Predictors of nonuse of donation after circulatory death lung allografts

Ashley Y. Choi, MHS,[a] Oliver K. Jawitz, MD,[b] Vignesh Raman, MD,[b] Michael S. Mulvihill, MD,[b] Samantha E. Halpern, BA,[a] Yaron D. Barac, MD, PhD,[c] Jacob A. Klapper, MD,[b] and Matthew G. Hartwig, MD[b]

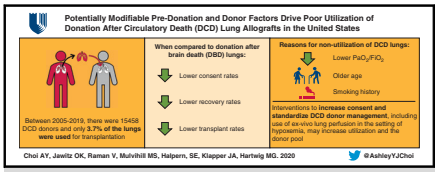
ABSTRACT

Objective: Despite growing evidence of comparable outcomes in recipients of donation after circulatory death and donation after brain death donor lungs, donation after circulatory death allografts continue to be underused nationally. We examined predictors of nonuse.

Methods: All donors who donated at least 1 organ for transplantation between 2005 and 2019 were identified in the United Network for Organ Sharing registry and stratified by donation type. The primary outcome of interest was use of pulmonary allografts. Organ disposition and refusal reasons were evaluated. Multivariable regression modeling was used to assess the relationship between donor factors and use.

Results: A total of 15,458 donation after circulatory death donors met inclusion criteria. Of 30,916 lungs, 3.7% (1158) were used for transplantation and 72.8% were discarded primarily due to poor organ function. Consent was not requested in 8.4% of donation after circulatory death offers with donation after circulatory death being the leading reason (73.4%). Nonuse was associated with smoking history ($P < .001$), clinical infection with a blood source (12% vs 7.4%, $P = .001$), and lower PaO_2/FiO_2 ratio (median 230 vs 423, $P < .001$). In multivariable regression, those with PaO_2/FiO_2 ratio less than 250 were least likely to be transplanted (adjusted odds ratio, 0.03; $P < .001$), followed by cigarette use (0.28, $P < .001$), and donor age >50 (0.75, $P = .031$). Recent transplant era was associated with significantly increased use (adjusted odds ratio, 2.28; $P < .001$).

Conclusions: Nontransplantation of donation after circulatory death lungs was associated with potentially modifiable predonation factors, including organ procurement organizations' consenting behavior, and donor factors, including hypoxemia. Interventions to increase consent and standardize donation after circulatory death donor management, including selective use of ex vivo lung perfusion in the setting of hypoxemia, may increase use and the donor pool. (J Thorac Cardiovasc Surg 2021;161:458-66)



Potentially modifiable predonation and donor factors drive poor use of DCD lungs.

CENTRAL MESSAGE

Use of DCD lungs can be improved with appropriate interventions. International guidelines should be developed to facilitate improved organ recovery.

PERSPECTIVE

Wait-list mortality is currently at an all-time high in LTx in the United States. DCD lungs have shown promise in expanding the donor pool, yet the United States lags behind several other countries in using these organs. With appropriate interventions such as EVLP, many factors that influence these practice patterns can potentially be improved.

See Commentary on page 467.

Despite the number of lung transplants performed in the United States having doubled since 2004, wait-list mortality is currently at an all-time high at 17.2 deaths per 100 wait-list years.[1] The increasing wait-list mortality rate despite an upward trend in transplant number necessitates continuous reevaluation and improvement of current practices of organ allocation and use.

First described in 1967,[2] donation after circulatory death (DCD) allograft use has shown promising results in mitigating the supply-demand mismatch, including an increase

From the [a]School of Medicine, Duke University, Durham, NC; [b]Department of Surgery, Duke University Medical Center, Durham, NC; and [c]The Division of Cardiovascular and Thoracic Surgery, Rabin Medical Center, Petach-Tikva, Israel.

Institutional funding was used for this study. Choi is supported by the National Center for Advancing Translational Sciences of the National Institutes of Health (NIH) under award Number TL1TR002555. Jawitz and Raman are supported by the NIH T32 Grants 5T32HL069749 and 5T32CA093245, respectively. Halpern is supported by a Pfizer Foundation grant and the Duke Clinical Translational Science Institute. The content is solely the responsibility of the authors and does not necessarily represent the official views of the NIH, Pfizer Foundation, or Duke Clinical Translational Science Institute.

This study was a podium presentation at the International Society for Heart and Lung Transplantation 39th Annual Meeting and Scientific Session in Orlando, Florida, on April 3-6, 2019.

Received for publication Sept 21, 2019; revisions received April 7, 2020; accepted for publication April 8, 2020; available ahead of print May 7, 2020.

Address for reprints: Ashley Y. Choi, MHS, Duke University Medical Center, Box 3863, Durham, NC 27710 (E-mail: choi.ashley@duke.edu).

0022-5223/$36.00

https://doi.org/10.1016/j.jtcvs.2020.04.111

Abbreviations and Acronyms

AOR = adjusted odds ratio
DBD = donation after brain death
DCD = donation after circulatory death
EVLP = ex vivo lung perfusion
LTx = lung transplantation
OPO = Organ Procurement Organization
P/F = PaO_2/FiO_2 ratio
PGD = primary graft dysfunction
UNOS = United Network for Organ Sharing

Scanning this QR code will take you to the article title page to access supplementary information.

in transplant activity by 6% and the donor pool by 15% in the United States.[3,4] However, most of the use in the United States remains limited to kidney and liver transplantation, and use in lung transplantation (LTx) lags behind many other countries.[5,6] DCD is generally stratified by the modified Maastricht classification (Paris 2013), in which uncontrolled DCD (categories I, II, IV) refers to organ procurement after unexpected cardiopulmonary arrest or unsuccessful resuscitation, while in controlled DCD (category III), arrest occurs after a planned withdrawal of life support, often performed in the intensive care unit or in the operating room.[7] Controlled DCD is the predominant approach to DCD in the United States, in part due to superior ability to minimize warm ischemic time.[1] In the past 2 decades, studies have emerged suggesting that DCD lung transplants have comparable survival outcomes and primary graft dysfunction (PGD) rates to donation after brain death (DBD).[8-16] Although these findings are important, they provide insufficient evidence to improve the current practices of DCD organ use. Opportunities to increase DCD organ use require identifying reasons for refusal, which can potentially be modified with appropriate interventions.

Reasons for continued underuse of DCD donors for LTx are not well understood. In an effort to describe reasons for this practice pattern, we investigated use of DBD and DCD lungs, predictors of nonuse, and organ disposition for each DCD lung allograft.

