers were accepted for transplantation. Comparatively, 6,310 offers were declined, most commonly due to poor function (35.8%) and 'donor past medical history (PMH)' (20.4%), together accounting for 56% of all declined heart offers. The largest category was 'organ-related' reasons (47.6%), and the smallest group was 'logistical' reasons (1.0%). Recipient-related factors accounted for only 7.8% of declined offers.

Conclusions: Donor heart function and PMH are the most common reasons for declining heart offers, with non-clinical factors also contributing to offer declines. Greater acceptance rates can be achieved with greater logistical support for the UK heart transplantation networks and the implementation of more robust and objective assessment methods for offered hearts, including biomarkers and coronary angiography, particularly in DCD donation.

Keywords: Heart transplantation; acceptance; biomarkers; determination of death (DCD); donation after brainstem death (DBD)

Submitted May 26, 2024. Accepted for publication Sep 09, 2024. Published online Nov 07, 2024.
doi: 10.21037/acs-2024-dcd-24
View this article at: https://dx.doi.org/10.21037/acs-2024-dcd-24

Introduction

In the United Kingdom (UK), over 300 patients are waiting for a heart transplant. With only 200 heart transplants performed annually, approximately 100 patients are left waiting (1). Transplantation rates are restricted by donor availability. Attempts to increase donor availability have included the use of extended-criteria donors (ECD) and the successful implementation of donation after circulatory determination of death (DCD) in the UK since 2015, with the latter resulting in a 20% increase in cardiac transplant activity.

However, a supply-demand mismatch remains. Declining

offered organs significantly limits the availability of donor hearts. The UK acceptance criteria for donation after brainstem death (DBD) and DCD are similar, except for donor age (<50 years for DCD) (2). However, the interpretation of these criteria can be subjective, including left ventricular (LV) function (3,4) and age (3). Questioning these criteria is necessary to avoid declining hearts that may be suitable for transplantation. A more liberal approach to donor organ offers may increase the risk of transplantation, but this is outweighed by improved transplantation rates and reduced waitlist mortality and morbidity (3,5).

In 2023, the national UK offer decline rate was 76.8%. This was higher than in 2022 (72.4%) but lower than in 2020 and 2021 (78.2% and 79.8%, respectively), with these years being hindered by the coronavirus disease 2019 (COVID-19) pandemic (1,6). Furthermore, unit-level offer decline rates vary regularly across the six UK cardiothoracic transplant centres (1,6). Unfortunately, reviews into reasons for offer decline are rarely reported in the UK or internationally (7,8). UK reports describe decline rates but provide no clear indication as to the reasons (1). We have therefore sought to review the reasons why donor heart offers were declined in the UK and aim to address this problem.

Methods

All UK transplant data are held in the Transplant Registry, managed by the National Health Service Blood and Transplant (NHSBT). Data for this study were provided in anonymised form by the NHSBT Statistics Department. Coded primary reasons for declined offers were obtained retrospectively from this registry for all DCD (since 2015) and DBD heart offers between 1st January 2008 and 31st December 2022. These reasons were then categorised into five groups: donor factors, recipient factors, organ factors, logistical factors, and other, based on expert opinion and supported by similar categories performed by the United Network for Organ Sharing (UNOS) in the United States (US) (9).

Statistical analysis

Data were analysed in RStudio (version 4.3.1, 2023-06-16). Absolute values for each reason were entered, and percentages were calculated relative to the total number of offers and to total offers per category. Graphs were produced using the 'ggplot' package.

Results

In the UK, over this 16-year period, 9,044 hearts were offered for transplantation. Of these, 6,310 heart offers were declined, with 6,044 (95.8% of all) having a coded decline reason on the NHSBT Transplant Registry. The remaining 2,734 hearts were accepted for donation, resulting in 2,673 (97.8%) transplanted (*Figure 1*) (1,10). Forty-three reasons for offer decline were recorded in this period (*Figure 2*, *Table 1*). The most common reason for declining an offer was 'poor function', accounting for 35.8% (n=2,166) of declined offers (of those coded), followed by 'donor unsuitable—past medical history (PMH)', accounting for 20.4% (n=1,230). Together, these two factors alone contributed to 56% of declined offers.

