Improving National Results in Liver Transplantation Using Grafts From Donation After Cardiac Death Donors

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Background. Published reports describing the national experience with liver grafts from donation after cardiac death (DCD) donors have resulted in reservations with their widespread utilization. The present study aimed to investigate if temporal improvements in outcomes have been observed on a national level and to determine if donor and recipient selection have been modified in a fashion consistent with published data on DCD use in liver transplantation (LT). **Methods.** Patients undergoing DCD LT between 2003 and 2014 were obtained from the United Network of Organ Sharing Standard Transplant Analysis and Research file and divided into 3 equal eras based on the date of DCD LT: era 1 (2003-2006), era 2 (2007-2010), and era 3 (2011-2014). **Results.** Improvement in graft survival was seen between era 1 and era 2 ($P = 0.001$) and between era 2 and era 3 ($P < 0.001$). Concurrently, an increase in the proportion of patients with hepatocellular carcinoma and a decrease in critically ill patients, retransplant recipients, donor age, warm ischemia time greater than 30 minutes and cold ischemic time also occurred over the same period. On multivariate analysis, significant predictors of graft survival included: recipient age, biologic MELD score, recipient on ventilator, recipient hepatitis C virus + serology, donor age and cold ischemic time. In addition, even after adjustment for all of the aforementioned variables, both era 2 (hazard ratio, 0.81; confidence interval, 0.69-0.94; $P = 0.007$), and era 3 (hazard ratio, 0.61; confidence interval, 0.5-0.73; $P < 0.001$) had a protective effect compared to era 1. **Conclusions.** The national outcomes for DCD LT have improved over the last 12 years. This change was associated with modifications in both recipient and donor selection. Furthermore, an era effect was observed, even after adjustment for all recipient and donor variables on multivariate analysis.

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Liver transplantation (LT) using donation after cardiac death donors (DCD) represents 1 potential means to help address the rising discrepancy between the number of LT candidates and the availability of organs.[1] Initial reports examining the use of liver grafts from DCD described inferior long term outcomes when compared with donation after brain death donors (DBD). These inferior results were ascribed to high rates of biliary complications, as well as increased rates of primary nonfunction and hepatic artery thrombosis.[2-6] These initial reports have resulted in reservations with the use of liver grafts from DCD donors; as a result, the number of LT using these organs has not increased as much as initially projected.[7]

Multiple studies have described both donor and recipient factors associated with inferior results with DCD LT. As with all innovations in surgical and medical care of patients, there is likely a learning curve for the optimal utilization of liver grafts from DCD. Collectively, because community behaviors are often modified based on published reports, resulting in improvement of results. More recent publications using new techniques and better patient selection when implanting DCD organs have suggested that lower rates of complications for ischemic cholangiopathy (IC), primary nonfunction, and hepatic artery thrombosis along with higher survival rates can be achieved.[8-12] These temporal differences in outcome highlight learning curve associated with experience in both donor and recipient selection with the use of DCD grafts.

The present study aimed to investigate if temporal improvements in DCD outcomes have been observed on a national level and to determine if donor and recipient selection have been modified in a fashion consistent with published data on DCD LT.

MATERIALS AND METHODS

After approval from the Mayo Clinic Institutional Review Board, data were obtained and extracted from the United Network of Organ Sharing (UNOS) Standard Analysis and Research file. The study population included all DCD LT

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performed in the United States from January, 1 2003, to December 31, 2014. DCD LTs were divided into 3 equal eras based on the date of LT: era 1 (2003-2006), era 2 (2007-2010), and era 3 (2011-2014).

Donor and recipient factors were examined, including all the components of the liver donor risk index, donor sex, donor body mass index (BMI), donor warm ischemia time (dWIT), recipient age, recipient BMI, recipient sex, recipient etiology of liver disease, model for end-stage liver disease (MELD) score at transplant, presence of hepatocellular cancer (HCC) as a secondary diagnosis, retransplantation, mechanical ventilation at the time of transplant, and medical condition at the time of transplant.

Graft survival was calculated from the time of transplant until death, graft loss, or date of last follow-up. The occurrence and the date of death were obtained from data reported to the Scientific Registry of Transplant Recipients (SRTR) by transplant centers and were completed by data from the US Social Security Administration and from the Organ Procurement Transplant Network.

All statistical analyses were performed using STATA 12 (Stata Corp., College Station, TX). Differences between groups were analyzed using the unpaired *t* test for continuous variables and by the χ^2 test or continuity correction method for categorical variables. Wilcoxon rank-sum was used for variables that did not display a normal distribution. Survival curves for patient or graft survival were generated using the Kaplan-Meier method and compared by the log-rank test. Cox proportional hazard multivariate regression with backwards stepwise selection for graft survival was performed. All statistical tests were 2-sided, and differences were considered significant when *P* value is less than 0.05.