MATERIALS AND METHODS

Data Source

We performed a retrospective analysis of United Network for Organ Sharing (UNOS) data from the Scientific Registry of Transplant Recipients. This study was deemed exempt by our Institutional Review Board.

Study Population and Design

All donors who donated at least 1 organ for transplantation between 2005 and 2019 were identified in the UNOS registry and stratified based on DCD and DBD status. Donor baseline characteristics were recorded for DCD donors who have consented for LTx. Study design is summarized in Figure 1.

Outcomes

The primary outcome of interest was use of DCD lung allografts. Donor-associated characteristics that correlated with use for transplantation were examined, including annualized Organ Procurement Organization (OPO) volume, which is the odds of using a DCD lung with every 20 additional donors managed by the OPO. Use rates were compared in DBD and DCD lung allografts. Organ disposition and reasons for nonuse of donor lungs were evaluated. Individual organ-level and donor-level analyses were performed. Finally, use patterns across the United States were mapped to demonstrate DCD lung use in each state as well as proportion of lung donors that are DCD versus DBD.

Statistical Analysis

Baseline demographics and clinical characteristics were compared using the Wilcoxon rank-sum test for continuous variables and the Pearson chi-square test or Fisher exact test for categoric variables. Categoric data were reported as count and percentage while continuous data were reported as median and interquartile range. Comparisons were 2-tailed for all analyses. Multivariable logistic regression was fit to assess the relationship between donor variables and use. Approximately 1.7% of PaO_2/FiO_2 (P/F) ratio were missing from our data and regression was performed as a complete case analysis. Summary of all missing variables is shown in Table E1. Statistical analysis was completed using R version 3.5.1 (Vienna, Austria).

RESULTS

Comparison of Use Rates Between Donation After Brain Death and Donation After Circulatory Death Lungs

Use rates increased for both DBD and DCD lungs over time, consistent with rates shown in Table 1 (2005-2009, 2010-2014, and 2015-2019). Furthermore, use of DBD grafts increased at a faster pace than DCD grafts, reaching a difference of over 20% in 2019 from 15% in 2005 (Figure E1).

Donor Baseline Characteristics Stratified by Use for Lung Transplantation

A total of 15,458 DCD donors met inclusion criteria. Of those, 709 were excluded from donor-level analysis as they did not consent for LTx. Excluding these individuals was to ensure that all donors in this analysis had the potential to be transplanted. A final cohort of 14,749 donors were analyzed and stratified by LTx use. Donors whose lungs were not transplanted outnumbered donors whose lung(s) was transplanted (14,117 vs 632). DCD lungs were less likely to be transplanted if the donor had any smoking history ($P < .001$), clinical infection with a blood source (12% vs 7.4%, $P = .001$), and a lower P/F ratio (median 230 vs 423, $P < .001$). When stratified by era, most DCD lungs were transplanted (67.6%) in 2015-2019, followed by 2010-2014 (20.3%) and 2005-2009 (12.2%), but also

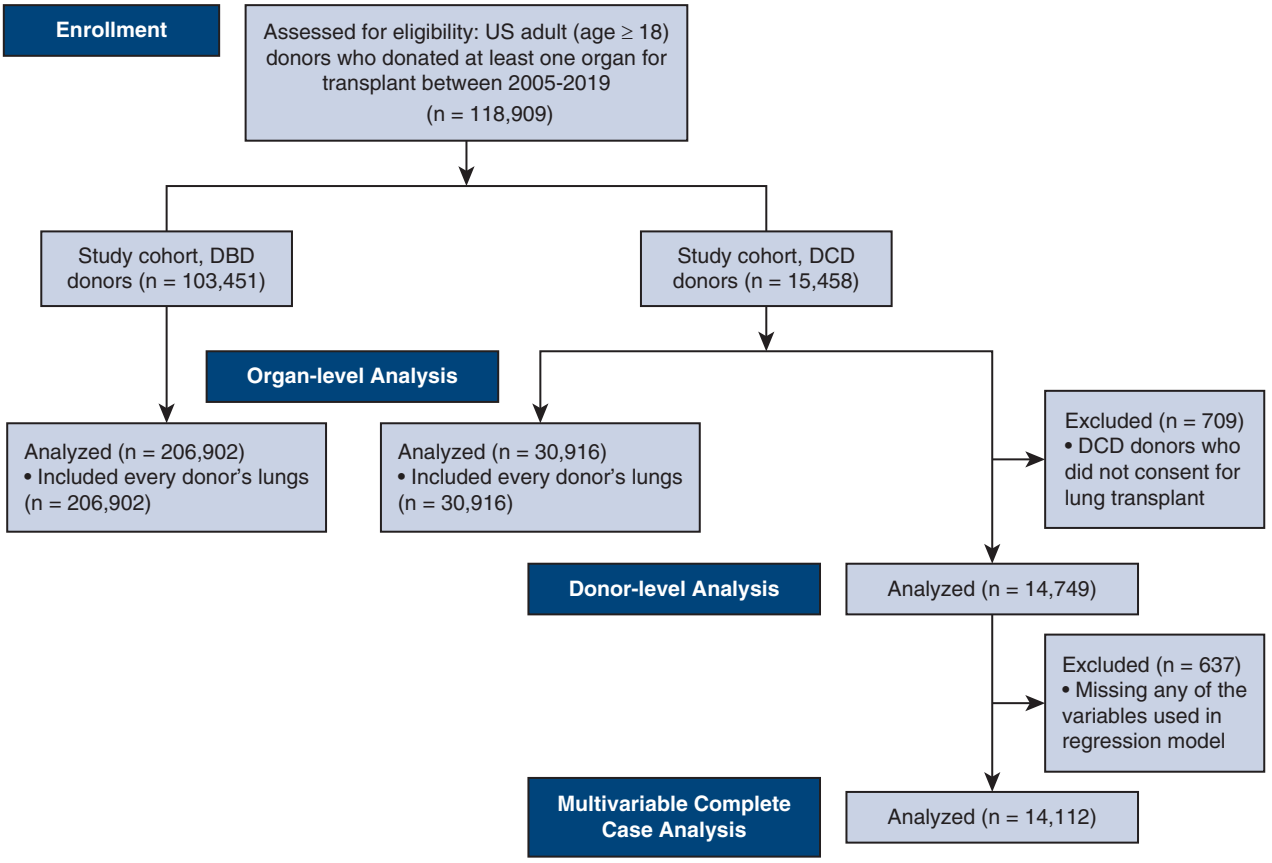


FIGURE 1. CONSORT diagram of study design. All donors who donated at least 1 organ for transplantation between 2005 and 2019 were identified in the UNOS registry and stratified on the basis of DCD and DBD status. Individual organ-level and donor-level analyses were performed. DCD donors who did not consent for LTx were excluded from further analysis because their lungs could not be evaluated or used for transplantation. *DBD*, Donation after brain death; *DCD*, donation after circulatory death.