The organ-related factors category accounted for the largest proportion of declined offers, comprising 47.6% (n=2,877) hearts. 'Poor function' (35.8%) and 'size' (9.4%) accounted for 45% out of the 47% offers declined within this group. Immunological incompatibility (HLA/ABO/Crossmatch) resulted in 67 declined offers (1.1%), whilst prolonged ischaemic time (warm or cold) accounted for 7 declined hearts (0.12%).

Donor factors were the second-largest category at 33.8% (n=2,043), in particular, 'PMH' and 'age', accounting for 20.4% (1,230 hearts) and 7.2% (434 hearts), respectively. 'Virology' (1.8%) and other donor-related diseases (2.2%) accounted for 243 declined offers (4.0%). Circumstances around donor death accounted for 65 (1.1%) declined offers, including cases of unstable donors (0.8%), cause of death (0.1%), non-heart beating donation (until 2015) (0.3%) and donor arrest (0.1%).

Excluding 'poor function' and 'donor-PMH', all 41 remaining reasons individually accounted for less than 10% of declined offers, with 32 accounting for less than 1% of declines. Eighteen offers were sent for research purposes (0.3%), and two were retrieved specifically for heart valves. Almost all recipient-related factors were due to the lack of available recipients (99% of the group), accounting for 465 declined offers (7.7%).

The smallest category was logistical factors, accounting for 1% (n=61) of declines, mostly due to loss of fast-track offers (0.2%) and unavailability of transportation (0.4%), the retrieval team (0.1%) and bed (0.1%).

Discussion

When assessing lost opportunities for heart transplantation, the underlying reasons for declining heart offers must be