RESULTS

Between January 1, 2003, and December 31, 2014, a total of 3199 DCD LT was performed in the United States. Median number of DCD LT performed annually was 214 in era 1, 285 in era 2, and 300 in era 3 (Figure 1). Median number of DCD LT performed by each transplant center over the study period was 16 (range, 1-256). UNOS regions with highest proportion of DCD LT included regions 7 and 6 (8.3% and 8.2%, respectively), whereas UNOS regions with the lowest proportion of DCD LT included region 4, region 11, region 9, and region 5 (1.4%, 2.9%, 3.2%, and 3.5%, respectively). Median match MELD score, biologic MELD score, and percentage DCD by region over the 3 eras can be seen in **Supplemental Table** (**SDC,** http://links.lww.com/TP/B346). The proportion of DCD LT also varied significantly by organ procurement organization, ranging from 0.4% to 14.8% (Figure 2).

Recipient characteristics in each of the 3 eras can be seen in Table 1A. Mean recipient age at LT increased between era 1 (52.7 ± 11.6) and era 2 (54.2 ± 11.0) ($P = 0.003$) and between era 2 and era 3 (56.0 ± 10.1) ($P < 0.001$). No statistically significant differences in recipient BMI or sex were seen over the 3 eras.

A higher proportion of recipients with hepatitis C virus (HCV)–positive serology were seen between era 1 (38%) and era 2 (44%) ($P = 0.02$) and between era 2 and era 3 (49%) ($P = 0.005$). The proportion of patients with alcoholic cirrhosis and nonalcoholic steatohepatitis increased between era 1 and era 2 (5% to 12%; $P = 0.03$ and 3% to 7%; $P < 0.001$, respectively). The proportion of recipients with cholestatic liver disease decreased between era 1 and era 3 (7% to 5%; $P = 0.02$). The number of patients with a secondary diagnosis of HCC increased between era 1 (19%) and era 2 (26%) ($P < 0.001$) and between era 2 and era 3 (34%) ($P < 0.001$). Biologic MELD score did not change significantly over the 3 eras, whereas a significant increase in match MELD was seen between era 1 and era 3 (21.8 ± 7.4 to 25.5 ± 6.6; $P < 0.001$). The proportion of DCD liver grafts used for retransplants decreased over the 3 eras (6% to 2%; $P < 0.001$) as did the proportion of critically ill recipients in the intensive care unit at the time of

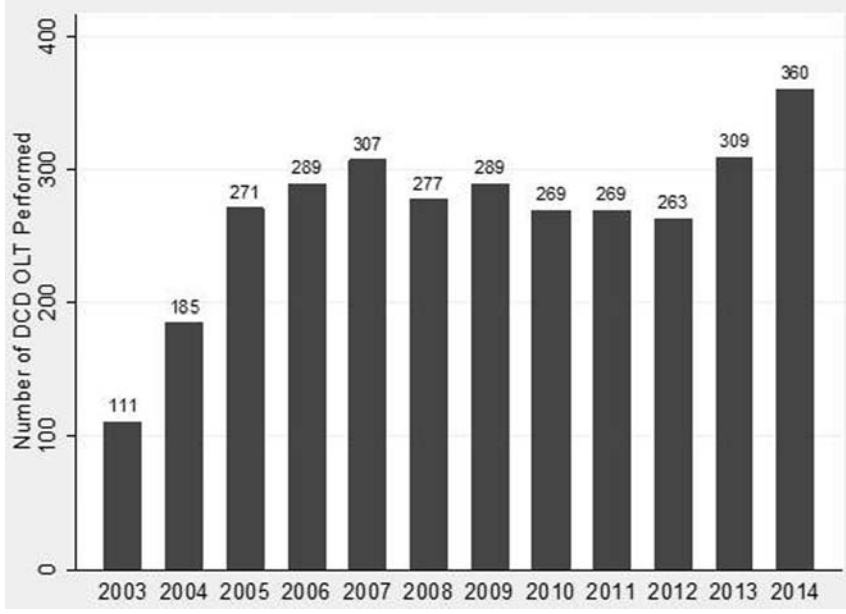

FIGURE 1. Number of liver transplantation using grafts from donation after cardiac death donors performed by year.

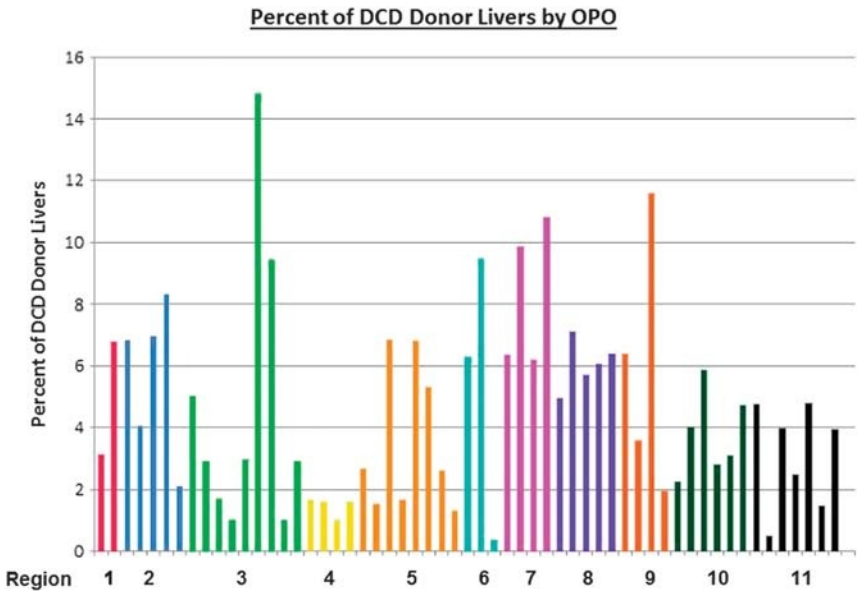

FIGURE 2. Percentage of DCD liver donors by OPO and region.

transplant (13% to 8% $P < 0.001$). The proportion of recipients undergoing a simultaneous liver-kidney (SLK) transplant increased over the 3 eras (4% to 6% $P = 0.006$).