discarded to the largest extent (47%) in 2015-2019. Annual OPO volume was not significantly different between transplanted and not transplanted groups. Complete baseline characteristics are presented in Table 1. In multivariable regression, P/F ratios below 250 were most strongly associated with nonuse (adjusted OR [AOR], 0.03; $P < .001$), followed by P/F ratios 250-300 (AOR, 0.09; $P < .001$), cigarette use (AOR, 0.28; $P < .001$), P/F ratios 300-350 (AOR, 0.29; $P < .001$), and donor age >50 (AOR, 0.75, $P = .031$) (Figure 2). Conversely, the most recent era, 2015-2019, was associated with an increase in use (AOR, 2.28; $P < .001$).

Organ Disposition and Reasons for Nonuse

All potential lung allografts (30,916) from DCD donors in the study were included in analysis. Of those, 3.7% (1158 lungs) were transplanted and 72.8% (22,513) were discarded, most frequently due to poor organ function and concerns about ischemic time (Figure 3). Consent was not requested in 8.4% of DCD offers. Consent was not obtained from the donor/donor family when requested in 4.6% of DCD lungs. When all potential lung allografts from DBD donors (n = 206,902) were analyzed, the proportions of allografts discarded and consent not obtained were comparable to DCD lungs (DBD 63.3% vs DCD 72.8%, 2.6% vs 4.6%). However, consent not requested in DBD lungs was only one quarter as frequent as in DCD lungs (2.2% vs 8.4%, $P < .001$), with non–heart beating donor being the leading reason (73.4%) not to request consent in the DCD setting. Organ disposition per lung and reasons for nonuse are summarized in Table 2, Figures 3 and 4, and Table E2.

Regional Patterns Associated With DCD Lung Use

When plotted on the map of the United States, DCD LTx rates varied greatly across 11 UNOS regions from 2.5% (Region 6) to 8.1% (Region 10) (Figure 5, *A*). Highest rates of DCD LTx were observed in regions 1, 7, 9, and 10, which corresponded to regions with the highest proportions of DCD (Figure 5, *B*). These regions are from the lower half of regions with respect to the total number of lung transplants performed. All regions are shown on the UNOS website: https://unos.org/community/regions/.

TABLE 1. Donor characteristics stratified by use for transplantation

Donor variable	Not transplanted (n = 14,117)	Transplanted (n = 632)	*P* value
Age, y	40 (26-51)	37 (26-48)	.002
Male gender	9335 (66.1%)	379 (60.0%)	.002
BMI	26.9 (23.1-31.7)	25.6 (22.7-29.5)	<.001
Donor ethnicity			.342
White	11,592 (82.1%)	514 (81.3%)	
Black	1014 (7.2%)	45 (7.1%)	
Hispanic	1161 (8.2%)	50 (7.9%)	
Other	350 (2.5%)	23 (3.6%)	
Cigarette use			<.001
<20 pack-y	10,706 (76.8%)	581 (93.4%)	
20+ pack-y	524 (3.8%)	4 (0.6%)	
20+ pack-y with recent 6-mo use	2704 (19.4%)	37 (5.9%)	
Cocaine use	2580 (18.5%)	107 (17.1%)	.404
Alcohol abuse	3131 (22.5%)	131 (21.1%)	.414
Diabetes	998 (7.1%)	37 (5.9%)	.281
Hypertension	3696 (26.3%)	142 (22.6%)	.044
Cancer	341 (2.4%)	11 (1.7%)	.345
Donor cause of death			<.001
Anoxia	6505 (46.1%)	251 (39.7%)	
Cerebrovascular/stroke	2521 (17.9%)	156 (24.7%)	
Head trauma	4343 (30.8%)	210 (33.2%)	
CNS tumor	26 (0.2%)	2 (0.3%)	
Other	722 (5.1%)	13 (2.1%)	
ABO blood type			.001
A	5526 (39.1%)	235 (37.2%)	
B	1553 (11.0%)	59 (9.3%)	
AB	492 (3.5%)	7 (1.1%)	
O	6546 (46.4%)	331 (52.4%)	
Bilirubin (median, IQR)	0.6 (0.4-0.9)	0.6 (0.4-0.9)	.078
Creatinine (median, IQR)	0.8 (0.6-1.1)	0.8 (0.6-1.0)	.187
AST (median, IQR)	59 (36-104)	51 (32-82)	<.001
ALT (median, IQR)	46 (27-87)	41 (23-75)	<.001
Clinical infection, blood source	1687 (12.0%)	47 (7.4%)	.001
P/F ratio (median, IQR)	230 (145-330)	423 (360-484)	<.001
Era			<.001
2005-2009	2955 (20.9%)	77 (12.2%)	
2010-2014	4532 (32.1%)	128 (20.3%)	
2015-2019	6630 (47.0%)	427 (67.6%)	
Annual OPO volume (median, IQR)*	162 (120-265)	160 (125-250)	.924

This table includes all DCD donors except those who did not consent for LTx. *BMI*, Body mass index; *CNS*, central nervous system; *IQR*, interquartile range; *AST*, aspartate aminotransferase; *ALT*, alanine aminotransferase; *P/F*, PaO2/FiO2 ratio; *OPO*, Organ Procurement Organization. *OPO volume is defined as the annualized number of donors (DCD or DBD) that fit study inclusion criteria managed by OPO.

DISCUSSION

In this retrospective analysis of the 2005-2019 UNOS database, we analyzed DCD donor factors associated with nonuse of donated lungs. Although any smoking history, older age, and lower P/F ratios predicted nonuse, sex and race did not. After our evaluation of organ disposition, we demonstrated that the OPO's consenting practices may represent the largest modifiable predonation factor resulting in nonuse of 4008 lungs (13%).