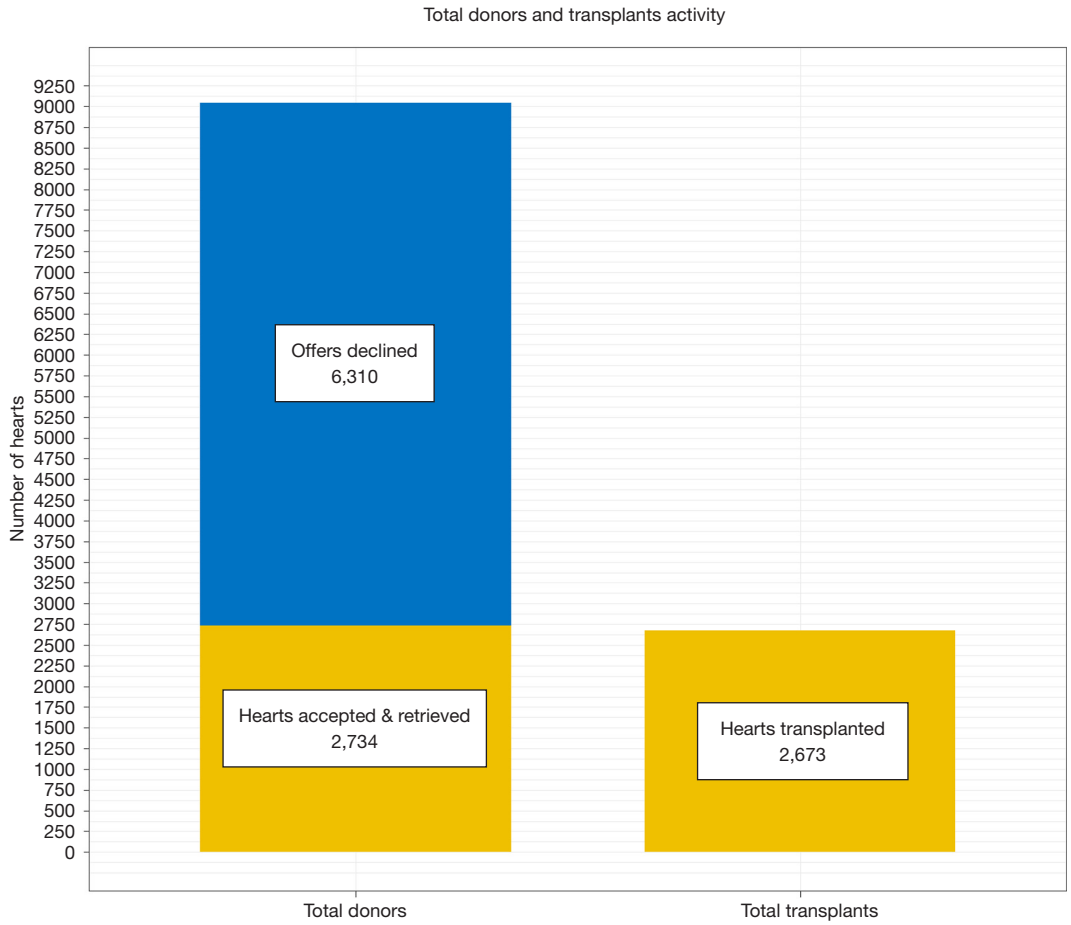

Figure 1 Total number of UK heart offers and heart transplants between 1st January 2008 and 31st December 2022.

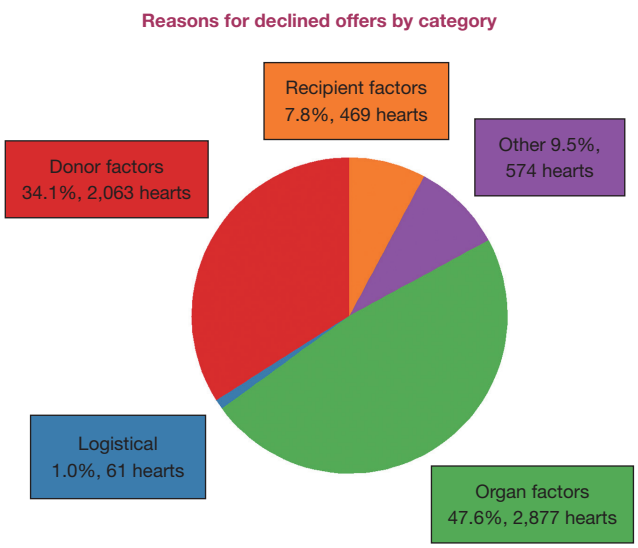

Figure 2 Proportion of UK donor heart offers declined between 1st January 2008 and 31st December 2022, by category.

reviewed. Unfortunately, this is rarely performed, with activity reports typically considering utilisation rates after offer acceptance. The latest heart transplantation rates per million population, show the UK (3.0) lagging behind both Europe (3.5) and the US (12.4) (11). Despite the UK's impressive 97.6% utilisation of accepted offers, this is likely due to the UK's markedly lower offer acceptance rate of only 32.8%, emphasizing the urgent need for improvement in this area.

We have demonstrated that organ-related factors are the most common reason for offer decline (48%), particularly poor organ function (35.8%). Donor PMH was the second-largest reason for declining offers (20.4%), and donor-related factors were the second-largest category (34%). This suggests that the assessment of organ function and donor selection are the most critical components determining offer acceptance.