Donor characteristics for the 3 eras can be seen in Table 1B. The proportion of donors aged 60 years or older (5% to 0.7%; $P < 0.001$) and the proportion of donors between ages 50 and 59 years (18% to 11%; $P < 0.001$) decreased significantly over the 3 eras. No significant changes in donor sex, BMI, or ethnicity were seen over the 3 eras. Donor warm ischemic time data were missing in a high number of DCD cases in era 1 (11%) compared with era 3 (0.2%). Of the patients who had complete data on dWIT, there were trends of a lower proportion of patients with long dWIT (>30 minutes); however, these differences were not statistically significant. Mean dWIT remained similar between era 1 (15.6 ± 9.2 minutes) and era 2 (16.2 ± 8.6 minutes) ($P = 0.12$), but did increase significantly between era 2 and era 3 (17.5 ± 7.7 minutes) ($P < 0.001$). Cold ischemia time decreased significantly over the 3 eras (7.7 ± 3.5 hour in era 1 to 5.9 ± 2.9 hour in era 3, $P < 0.001$). The proportion of locally shared organs increased ($P < 0.001$), whereas the proportion of nationally shared organs decreased ($P < 0.001$).

Graft survival for the 3 eras can be seen in (Figure 3). A significant improvement in graft survival was seen between era 1 and era 2 ($P = 0.001$) and between era 2 and era 3 ($P < 0.001$). Graft survival at 1, 3, and 5 years was 72%, 62%, and 55% in era 1; 79%, 69%, and 63% in the era 2; and 85%, 75%, and 67% in era 3. Patient survival for the 3 eras can be seen in Figure 4. No significant change in patient survival was seen between era 1 and era 2 ($P = 0.43$); however, a significant improvement was seen between era 2 and era 3 ($P = 0.03$) and between era 1 and era 3 ($P = 0.001$). Patient survival at 1, 3, and 5 years was 83%, 74%, and 69% in era 1, 86%, 77%, and 71% in the era 2; and 88%, 81%, and 78% in era 3. When comparing the gap in graft survival between DCD and DBD donors over time, a significant improvement in DCD graft survival can be seen by a reduced gap in era 3 compared with era 1 and era 2 (Figure 5).

A multivariate analysis with backward stepwise regression predicting graft survival looking at recipient and donor variables was performed (Table 2). Eras 2 and 3 were included in the model with era 1 as the reference. Variables with significance retained in the model included recipient age (hazard ratio [HR], 1.04; confidence interval [CI], 1.01-1.07; $P = 0.035$), biologic MELD score (HR, 1.07; CI 1.03-1.11; $P = 0.002$), recipient on a ventilator at the time of transplant (HR, 1.65; CI, 1.2-2.2; $P = 0.001$), HCV-positive serology (HR, 1.24; CI, 1.1-1.4; $P = 0.002$), donor age (HR, 1.06; CI, 1.03-1.08; $P < 0.001$), and cold ischemic time (CIT) (HR, 1.03; CI, 1.01-1.05; $P < 0.001$). Even after adjustment for all of the aforementioned variables, both era 2 (HR, 0.81; CI, 0.69-0.94; $P = 0.007$) and era 3 (HR, 0.61; CI, 0.5-0.73; $P < 0.001$) had a protective effect compared to era 1.

DISCUSSION

Due to the inferiority of DCD LT results in early reports, there has been reluctance among many centers to use DCD liver grafts.[3] As with all innovations in transplant practice, there is undoubtedly a learning curve associated with the optimal utilization of liver grafts from DCD donors which has taken place as new data and analyses have become available. Single-center experiences are valuable; however, these provide smaller sample size with underpowered associations. They are also subject to individual practice differences with donor and recipient selection bias as well as surgical technique and medical management of recipients after LT. The current study provides data and analyses to give a broader picture of practice and provides long-term outcomes for recipients of DCD LT. The current study is designed to provide data after implementation of MELD. The present study demonstrates a national improvement in graft survival with DCD LT from 2003 to 2014. Concurrently, there were changes that occurred over the same period in recipient variables, such as the proportion of patients with a diagnosis of HCC, patients who were critically ill or required retransplantation along with donor variables, such as donor age, prolonged

TABLE 1A.