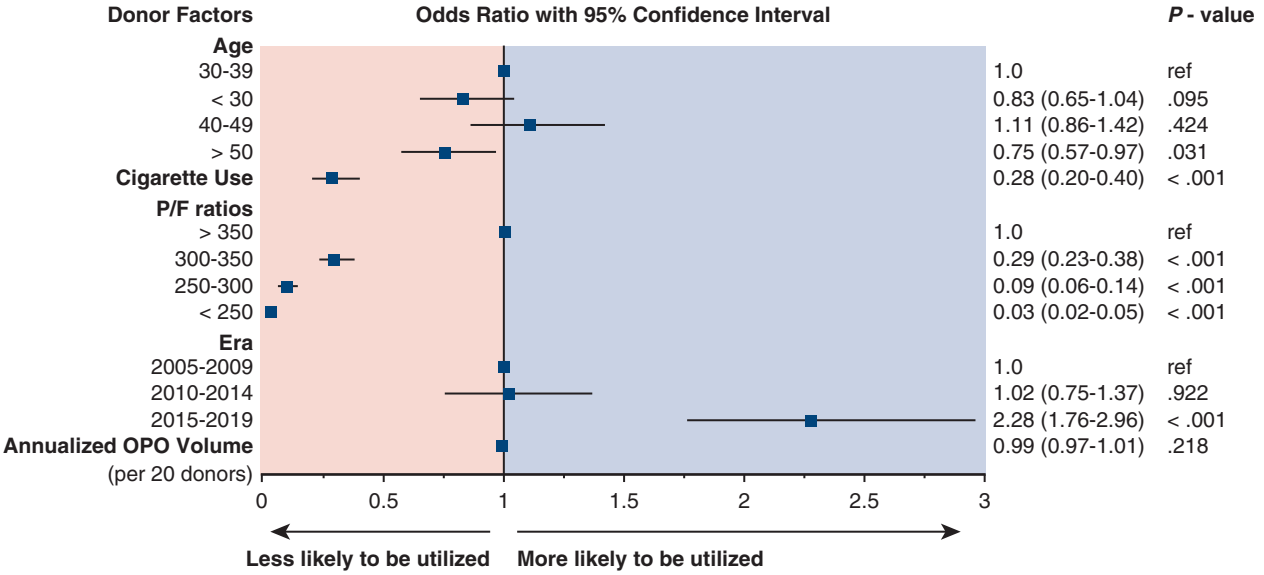


FIGURE 2. Forest plot of donor factors leading to use for transplantation. Multivariable regression modeling was fit to assess the relationship between donor factors and use. P/F less than 250 was most strongly associated with nonuse (adjusted OR [AOR], 0.03; $P < .001$), followed by P/F ratios 250 to 300 (AOR 0.09, $P < .001$), cigarette use (AOR, 0.28; $P < .001$), P/F ratios 300-350 (AOR, 0.29; $P < .001$), and donor age more than 50 years (AOR, 0.75; $P = .031$). Conversely, the most recent era, 2015-2019, was associated with an increase in use (AOR, 2.28; $P < .001$). *P/F*, PaO2/FiO2 ratio; *OPO*, Organ Procurement Organization.

This is the first study, to our knowledge, to examine predonation and donor characteristics of DCD lungs that were not transplanted using a large national transplant database. Underuse of DCD lungs in the United States remains consistent with prior studies, and despite growing evidence showing comparable outcomes in DBD and DCD LTx,[8-16] is lower than in several other countries reporting rates of greater than 20%.[1,5,6] The discrepancy between DBD and DCD lung allograft use has grown in the United States. At present, no international guidelines exist to standardize DCD allograft use practices, and such practices become highly dependent on an institution's available resources and familiarity with DCD procedures. A clear message from our study is that higher DCD donor availability translates to more DCD LTx performed within the region, and thus identifying predonation

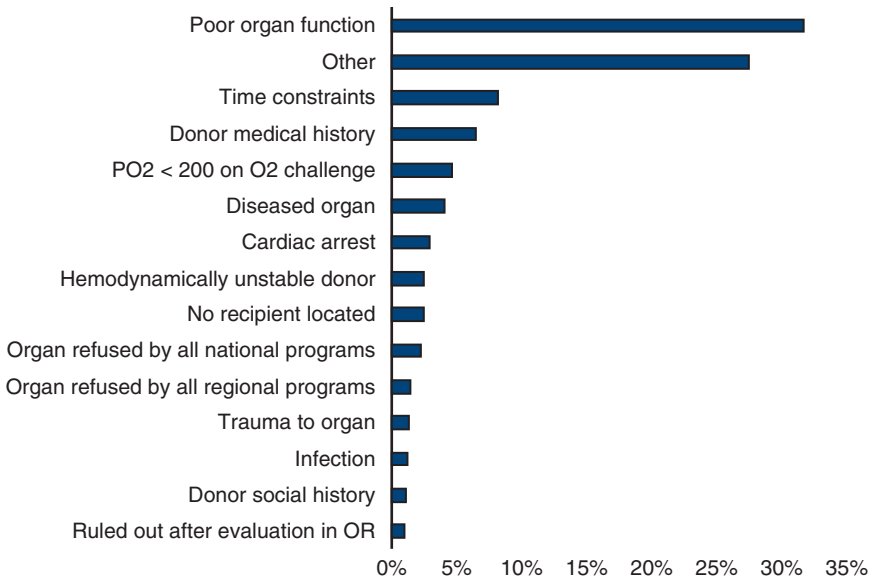


FIGURE 3. Leading reasons for DCD lungs not recovered (n = 22,513). Transplant coordinators record these reasons, and organs were most frequently discarded because of poor organ function and concerns about ischemic time. *OR*, Operation room.

TABLE 2. Comparison of organ disposition per donation after circulatory death lung versus donation after brain death lung, 2005-2019

	DCD lungs (n = 30,916)	DBD lungs (n = 206,902)	*P* value
Consent not requested	8.4% (2590)	2.2% (4588)	<.001
Consent not obtained	4.6% (1418)	2.6% (5315)	<.001
Organ not recovered	72.8% (22,513)	63.3% (130,934)	<.001
Recovered not for transplantation	9.3% (2864)	8.6% (17,787)	<.001
Recovered for transplantation but not transplanted	1.2% (373)	1.0% (1974)	<.001
Transplanted	3.7% (1158)	22.4% (46,304)	<.001

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

factors is just as important as identifying donor factors that lead to nonuse.

At the donor level, smoking history, lower P/F ratios, and older donor age predicted nonuse in DCD LTx. We suspect that these were clinical decisions driven by efforts to avoid adverse outcomes, such as PGD and early mortality. However, these decisions may not be consistent with our current knowledge of the risk factors. In a multicenter study of 1255 LTx recipients, the single donor factor shown to increase the risk for stage 3 PGD was smoking history, whereas a myriad of other factors came from the recipients, including a high body mass index of 25 kg/m^2 or greater, elevated reperfusion fraction of inspired oxygen, and use of cardiopulmonary bypass.[17] Bonser and colleagues[18] demonstrated that recipient survival was, indeed, worse after receipt of a lung from a smoking donor compared with a nonsmoking donor, but that overall survival was significantly better than if the recipient had continued on the wait-list. This suggests that donor smoking history should be carefully evaluated but balanced with considerations for urgency.