Donor heart function emerged as the greatest reason for

Table 1 Reasons for donor heart offer decline between 1st January 2008 and 31st December 2022, by category

Factors	No. of hearts	Percentage—per category (%)	Percentage—all hearts (%)
Donor factors			
Donor unsuitable—past history	1,230	59.6	20.4
Donor unsuitable—age	434	21.0	7.2
Donor unsuitable—virology	108	5.2	1.8
Donor unstable	51	2.5	0.8
Family permission refused	36	1.7	0.6
Donor unsuitable—medical reason	28	1.4	0.5
Donor unsuitable—cause of death	9	0.4	0.1
Medication	7	0.3	0.1
Donor arrested	5	0.2	0.1
Other disease	135	6.5	2.2
Non-heart beating donor (until 2015)	20	1.0	0.3
Total	2,063	100	34.1
Recipient factors			
No suitable recipients	465	99.1	7.7
Recipient did not need transplant	2	0.4	0.03
Recipient refused	1	0.2	0.02
Recipient unfit	1	0.2	0.02
Total	469	100	7.8
Organ factors			
Poor function	2,166	75.3	35.8
Donor unsuitable—size	567	19.7	9.4
HLA/ABO type	65	2.3	1.1
Organ unsuitable for transplant	21	0.7	0.3
Infection	20	0.7	0.3
Organ damaged	11	0.4	0.2
Tumour	11	0.4	0.2
Anatomical	6	0.2	0.1
Ischaemia time too long—warm	4	0.1	0.1
Ischaemia time too long—cold	3	0.1	0.05
X-match positive	2	0.1	0.03
Fatty organ	1	0.03	0.02
Total	2,877	100	47.6

Table 1 (*continued*)

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Factors	No. of hearts	Percentage—per category (%)	Percentage—all hearts (%)
Logistical factors			
No response to fast-track offer	11	18.0	0.2
Transport difficulties	9	14.8	0.1
Centre already retrieving/transplanting	8	13.1	0.1
No beds	8	13.1	0.1
No staff	1	1.6	0.02
Centre criteria not achieved	1	1.6	0.02
Distance	1	1.6	0.02
No theatre	1	1.6	0.02
Poor weather	4	6.6	0.1
No time	17	27.9	0.3
Total	61	100	1.0
Other			
Other	523	93.9	8.7
Used for research after declined by centres	18	3.2	0.3
Permission refused by coroner	11	2.0	0.2
Unknown	3	0.5	0.05
Heart retrieved for valves only	2	0.4	0.03
Organ used elsewhere	17	3.0	0.3
Total	574	100	9.5

HLA, human leukocyte antigen.

declining offers in this dataset, similar to trends observed in Australia, Korea and the US (7,12-14). Prior UK studies have outlined similar findings (3,15) but did not investigate these factors further. Globally, functional assessment, especially LV function, is predominantly performed using echocardiography (3,4,7,14,16). However, echocardiography thresholds for LV function can be misleading, as they do not consider the temporary LV dysfunction across the donation process (3,4,8,14,16-18). Donated hearts should undergo adequate resuscitation before determining their final functional capacity, distinguishing them from irrecoverably damaged hearts (3,4,8,14,16-18). Machine perfusion (MP) may be useful for this purpose. It is well-established in DCD donation and may benefit DBD donation (19), providing an opportunity for continued resuscitation and greater restoration of function. However, there is a lack of objective assessments of donor cardiac function on the ex-situ perfusion device (14). Lactate has historically been used (20), but has been demonstrated to be inadequate for this purpose in DCD hearts, with poor sensitivity and specificity (21,22). Consequently, approximately 30 hearts may potentially be inappropriately declined at this stage due to lactate-defined poor function (21). If MP is increasingly used, new biomarkers are urgently required to fulfil this role. Thoraco-abdominal normothermic regional perfusion (taNRP) offers better functional assessment using trans-oesophageal echocardiography and thermo-dilution cardiac output studies (23).

Echocardiography interpretation is also subjective. Khush *et al.* showed a significant difference in echocardiography image interpretation between echo experts and non-expert cardiologists, with non-expert cardiologists reporting a lower LV ejection fraction and overstating LV dysfunction (24). Furthermore, the same image was

interpreted differently by the same person at two different times in 6% of cases (24). This is critical in donor heart assessment when images are reviewed by healthcare professionals who are not echocardiographic experts (14,16). Such variability in echo interpretation is extremely concerning given its importance in offer acceptance decisions, potentially wasting viable donor hearts. Evaluation of echocardiographic images in centralised centres, including assessment and recovery centres (ARC) (14,25) may help mitigate this issue. However, these centres are beset with financial and logistical issues that are unlikely to be resolved in the near future. A precise and accurate functional measurement tool, especially one less susceptible to human error, is crucial.