Characteristics in recipients undergoing DCD LT in the 3 eras

Recipient characteristics	Era 1 (2003-2006) N = 856	Era 1 (2003-2006) N = 1142	Era 3 (2011-2014) N = 1201	Era 3 (2011-2014) *P*	Era 2 vs Era 3 *P*	Era 1 vs Era 3 *P*
Age at transplant, y	52.7 ± 11.6	54.2 ± 11.0	56.0 ± 10.1	0.003	<0.001	<0.001
Body mass index	27.9 ± 5.6	28.3 ± 5.8	28.1 ± 5.5	0.12	0.39	0.42
Sex (male)	590 (69%)	770 (67%)	839 (70%)	0.48	0.2	0.65
Diagnosis						
Hepatitis C virus serology	327 (38%)	498 (44%)	584 (49%)	0.02	0.005	<0.001
EtOH	129 (5%)	135 (12%)	149 (12%)	0.03	0.66	0.08
NASH	29 (3%)	80 (7%)	93 (8%)	<0.001	0.49	<0.001
Cholestatic	63 (7%)	73 (6%)	59 (5%)	0.4	0.12	0.02
HCC exception	160 (19%)	296 (26%)	409 (34%)	<0.001	<0.001	<0.001
Calculated MELD score	19.5 ± 9.0	19.9 ± 9.5	19.5 ± 9.8	0.34	0.32	>0.99
Match MELD score	21.8 ± 7.4	23.5 ± 6.8	25.5 ± 6.6	<0.001	<0.001	<0.001
Retransplant	55 (6%)	30 (3%)	20 (2%)	<0.001	0.11	<0.001
SLK	31 (4%)	59 (5%)	76 (6%)	0.1	0.23	0.006
Days on waitlist (at transplanting center)	59	84.5	115			
Mechanical, ventilated or organ perfusion support at transplant	46 (5%)	67 (6%)	46 (4%)	0.64	0.02	0.1
Medical condition						
At home	634 (74%)	886 (78%)	931 (78%)	0.07	0.97	0.07
In hospital (not ICU)	115 (13%)	147 (13%)	175 (15%)	0.71	0.23	0.47
In ICU	107 (13%)	109 (10%)	95 (8%)	0.04	0.16	<0.001

NASH, nonalcoholic steatohepatitis; ICU, intensive care unit.

TABLE 1B.

Characteristics in DCD donors in the 3 eras

Donor Characteristics	Era 1 (2003-2006) N = 856	Era 2 (2007-2010) N = 1142	Era 3 (2011-2014) N = 1201	Era 1 vs Era 2 *P*	Era 2 vs Era 3 *P*	Era 1 vs Era 3 *P*
Age, y						
<18	**108 (13%)**	**137 (12%)**	**128 (11%)**	**0.68**	**0.31**	**0.17**
18-49	553 (65%)	828 (73%)	931 (78%)	<0.001	0.005	<0.001
50-59	152 (18%)	158 (14%)	133 (11%)	0.02	0.04	<0.001
≥60	43 (5%)	19 (1.7%)	9 (0.7%)	<0.001	0.04	<0.001
Sex (male)	563 (66%)	789 (69%)	800 (67%)	0.12	0.2	0.69
BMI	26.1 ± 5.7	26.1 ± 5.7	26.3 ± 5.7	>0.99	0.4	0.43
Race/ethnicity						
White	730 (85%)	960 (84%)	986 (82%)	0.46	0.21	0.06
Black	67 (8%)	89 (8%)	110 (9%)	0.98	0.24	0.29
other	59 (7%)	93 (8%)	105 (9%)	0.3	0.6	0.13
Cause of death						
Anoxia	266 (31%)	403 (35%)	521 (43%)	0.048	<0.001	<0.001
Stroke	183 (21%)	206 (18%)	199 (17%)	0.06	0.35	0.006
Trauma	359 (42%)	473 (41%)	447 (37%)	0.82	0.04	0.03
Other	48 (6%)	60 (5%)	34 (3%)	0.73	0.003	0.002
dWIT, min						
<15	424 (50%)	538 (47%)	462 (38%)	0.28	<0.001	<0.001
15-20	163 (19%)	244 (21%)	345 (29%)	0.2	<0.001	<0.001
20-25	77 (9%)	167 (15%)	217 (18%)	<0.001	0.02	<0.001
25-30	39 (4.6%)	87 (7.6%)	116 (9.7%)	0.005	0.08	<0.001
>30	60 (7.0%)	60 (5.3%)	58 (4.8%)	0.1	0.64	0.036
Unknown	93 (11%)	46 (4%)	3 (0.2%)	<0.001	<0.001	<0.001
Cold ischemia time, h	7.7 ± 3.5	6.9 ± 3.3	5.9 ± 2.9	<0.001	<0.001	<0.001
Share type						
Local	541 (63%)	778 (68%)	860 (72%)	0.02	0.07	<0.001
Regional	213 (25%)	245 (21%)	280 (23%)	0.07	0.28	0.41
National	102 (12%)	119 (10%)	61 (5%)	0.29	<0.001	<0.001

dWIT and CIT. Notwithstanding these modifications, an era effect remained when controlling for the aforementioned changes in multivariate analysis. The improvements in graft survival were likely multifactorial, with the transplant community's behavior being influenced by the emerging data in the field.