In the LTOG results, a lower donor P/F ratio was not found to be associated with PGD.[17] However, when interpreting these results, the authors pointed out that a low donor PaO_2 often eliminates a potential organ from use for transplantation. Precluding donation from donors with lower P/F ratios is an important observation validated by the present study. Therefore, the LTOG results may underestimate this potential predictor, and future guidelines must consider preoperative and intraoperative management of donors to improve assessment before procurement. For instance, variations in donor hospital policies and management of DCD donors by OPOs in the United States, such as limitations on bronchoscopy and diuresis, may lead to falsely low P/F ratios. Selective use of ex vivo lung perfusion (EVLP) for additional assessment is advocated by some; however, many of the good results obtained with

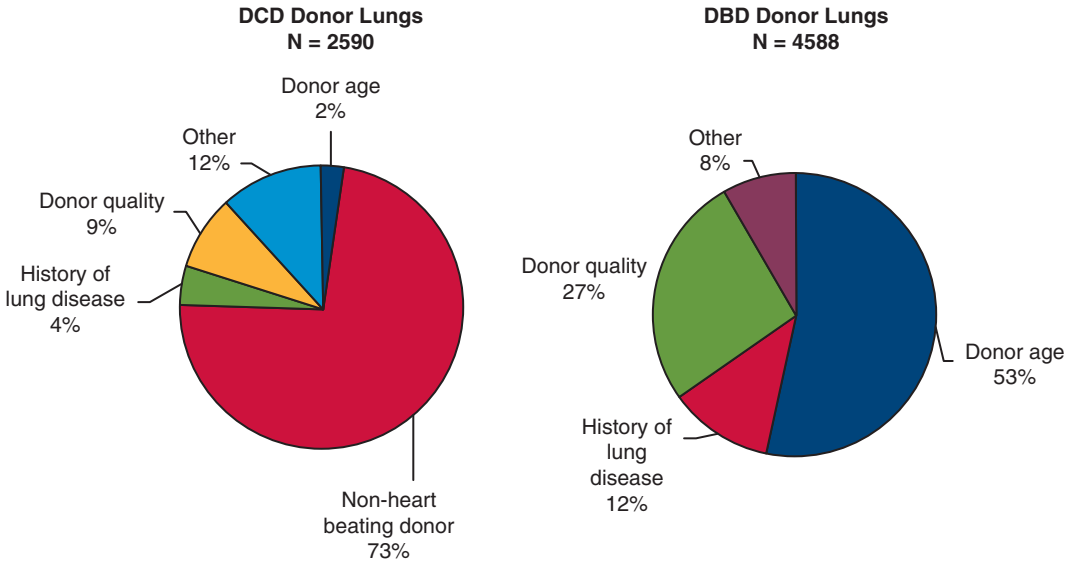
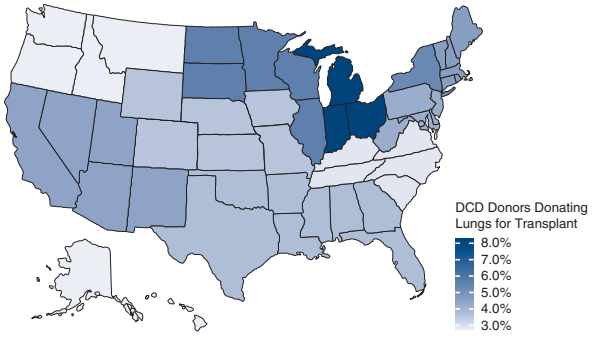


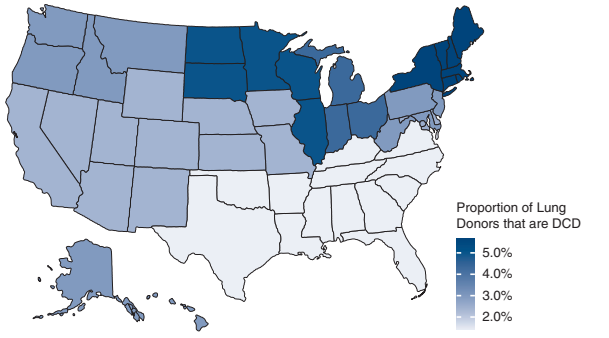
FIGURE 4. Reason for consent not requested by donation type. Regardless of donation type, OPO approach potential donors and their families to request consent for donation in most cases in the United States. In direct comparison of the 2 donation types, DCD and DBD, consent was not requested in 8.4% of DCD offers, whereas this rate was significantly lower in DBD offers at 2.2% ($P < .001$). *DCD*, Donation after circulatory death; *DBD*, donation after brain death.



DCD donors only

UNOS Region	1	2	3	4	5	6	7	8	9	10	11
Not transplanted	923	2204	1421	1094	2004	826	1616	1382	689	1359	1308
Transplanted	39	83	46	34	78	21	97	42	37	120	35
% transplanted	4.1%	3.6%	3.1%	3.0%	3.7%	2.5%	5.7%	2.9%	5.1%	8.1%	2.6%

A



DCD and DBD donors

UNOS Region	1	2	3	4	5	6	7	8	9	10	11
DBD lung transplants	669	2839	3771	2768	3994	742	1945	2057	632	2606	2949
DCD lung transplants	39	83	46	34	78	21	97	42	37	120	35
% DCD	5.5%	2.8%	1.2%	1.2%	1.9%	2.8%	4.8%	2.0%	5.5%	4.4%	1.2%

B

FIGURE 5. A, Proportion of DCD donors donating lungs that resulted in completed transplantation by UNOS region during study period. B, Proportion of lung donors that are DCD by UNOS region during study period. Highest rates of DCD LTx were observed in regions 1, 7, 9, and 10, which corresponded to regions with the highest proportions of DCD. These regions are from the lower half of regions with respect to the total number of lung transplants performed. All regions are shown on the UNOS website: https://unos.org/community/regions/. *DCD*, Donation after circulatory death; *UNOS*, United Network for Organ Sharing; *DBD*, donation after brain death.

lungs from DCD donors were done without the adjunctive use of EVLP.[8,15] The national data collection on EVLP use in donor lungs began in 2018 and should facilitate identification of appropriate opportunities for ex vivo assessments of DCD lungs, including low P/F ratios. The appropriateness may vary tremendously among countries because of differences in management of DCD donors. Ultimately, variations and limitations in donor management policies will affect the utility of EVLP in increasing DCD lung donation, and increasing access to such technology, along with evolving patient evaluation methods and immunosuppressive regimens, likely explains the higher use of DCD lungs in 2015-2019 compared with earlier years.