Pulmonary artery catheters (PACs) offer a more objective functional assessment, with established cardiac output results that correlate well with post-transplant outcomes (3,16). However, the use of PACs requires additional specialised expertise, which is often unavailable outside of cardiothoracic centres. In the UK, a PAC is usually inserted by the cardiothoracic retrieval team at the donor hospital. This delay prevents early, targeted resuscitation and organ assessment prior to the deployment of limited retrieval teams, potentially wasting valuable time and resources, especially if the heart is later deemed unsuitable. Improved assessment methods that can be interpreted by all transplant healthcare professionals are necessary, enabling earlier and more efficient assessment of organs.

Donor factors were the second-largest category of offer decline reasons. In particular, donor PMH was the second most common reason for offer decline overall. Coronary artery disease (CAD) risk factors are often the most significant concerns (26-28), with physical coronary assessment performed by palpation of the coronary arteries by the retrieving surgeon to determine final utilisation decisions once accepted. Both approaches, however, are subjective, leading to widespread variation in regional acceptance. Furthermore, CAD is both a donor-related issue, through donor risk factors of disease, and an organ-related problem, as poor coronary perfusion can impair cardiac function. As such, robust assessment of CAD must involve both a review of risk factors and an assessment of the organ itself, including adequate functional assessment. Unfortunately, coronary assessment is often based solely on donor risk factors, with many offers declined as a result (26,28). Using echocardiography to show regional wall motion abnormalities (RWMA) may be less subjective than risk factors alone, but it does not always translate accurately to CAD burden. Catecholamine stunning can cause RWMA without CAD, which can resolve on repeat echocardiography after resuscitation (8,17,29).

Coronary angiography provides an objective tool for CAD assessment and is recommended in cases of RWMA on echocardiography, reduced ejection fraction, or donor risk factors internationally (8,26,27,29). In Europe, angiography is extended to all men aged 55 years and above, women aged 55 years and above with one risk factor, and all donors between 46 and 55 years with two risk factors (16). However, with limited resources, final decisions on angiograms are still based on clinical judgment, which is highly inconsistent and unfair to donor wishes and waiting recipients (26). With a standardised assessment of CAD, the use of coronary angiography can increase acceptance rates by 9% (27), including wider use of older donors, who are more likely to have risk factors but may not have significant CAD (sCAD) (16,26). Moreover, 7% of clinician-defined 'normal' hearts may have CAD on angiography (30), which is overlooked by the surgeon, leading to inappropriate transplantation (26). In the DONOR-CAD trial, only 4 out of 937 transplanted hearts received a pretransplant angiogram, and the incidence of sCAD was 6.9%, up to half the incidence of donor risk factors. Had the assessment been based solely on risk factors, 116 (12%) hearts would have been inappropriately declined (28). Applied to our cohort, angiography could have saved an additional 723 lives over the 16-year study period (45 lives/year) by preventing offered hearts from being incorrectly declined. Clinicians can both overestimate and underestimate CAD burden. Angiography reduces such occurrences, improving the offer acceptance rate, whilst reducing the burden of decision-making on the surgical team.