Recipient Selection

Previous reports have demonstrated that LT using DCD grafts is associated with inferior outcomes when used in critically ill patients.[13,14] Over the 3 eras in the present study, a decrease in the proportion of recipients in the intensive care unit before LT was observed as was the proportion of ventilated patients between era 2 and era 3. This suggests that programs were avoiding DCD organs for critically ill recipients. The multivariate analysis confirmed that one of the most significant variables in predicting graft survival was the recipient being on a ventilator at the time of LT. Other data also suggested inferior outcomes when DCD organs were used in cases of retransplantation—a decrease in the proportion of retransplant recipients was also observed over the 3 eras.[15]

An inverse relationship has been reported between an increasing MELD score and post-LT outcome when DCD organs are used. Mathur et al[16] noted an HR of 1.47 with the use of DCD LT for patients with a MELD score of 35 or higher in a previous analysis of UNOS data. Biologic MELD score was shown to be a significant predictor of graft survival in the present study. Although the match MELD score increased over the 3 eras, the biological MELD remained relatively low (19.5). This dichotomy can be explained by the increasing proportion of patients with HCC receiving DCD LT. Although early reports speculated on inferior survival when DCD organs were implanted in patients with HCC, more recent data specifically looking at recurrence demonstrated no difference between recipients of DCD and DBD organs.[17,18] Indeed, patients with HCC may represent ideal DCD LT candidates due to their relatively low biological MELD. This may be particularly important in regions of the country where high MELD scores are required to receive a liver offer, especially where MELD exception scores for HCC are now capped at 34.

Data regarding the appropriateness of DCD LT in patients with HCV have been inconsistent.[16,19-23] Several reports suggested that recurrence may be more severe in patients receiving DCD LT, whereas others suggested no difference between DCD and DBD LT. An increase in the proportion of patients with HCV-positive serology was seen over the 3 eras in the present study. This may be partially correlated with an increase in recipients with a secondary diagnosis of HCC. HCV-positive serology was negatively associated with graft survival on multivariate analysis. Most of the current data on the use of DCD organs in patients with HCV came from

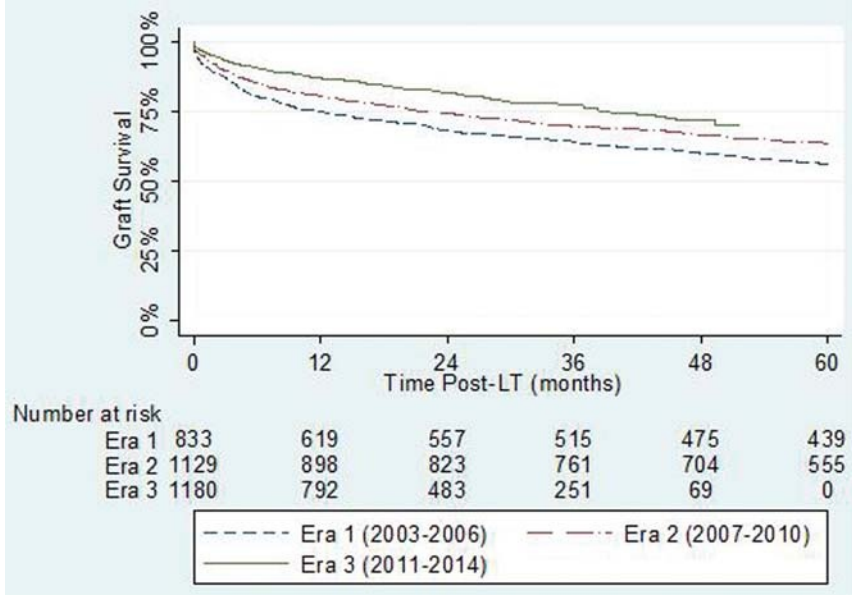

FIGURE 3. Kaplan-Meier graft survival estimates by era of DCD LT. Era 1 versus era 2 ($P = 0.001$), era 2 versus era 3 ($P < 0.001$), era 1 versus era 3 ($P < 0.001$).

the time before the introduction of highly effective direct acting antiviral therapy. With advent of all oral, non–interferon-based regimens, to treat recurrent HCV infection, any discussion about the appropriateness of DCD grafts in this setting can reasonably exclude concerns about the impact of the virus itself. UNOS registry data have also suggested a higher rate of graft failure in patients with primary sclerosing cholangitis (PSC) receiving a DCD LT with an interaction term between DCD and PSC HR of 1.76.[24] Potential mechanisms for inferior outcome in this situation could be related to increased ischemia-reperfusion injury, leading to an autoimmune insult and a predisposition to recurrent PSC.[24] A slight decrease in the proportion of patients with PSC receiving DCD LT was observed over the 3 eras in the present study. This may reflect modifications to practice based on the above data or perhaps concerns with regards to access to the biliary tree with a Roux-en-Y hepaticojejunostomy in patients that may have higher risk of biliary complications.

A slight increase in the proportion of patients undergoing SLK transplantation with DCD grafts as seen over the 3 eras. There has been 1 report that suggested inferior results when using DCD grafts or SLK, whereas others have suggested no differences compared with DBD.[25-27] Data on the role of DCD organs in SLK remain limited. The slight increase in DCD organs for SLK transplantation may reflect the overall increase in patients listed for SLK transplant over that period as well as the difficulty in matching organs for these patients particularly for those with lower biological MELD scores.