Early published studies suggested that donor age greater than 50 years, when combined with prolonged ischemic time (>7 hours), demonstrated worse survival after LTx.[19] However, in a more contemporaneous study evaluating this question, prolonged ischemic time was not associated with worse survival, whereas donor age greater than 50 years was.[20] In a separate study focused on DCD LTx, donor age was further shown to be associated with worse survival, but lacked any data regarding cutoff at which worse survival was observed.[10] Age was predictive of nonuse in our study for DCDs more so than DBD. In contradistinction, previously identified donor risk factors for PGD and early mortality, such as sex and race,[19,21-23] were not associated with nonuse for transplantation.

Consent issues represented a sizeable portion of lungs that were not used for clinical transplantation. The proportion of consent not provided by the donor family was slightly higher in the DCD setting, raising the suspicion that family perception does not vary significantly between types of donation. Conversely, we observed a 4-fold difference in the proportion of consent requested, which suggested that consent-seeking behavior of OPOs may explain the difference in the consent rates between DBD and DCD. Although DCD appears to have an impact on the consent process, the Institute of Medicine, Society of Critical Care Medicine, and Scientific Registry of Transplant Recipients, all of which are leading organizations influencing organ-procurement practices in the United States, provide little guidance regarding the consent process for DCD. As such, wide variability in the process has been reported.[24]

With the Centers for Medicare and Medicaid Services' proposed update to OPO performance evaluation scheduled to take effect in 2022 or earlier, now is a critical time to discuss strategies to effectively partner with OPOs to increase awareness. In the proposed update, both donation and transplantation rate outcome measures for OPOs will rely on the number of transplanted organs from each OPO rather than those that are recovered.[25,26] In theory this will incentivize OPOs to pursue all viable organs, but if the centers are not willing to transplant the organs that are pursued by the OPOs, then that will ultimately reflect poorly on the OPOs in this new system. An unintended consequence would be that OPOs' decision to pursue an organ may be more heavily influenced by donor factors such as age, smoking history, and DCD status. In general, the community should discourage OPOs from not evaluating certain donors on the basis of such history without at least extending offers to transplant centers. A few strategies can address

some of these concerns. Increasing communication between centers and OPOs can help ensure that OPOs are aware of whether their affiliated centers are willing to consider DCD lungs. Lowering penalty imposed on OPOs when extended criteria donors, such as DCD donors, are not transplanted would increase pursuit of these organs and subsequent evaluation by procurement teams. Continued discussion is necessary to ensure the evaluation system achieves its intended goals and avoids unintended consequences.

Study Limitations

There are several limitations in the study. Retrospective reviews using large, national databases have the inherent limitation of unmeasured confounders that cannot be accounted for within the analysis. For instance, the database does not account for the use of neuroprotective agents that may aid in prognosis of donor death, aspects of DCD donor assessments that lead to nonuse such as barriers to obtaining studies (computed tomography scans, bronchoscopies) and potentially inflexible withdrawal and operative timing that preclude organ donation. Center volume and travel distance are important variables that influence use of DCD organs but were not included in our analysis because DCD donors are not always associated with a transplant center. When their organs do not result in transplantation, there is no associated transplant center to analyze volume or any other transplant center–associated variables. This is an important variable that may be investigated with a new study cohort consisting of recipients of DCD lungs. Although travel distance from donor hospital to transplant center appears to have an impact on use as time constraint was a leading reason for organ refusal, this information was not available in the database for DCD lungs that were not transplanted. Because each DCD lung was the unit of analysis, lungs that did not result in transplantation would not have travel distance recorded and lead to a skewed analysis. We did not limit our analysis to organs that were transplanted because our primary objective was to examine disposition of every DCD lung. Another limitation was the lack of comprehensive data regarding text response to justify "poor organ quality," which poses a challenge to staging appropriate interventions to improve the quality of DCD organs. Furthermore, documentation of candidate donor P/F ratios before or after recruitment maneuvers was poorly standardized. Nonetheless, the UNOS/OPTN registry is an ideal data source for this analysis, because it captures 100% of transplants performed in the United States and provides a sample size that is able to generate meaningful trends that were deficient in previous single-center retrospective studies.

CONCLUSIONS

Potentially modifiable predonation factors, such as consenting behavior of OPOs, as well as donor factors, including hypoxemia, were associated with nontransplantation of DCD lungs (Figure 6). The initial P/F ratio and other modifiable factors have become relative in the era of ex vivo lung assessment. Thus, every donor should be assessed on a case-by-case basis rather than following predetermined criteria of P/F ratio and age cutoffs. Although this is well known and practiced for DBD donors, the importance of this strategy is acutely increased in DCD donors if the collective goal is to increase the number of available organs suitable for transplantation. With emerging evidence contradicting our previous understanding that certain donor