Unfortunately, little evidence exists to support the use of angiography in donor heart assessment (26,29). Additionally, routine coronary angiography in the UK would pose significant financial and logistical challenges for the National Health Service (NHS), especially as coronary catheterisation laboratories are not always available (26). Ante-mortem investigations, including invasive angiography, are currently not allowed in the UK (31,32), as they are deemed not in the best interests of donor care. Conversely, angiography could increase the likelihood of donor wishes being supported and respect for donor autonomy. This should be considered in discussions about the donor's best interest (31). Angiography can be performed post-mortem whilst on the Organ Care System (OCS) machine (27), but necessitates the use of an expensive OCS machine for

a heart that may be rejected (26). Computed tomography (CT) coronary angiography has similar sensitivity to invasive angiography, but its use in this area is minimal, and poor image quality due to donor heart arrhythmias may be problematic (16). Overall, the use of angiography remains limited (26), further contributing to low offer acceptance rates. Maintaining coronary perfusion is ultimately vital for preserving cardiac function. Adequate functional assessments can therefore support the use of hearts with borderline CAD risk, particularly for marginal, older or urgent recipients (4). Survival with these hearts, even with eventual sCAD, is greater than a left ventricular assisted device (LVAD) or no transplant at all, offering better, life-prolonging treatment for urgent patients (28). However, this relies on adequate investigation of CAD to avoid misdiagnoses and erroneous offer decline.

Offer decline due to donor virology concerns was low (1.8%), with relatively moderate restrictions in the UK. Only human immunodeficiency virus (HIV)-positivity and intravenous drug use (IVDU) are absolute contraindications to donation, with hepatitis C used in ECD (33). In the US, increased use of hepatitis C-positive and IVDU donors (13,34) has supported acceptance and utilisation rates without affecting post-transplant outcomes. Similar progress should be considered in the UK, especially in otherwise acceptable hearts.

Donor age was the second-largest donor-related reason for offer decline, at 7.2% (434 offers). Forty-five years is generally considered the upper limit of donor age, but a clear cut-off has not been universally established (4,29). UK age thresholds are higher than in the US, where 59% of US donors are less than 35 years old (5). Furthermore, older ECDs above 60 years are increasingly tolerated in the UK and Europe (25). However, the UK remains behind Europe, with 42.8% of European donors above 60 years, compared to 75% of UK donors aged 58 years or below (6,34). Adequate CAD and functional assessment will encourage the use of older UK donors, increasing offer acceptance rates (5,29).

Similar ambiguity exists regarding organ size mismatch, causing 567 (9.48%) declined offers. In some US states, up to 58% of heart offers were declined due to size mismatch, whereas this posed no issue in other US states and Europe (5,13,14,16). Both under and oversized hearts can have positive outcomes (13,35). Predicted heart mass is increasingly tolerated as the best assessment method, but with low-level evidence and a number of locally-based caveats that affect the final offer decision (29,36,37), ultimately deferring to surgical judgment. Consequently, it is crucial that accurate assessment methods are provided for other donor criteria first, such as cardiac function, to facilitate effective decisions regarding more uncertain criteria such as donor age and organ size (34).

Unacceptably, 61 heart offers were declined based on non-clinical, logistical issues, most commonly due to 'no response to fast-track offer'. For UK fast-track offers, hearts that have been removed, are being removed, or are due to be removed within 90 minutes are offered rapidly to all transplant centres simultaneously. If no centre accepts the offer, these offers are declined. With 24/7 transplantation services in the UK, all centres must respond rapidly to maximise offer acceptance. Further information regarding these declined offers is required. Twenty-five hearts were declined due to bed unavailability, busy retrieval teams, or transportation difficulties. These issues highlight an overstretched retrieval service, the National Organ Retrieval Service (NORS), in the UK. To support maximal offer acceptance, cardiac NORS teams must be expanded, similar to the £1.78 million offered to expand abdominal retrieval in 2018 (25). Preventable losses of potentially viable hearts are unacceptable, and steps must be taken to eradicate this issue.

Overall, donor heart acceptability criteria are currently unclear, relying on subjective, inaccurate tools. Functional biomarkers are needed for objective functional assessment, avoiding interpreter variation whilst providing a cost-effective, repeatable assessment tool, particularly during initial resuscitation. This will improve the efficiency of UK NORS by utilising retrieval services and machines in hearts with higher transplant potential. These markers can work with other tools, enhancing donor functional assessment. Echocardiography can provide descriptive functional and valvular assessment, supported by objective biomarkers.