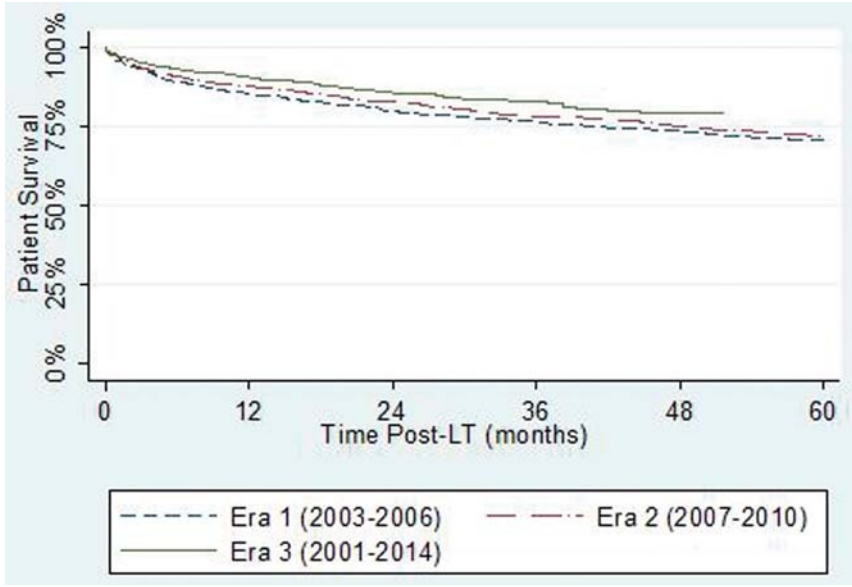

FIGURE 4. Kaplan-Meier patient survival estimates by era of DCD LT. Era 1 versus era 2 ($P = 0.43$), era 2 versus era 3 ($P = 0.03$), era 1 versus era 3 ($P = 0.001$).

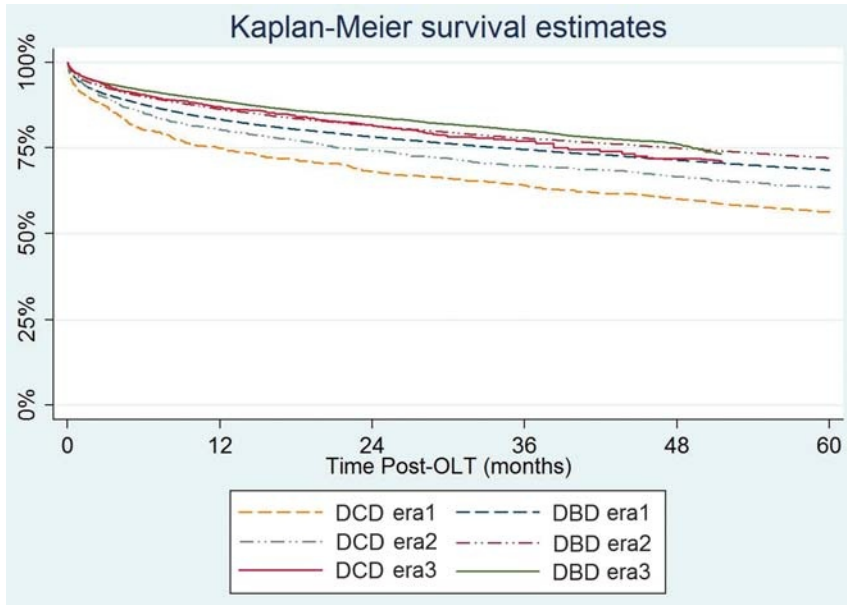

FIGURE 5. Kaplan-Meier patient survival estimates by era of DCD and DBD LT by era. DCD versus DBD: era 1 ($P < 0.001$), era 2 ($P < 0.001$), era 3 ($P = 0.01$).

Donor Selection

One of the variables with the strongest association with inferior outcome in DCD LT is advanced donor age.[2,3] Previous studies reviewing UNOS data have reported a HR for graft loss of 1.26 with donors older than 55 years.[16] The present study demonstrated a decline in the proportionate utilization of donors older than 50 and a larger decline in those older than 60 years throughout the 3 eras. Many centers no longer consider DCD older than 50 years with even fewer pursuing those donors older than 60 years.[16] Donor age was negatively associated with graft survival in our multivariate analysis. Perhaps, the second most widely accepted negative predictor of outcome with DCD LT is prolonged dWIT.[2,13,16] We found that a large proportion of cases in the era 1 (11%) had missing data on the dWIT, decreasing to less than 1% in era 3. This likely represents the transplant community's understanding of the potential pivotal importance dWIT as well as better recording and reporting. A decrease in the proportion of donors with dWIT longer than 30 minutes can be seen in the present study, however, dWIT was not shown to be a significant predictor of graft survival on multivariate analysis. Although CIT is known to be important in all solid organ transplants, particular attention has been given to minimizing CIT in DCD LT.[13,16] CIT decreased significantly over the 3 eras from a mean time 7.7 hours to 5.9 hours and was a significant predictor of graft survival on multivariate analysis.