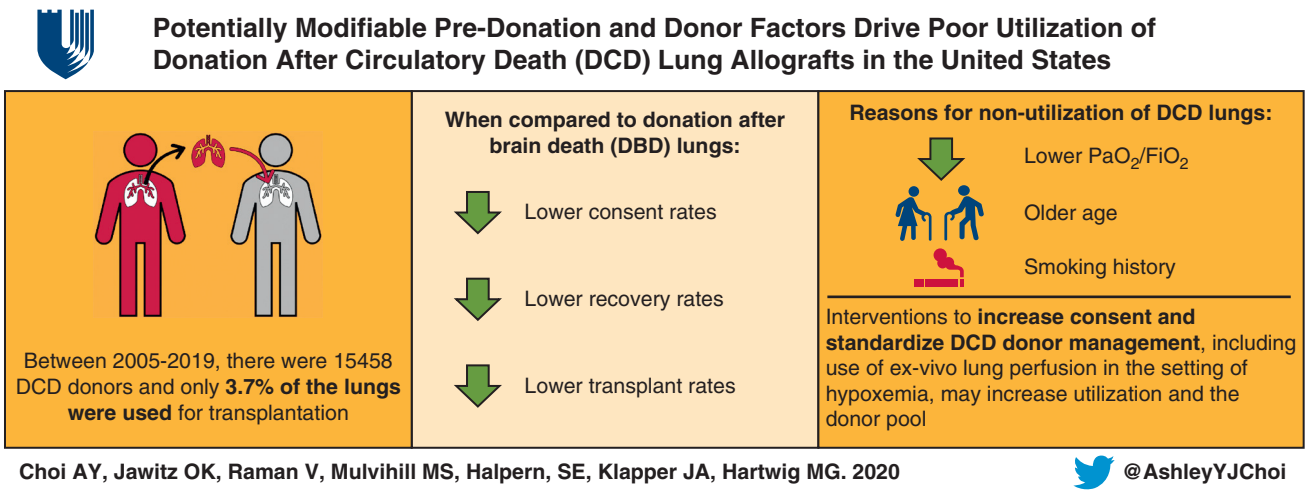


FIGURE 6. Standardized management and optimization of DCD donors within ethical constraints, including the selective use of EVLP, may increase use of DCD organs and expand the donor pool. *DCD*, Donation after circulatory death; *DBD*, donation after brain death.

factors, such as smoking history and donor age, are associated with poor graft survival, evidence-based reassessment of institutional protocols and partnership with OPOs will negate some of these nonmodifiable concerns to recovering DCD lungs.

Conflict of Interest Statement

The authors reported no conflicts of interest.

The *Journal* policy requires editors and reviewers to disclose conflicts of interest and to decline handling or reviewing manuscripts for which they may have a conflict of interest. The editors and reviewers of this article have no conflicts of interest.

References

1. Organ Procurement and Transplantation Network (OPTN) and Scientific Registry of Transplant Recipients (SRTR). OPTN/SRTR 2017 Annual Data Report. Rockville, MD: Department of Health and Human Services, Health Resources and Services Administration; 2019.
2. Steinbrook R. Organ donation after cardiac death. *N Engl J Med*. 2007;357:209-13.
3. Osaki S, Anderson JE, Johnson MR, Edwards NM, Kohmoto T. The potential of cardiac allografts from donors after cardiac death at the University of Wisconsin Organ Procurement Organization. *Eur J Cardiothorac Surg*. 2010;37:74.
4. Singhal AK, Abrams JD, Mohara J, Hasz JD, Nathan HM, Fisher CA, et al. Potential suitability for transplantation of hearts from human non-heart- beating donors: data review from the gift of life donor program. *J Heart Lung Transplant*. 2005;24:1657.
5. Levvey BJ, Harkess M, Hopkins P, Chambers D, Merry C, Glanville AR, et al. Excellent clinical outcomes from a national donation after cardiac death lung transplant collaborative. *Am J Transplant*. 2012;12:2406-13.
6. Cypel M, Sato M, Yildirim E, Karolak W, Chen F, Yeung J, et al. Initial experience with lung donation after cardiocirculatory death in Canada. *J Heart Lung Transplant*. 2009;28:753-8.
7. Thuong M, Ruiz A, Evrard P, Kuiper M, Boffa C, Akhtar MZ, et al. New classification of donation after circulatory death donors definitions and terminology. *Transplant Int*. 2016;29:749-59.
8. Snell GI, Levvey BJ, Oto T, McEgan R, Pilcher D, Davies A, et al. Early lung transplantation success utilizing controlled donation after cardiac death. *Am J Transplant*. 2008;8:1282-9.
9. De Oliveira NC, Osaki S, Maloney JD, Meyer KC, Kohmoto D, D'Alessandro AM, et al. Lung transplantation with donation after cardiac death donors: long-term follow-up in a single center. *J Thorac Cardiovasc Surg*. 2010;139:1306-15.
10. Villavicencio MA, Axtell AL, Spencer PJ, Heng EE, Kilmarx S, Dalpozzal N, et al. Lung transplantation from donors after circulatory death: United States and single center experience. *Ann Thorac Surg*. 2018;106:1619-27.
11. Cypel M, Levvey BJ, Van Raemdonck D, Erasmus M, Dark J, Love R, et al. ISHLT donation after circulatory death registry report. *J Heart Lung Transplant*. 2015;74:1278-82.
12. Mooney JJ, Hedlin H, Mohabir PK, Vazquez R, Nguyen J, Ha R, et al. Lung quality and utilization in controlled donation after circulatory determination of death within the United States. *Am J Transplant*. 2016;16:1207-15.
13. Costa J, Shah L, Robbins H, Raza K, Sreekandth S, Arcasoy S, et al. Use of lung allografts from donation after cardiac death donors: a single-center experience. *Ann Thorac Surg*. 2018;105:271-8.
14. Krutsinger D, Reed R, Blevins A, Puri V, De Oliveira NC, Zych B, et al. Lung transplantation from donation after cardiocirculatory death: a systematic review and meta-analysis. *J Heart Lung Transplant*. 2015;34:675-84.
15. Van Suylen V, Luijk B, Hoek RAS, van de Graaaf EA, Vershuuren EA, Van De Wauwer C, et al. A multicenter study on long-term outcomes after lung transplantation comparing donation after circulatory death and donation after brain death. *Am J Transplant*. 2017;17:2679-86.
16. Mason DP, Thuita L, Alster JM, Murthy SC, Budev MM, Mehta AC, et al. Should lung transplantation be performed using donation after cardiac death? The United States experience. *J Thorac Cardiovasc Surg*. 2008;136:1061-6.
17. Diamond JM, Lee JC, Kawut SM, Shah RJ, Localio AR, Bellamy SL, et al. Clinical risk factors for primary graft dysfunction after lung transplantation. *Am J Respir Crit Care Med*. 2013;187:527-34.
18. Bonser RS, Taylor R, Collett D, Thomas HL, Dark JH, Neuberger J, on behalf of members of the Cardiothoracic Advisory Group to NHS Blood and Transplant and the Association of Lung Transplant Physicians (UK). Effect of donor smoking on survival after lung transplantation: a cohort study of a prospective registry. *Lancet*. 2012;380:747-55.
19. De Perrot M, Bonser RS, Dark J, Kelly RF, McGiffin D, Menza R, et al. Report of ISHLT working group on primary lung graft dysfunction part III: donor-related risk factors and markers. *J Heart Lung Transplant*. 2005;24:1460-7.
20. Mulvhill MS, Gulack BC, Ganapathi AM, Speicher PJ, Englum BR, Hirji SA, et al. The association of donor age and survival is independent of ischemic time following deceased donor lung transplantation. *Clin Transplant*. 2017;31:e12993.
21. Whitson BA, Nath DS, Johnson AC, Walker AR, Prekker ME, Radosevich DM, et al. Risk factors for primary graft dysfunction after lung transplantation. *J Thorac Cardiovasc Surg*. 2006;131:73-80.
22. Christie JD, Kotloff RM, Pochettino A, Arcasoy SM, Rosengard BR, Landis JR, et al. Clinical risk factors for primary graft failure following lung transplantation. *Chest*. 2003;124:1232-41.
23. Meyer DM, Bennett LE, Novick RJ, Hosenpud JD. Effect of donor age and ischemic time on intermediate survival and morbidity after lung transplantation. *Chest*. 2000;118:1255-62.
24. Wendler D, Dickert N. The consent process for cadaveric organ procurement: how does it work? How can it be improved? *JAMA*. 2001;285:329-33.
25. Centers for Medicare and Medicaid Services. Fact sheet organ procurement organization (OPO) conditions for coverage proposed rule: revisions to outcome measures for OPOs. CMS; 2019. Available at: www.cms.gov/newsroom/fact-sheets/organ-procurement-organization-opo-conditions-coverage-proposed-rule-revisions-outcome-measures-opos. Accessed April 5, 2020.
26. Snyder JJ, Musgrove D, Zaun D, Wey A, Salkowski N, Rosendale J, et al. The centers for Medicare and Medicaid services' proposed metrics for recertification of organ procurement organizations: evaluation by the scientific registry of transplant recipients. *Am J Transplant*. March 11, 2020 [Epub ahead of print].