The use of biomarkers during MP can support functional assessment in transit, replacing lactate, and providing continuous evaluation of potential cardiac recovery (38). Thus, biomarkers can enhance both offer acceptance and post-acceptance utilisation rates. Thorough and objective functional assessments will ensure that suitable hearts are transplanted, and poorly functioning hearts are correctly declined (3,38). Suggested biomarkers include troponin, brain natriuretic peptide (BNP), procalcitonin, mitochondrial products and inflammatory mediators (TNF-α and IL-6) (3,38). However, the best biomarkers are not yet known or correlated to recipient outcomes. More work is required to establish functional objective biomarkers

(3,38). Coronary angiography offers a straightforward objective measure of CAD, and wider implementation is urgently required.

Impact on DCD donation

In this study, 20 potential DCD hearts (0.3%) were rejected until 2015, as DCD donation was not established at time of offering. Currently, 33% of UK cardiac transplants are from DCD donations, compensating for the declining number of DBD donors (1,39). Of the 46,674 intensive therapy unit (ITU) deaths in the UK over the past 3 years, only 4% (n=1,932) were brainstem deaths, leaving over 40,000 individuals who would not meet the neurological criteria for brainstem death (39) and who may be potential DCD donors. DCD donation also offers these individuals and their families an opportunity to perform a heroic action in their passing. However, the increase in DCD donors underscores the need for adequate functional assessment. DCD imposes greater functional impairment on the donor heart through ischaemic reperfusion injury (IRI) compared to DBD donation. Therefore, the translation of lactate levels, assessed in DBD hearts, to this area is woefully inaccurate (23). In 2022–2023, 8% of hearts (n=55) were retrieved from DCD donors, compared to 20% (n=153) of DBD donors, despite similar donor availability (DBD: 772, DCD: 657) and a higher age acceptance for DCD donors. Older DCD donors, combined with IRI, necessitate increasingly more robust, objective functional tools. Controlled death in DCD donation also allows for greater opportunities for resuscitation, and adequate functional and CAD assessment. These opportunities must be explored to improve DCD acceptance and utilisation rates.

Limitations

This study is retrospective and dependent on NHSBT Registry completion. Two hundred and sixty-six hearts (4.2%) were declined but with no coded reason. Furthermore, only single primary reason codes were provided, meaning some hearts may have been declined for multiple reasons. Greater granularity surrounding offer decline circumstances, along with greater registry completion, may provide greater insights into UK offer acceptance issues. Greater reporting of offer decline reasons, supported by further reviews and national policies, is needed to understand why heart offers are declined and to develop improvement strategies.

Conclusions

Declined heart offers in the UK are largely related to organ function and donor risk factors. Both can be improved by using more objective assessment tools, including functional biomarkers and coronary angiography, to supersede existing subjective assessment techniques. This will support these criteria specifically and provide more robust information for combined clinical risk stratification, particularly when considering less well-defined criteria. Improved functional assessment measures are especially required, as donor organ dysfunction was the largest reason for offer decline in the UK. This study supports the growing need for new objective, clinician-independent biomarkers to clearly define donor heart suitability and function, especially with the expanding use of DCD donation. Maximising post-acceptance utilisation rates is futile without first improving offer acceptance rates, with well-defined acceptance criteria and accurate assessment tools. Heart donation is a selfless gift offered by donors. Healthcare professionals must fully support donor wishes by preventing inappropriate offer declines and saving as many lives as possible.

Acknowledgments

Funding: None.

Footnote

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

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Cite this article as: Asemota N, Louca J, Oechsner M, Williams L, Messer S, Manara A, Nunes J, Page A, Large S. A critical evaluation of donor heart offer acceptance in the United Kingdom. Ann Cardiothorac Surg 2025;14(1):37-46. doi: 10.21037/acs-2024-dcd-24