The improvements in graft survival seen over the 3 eras are undoubtedly multifactorial. Although modifications to both recipient and donor selection were demonstrated over time, an era effect was observed even when controlling for all of these factors in multivariate analysis. This likely represents improvements in technique and selection not captured in the variables reported to UNOS. While total dWIT is clearly important, dWIT is a composite period which includes different components and events from withdrawal of life support till perfusion of preservation solution. Unfortunately, more granular data on dWIT are not available through the SRTR database. We previously have shown that the time from asystole to cross clamping was the most significant predictor of outcome in the withdrawal process.[28,29] These reports have suggested that regardless of the total dWIT, a time from asystole or pulseless electrical activity to cross-clamping of greater than 10 minutes was negatively associated with outcome. Others have described the importance of the time from mean arterial pressure less than 50 mm Hg until perfusion with preservation solution.[30] We speculate that the large amount of missing data on dWIT in era 1 of the present study indicates that not only the length of dWIT but also how the patient progressed to cardiac death was more closely observed in the recent era. Other modifications to DCD LT have occurred that may have influenced the results. Recent reports have suggested that rates of biliary complications, particularly IC, could be reduced using tissue plasminogen activator (tPA).[11] Biliary strictures occurred less commonly in the tPA-treated group (16.5%) versus an historical control group (33.3%) with a much lower rate of diffuse intrahepatic strictures (3.5% versus 21.2%). However, because this study used an historical cohort, one cannot be certain if tPA was

TABLE 2.

Multivariate backwards stepwise regression predicting graft survival

Variable	HR	CI	*P*
Recipient age (per 5 y increase)	1.04	1.01-1.07	0.035
Biologic MELD score (per 5 unit increase)	1.07	1.03-1.11	0.002
On ventilator at LT	1.65	1.22-2.24	0.001
Recipient HCV+ serology	1.24	1.08-1.42	0.002
Donor age (per 5 y increase)	1.06	1.03-1.08	<0.001
Cold ischemic time (per 1 h increase)	1.03	1.02-1.05	<0.001
Era 2 (era 1 reference)	0.81	0.69-0.94	0.007
Era 3 (era 1 reference)	0.61	0.50-0.73	<0.001

solely responsible for the improved results or whether there was an era effect similar to what we have demonstrated herein. Although the use of tPA is promising, a randomized control trial will be required to determine if it has a beneficial effect on outcomes.

The present study shows that in the most recent era, there was significantly improved graft survival compared with previous published reports reviewing national data. A study published in 2006 demonstrated 1-year and 3-year graft survival rates of 70.1% and 60.5% in patients undergoing DCD LT.[13] The current study demonstrated 1-year and 3-year graft survival rates of 85% and 75%, respectively, in era 3. These new data revitalize the discussion about DCD organs providing a potential solution to the significant national shortage in liver grafts. A recent study revealed that 84% of the patients who die on the waiting list with a MELD score less than 15 previously had declined at least 1 organ offer.[31] Importantly, a DCD is not measured as an eligible donor death when calculating livers per eligible donor. Because OPOs are evaluated mainly on this metric, there is little incentive for the pursuit of DCD donors. Better communication between high-performing DCD OPOs and those OPOs with lower numbers of DCD allografts may help to identify strategies to successfully expand the donor pool. It is possible that deaths on the waiting list could be decreased with more widespread acceptance of DCD liver grafts. The current results with DCD LT, no longer support widespread reservations with their usage.

Weaknesses of the present study include its reliance on national registry data with lack of granular detail. In addition, because IC and biliary complications are not reported to SRTR, graft survival was the most accurate outcome measure available.

In conclusion, this study demonstrates a clear improvement in the outcomes of DCD LT in the United States over the last 12 years. Improvement in outcomes are likely multifactorial, partially related to increasing experience in recipient and donor selection. An era effect remains as a major factor even after adjustment for all recipient and donor variables on multivariate analysis, pointing to learning curve over the study period.