Key Words: transplantation, lung transplantation, donation after circulatory death, organ procurement, ex vivo lung perfusion

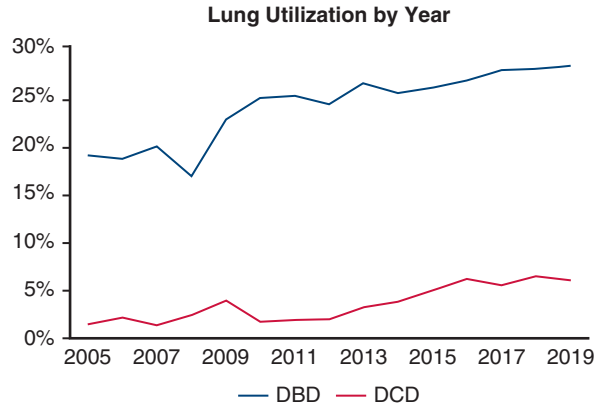


FIGURE E1. Lung use by year. *DBD*, Donation after brain death; *DCD*, donation after circulatory death.

TABLE E1. Summary of missing variables

Donor variable	Not transplanted (n = 14,117)	Transplanted (n = 632)
Age	0.0%	0.0%
Male gender	0.0%	0.0%
BMI	0.2%	0.2%
Donor ethnicity	0.0%	0.0%
Cigarette use	1.3%	1.6%
Cocaine use	1.4%	1.1%
Alcohol abuse	1.6%	1.6%
Diabetes	0.3%	0.5%
Hypertension	0.5%	0.6%
Cancer	0.2%	0.5%
Donor cause of death	0.0%	0.0%
ABO blood type	0.0%	0.0%
Bilirubin (median, IQR)	1.5%	0.3%
Creatinine (median, IQR)	0.0%	0.3%
AST (median, IQR)	1.3%	0.5%
ALT (median, IQR)	1.2%	0.5%
Clinical infection - blood source	0.0%	0.0%
P/F ratio (median, IQR)	3.1%	0.6%
Era	0.0%	0.0%
Annualized OPO volume	0.0%	0.0%

BMI, Body mass index; *IQR*, interquartile range; *AST*, aspartate aminotransferase; *ALT*, alanine aminotransferase; *P/F*, PaO2/FiO2 ratio; *OPO*, Organ Procurement Organization.

TABLE E2. Complete summary of leading reasons for donation after circulatory death (n = 22,513) and donation after brain death (130,934) lungs not recovered

	Reason for organ not recovered	DCD (n = 22,513)	DBD (n = 130,934)
200	Poor organ function	7136 (31.70%)	56,493 (43.15%)
201	Cardiac arrest	645 (2.87%)	82 (0.06%)
202	Infection	260 (1.15%)	2404 (1.84%)
203	Positive hepatitis	102 (0.45%)	3531 (2.70%)
204	Positive HIV	6 (0.03%)	106 (0.08%)
205	Diseased organ	905 (4.02%)	5459 (4.17%)
206	Anatomic abnormalities	11 (0.05%)	227 (0.17%)
207	Vascular damage	0 (0.00%)	31 (0.02%)
208	No recipient located	530 (2.35%)	6358 (4.86%)
209	Donor medical history	1442 (6.41%)	8977 (6.86%)
210	Donor social history	237 (1.05%)	1690 (1.29%)
211	Positive HTLV-1	2 (0.01%)	99 (0.08%)
212	Biopsy findings	0 (0.00%)	32 (0.02%)
213	Surgical damage in operating room	3 (0.01%)	46 (0.04%)
214	No local recovery team	18 (0.08%)	40 (0.03%)
215	Organ refused by all regional programs	317 (1.41%)	2719 (2.08%)
216	Organ refused by all national programs	498 (2.21%)	5790 (4.42%)
217	Organ refused by all programs with urgent need	60 (0.27%)	464 (0.35%)
218	Ruled out after evaluation in operating room	214 (0.95%)	7464 (5.70%)
219	Ruled out after biopsy	1 (0.00%)	19 (0.01%)
220	Ejection fraction <50%	0 (0.00%)	14 (0.01%)
221	Partial pressure of oxygen <200 on oxygen challenge	1043 (4.63%)	13,729 (10.49%)
222	Hemodynamically unstable donor	539 (2.39%)	1549 (1.18%)
223	Trauma to organ	278 (1.23%)	2974 (2.27%)
224	Positive Gram stain	44 (0.20%)	476 (0.36%)
225	Time constraints	1820 (8.08%)	1809 (1.38%)
226	Medical examiner restricted	212 (0.94%)	1416 (1.08%)
295	Donor history undetermined	2 (0.01%)	6 (0.00%)
299	Other	6188 (27.49%)	6930 (5.29%)

Transplant coordinators record these reasons, and organs were most frequently discarded due to poor organ function and concerns about ischemic time in both donation types.
DCD, Donation after circulatory death; *DBD*, donation after brain death; *HIV*, human immunodeficiency virus; *HTLV-1*, human T-cell leukemia virus 1.