REFERENCES

1. Washburn K, Pomfret E, Roberts J. Liver allocation and distribution: possible next steps. *Liver Transpl*. 2011;17:1005–1012.
2. Foley DP, Fernandez LA, Leverson G, et al. Donation after cardiac death: the University of Wisconsin experience with liver transplantation. *Ann Surg*. 2005;242:724–731.
3. Skaro AI, Jay CL, Baker TB, et al. The impact of ischemic cholangiopathy in liver transplantation using donors after cardiac death: the untold story. *Surgery*. 2009;146:543–552.
4. de Vera ME, Lopez-Solis R, Dvorchik I, et al. Liver transplantation using donation after cardiac death donors: long-term follow-up from a single center. *Am J Transplant*. 2009;9:773–781.
5. Jay C, Ladner D, Wang E, et al. A comprehensive risk assessment of mortality following donation after cardiac death liver transplant—an analysis of the national registry. *J Hepatol*. 2011;55:808–813.
6. Jay CL, Lyuksemburg V, Ladner DP, et al. Ischemic cholangiopathy after controlled donation after cardiac death liver transplantation: a meta-analysis. *Ann Surg*. 2011;253:259–264.
7. Parikh ND, Hutton D, Marrero W, et al. Projections in donor organs available for liver transplantation in the United States: 2014-2025. *Liver Transpl*. 2015;21:855–863.
8. Grewal HP, Willingham DL, Nguyen J, et al. Liver transplantation using controlled donation after cardiac death donors: an analysis of a large single-center experience. *Liver Transpl*. 2009;15:1028–1035.
9. DeOliveira ML, Jassem W, Valente R, et al. Biliary complications after liver transplantation using grafts from donors after cardiac death: results from a matched control study in a single large volume center. *Ann Surg*. 2011; 254:716–722.
10. Dubbeld J, Hoekstra H, Farid W, et al. Similar liver transplantation survival with selected cardiac death donors and brain death donors. *Br J Surg*. 2010;97:744–753.
11. Seal JB, Bohorquez H, Reichman T, et al. Thrombolytic protocol minimizes ischemic-type biliary complications in liver transplantation from donation after circulatory death donors. *Liver Transpl*. 2015;21:321–328.
12. Croome KP, McAlister V, Adams P, et al. Endoscopic management of biliary complications following liver transplantation after donation from cardiac death donors. *Can J Gastroenterol*. 2012;26:607–610.
13. Mateo R, Cho Y, Singh G, et al. Risk factors for graft survival after liver transplantation from donation after cardiac death donors: an analysis of OPTN/UNOS data. *Am J Transplant*. 2006;6:791–796.
14. Taner CB, Bulatao IG, Arasi LC, et al. Liver transplantation in the critically ill: donation after cardiac death compared to donation after brain death grafts. *Ann Hepatol*. 2012;11:679–685.
15. Perry DK, Willingham DL, Sibulesky L, et al. Should donation after cardiac death liver grafts be used for retransplantation? *Ann Hepatol*. 2011;10: 482–485.
16. Mathur AK, Heimbach J, Steffick DE, et al. Donation after cardiac death liver transplantation: predictors of outcome. *Am J Transplant*. 2010;10: 2512–2519.
17. Croome KP, Lee DD, Burns JM, et al. The use of donation after cardiac death allografts does not increase recurrence of hepatocellular carcinoma. *Am J Transplant*. 2015;15:2704–2711.
18. Croome KP, Wall W, Chandok N, et al. Inferior survival in liver transplant recipients with hepatocellular carcinoma receiving donation after cardiac death liver allografts. *Liver Transpl*. 2013;19:1214–1223.
19. Hernandez-Alejandro R, Croome KP, Quan D, et al. Increased risk of severe recurrence of hepatitis C virus in liver transplant recipients of donation after cardiac death allografts. *Transplantation*. 2011;92:686–689.
20. Taner CB, Bulatao IG, Keaveny AP, et al. Use of liver grafts from donation after cardiac death donors for recipients with hepatitis C virus. *Liver Transpl*. 2011;17:641–649.
21. Uemura T, Ramprasad V, Hollenbeak CS, et al. Liver transplantation for hepatitis C from donation after cardiac death donors: an analysis of OPTN/UNOS data. *Am J Transplant*. 2012;12:984–991.
22. Wells M, Croome KM, Janik T, et al. Comparing outcomes of donation after cardiac death versus donation after brain death in liver transplant recipients with hepatitis C: a systematic review and meta-analysis. *Can J Gastroenterol Hepatol*. 2014;28:103–108.
23. Tao R, Ruppert K, Cruz RJ, Jr, et al. Hepatitis C recurrence is not adversely affected by the use of donation after cardiac death liver allografts. *Liver Transpl*. 2010;16:1288–1295.
24. Sundaram V, Choi G, Jeon CY, et al. Donation after cardiac death liver transplantation in primary sclerosing cholangitis: proceed with caution. *Transplantation*. 2015;99:973–978.
25. Wadei HM, Bulatao IG, Gonwa TA, et al. Inferior long-term outcomes of liver-kidney transplantation using donation after cardiac death donors: single-center and organ procurement and transplantation network analyses. *Liver Transpl*. 2014;20:728–735.
26. Alhamad T, Spatz C, Uemura T, et al. The outcomes of simultaneous liver and kidney transplantation using donation after cardiac death organs. *Transplantation*. 2014;98:1190–1198.
27. LaMattina JC, Mezrich JD, Fernandez LA, et al. Simultaneous liver and kidney transplantation using donation after cardiac death donors: a brief report. *Liver Transpl*. 2011;17:591–595.
28. Taner CB, Bulatao IG, Perry DK, et al. Asystole to cross-clamp period predicts development of biliary complications in liver transplantation using donation after cardiac death donors. *Transpl Int*. 2012;25:838–846.
29. Taner CB, Bulatao IG, Willingham DW, et al. Events in procurement as risk factors for development of ischeminc cholangiopathy in liver transplantation using donation after cardiac death donors. *Liver Transpl*. 2012;18:100–111.
30. Foley DP, Fernandez LA, Leverson G, et al. Biliary complications after liver transplantation from donation after cardiac death donors: an analysis of risk factors and long term outcomes from a single center. *Ann Surg*. 2011;253:817–825.
31. Lai JC, Feng S, Roberts JP. An examination of liver offers to candidates on the liver transplant wait-list. *Gastroenterology*. 2012;143:1261–1265.