#### **ORIGINAL ARTICLE**



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# The volume-outcomes relationship in donation after circulatory death liver transplantation

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# Abstract

Background: Donation after circulatory death (DCD) liver transplantation (LT) has become an effective mechanism for expanding the donor pool and decreasing waitlist mortality. However, it is unclear if low-volume DCD centers can achieve comparable outcomes to high-volume centers.

Methods: From 2011 to 2019 utilizing the United Network for Organ Sharing (UNOS) database, liver transplant centers were categorized into tertiles based on their annual volume of DCD LTs. Donor selection, recipient selection, and survival outcomes were compared between very-low volume (VLV, n = 1-2 DCD LTs per year), low-volume (LV, n = 3-5), and high-volume (HV, n > 5) centers.

Results: One hundred and ten centers performed 3273 DCD LTs. VLV-centers performed 339 (10.4%), LV-centers performed 627 (19.2%), and HV-centers performed 2307 (70.4%) LTs. 30-day, 90-day, and 1-year patient and graft survival were significantly increased at HV-centers (all P < .05). Recipients at HV-centers had shorter waitlist durations (P < .01) and shorter hospital lengths of stay (P < .01). On multivariable regression, undergoing DCD LT at a VLV-center or LV-center was associated with increased 1-year patient mortality (VLV-OR:1.73, 1.12-2.69) (LV-OR: 1.42, 1.01-2.00) and 1-year graft failure (VLV-OR: 1.79, 1.24-2.58) (LV-OR: 1.28, .95-1.72).

Discussion: Increased annual DCD liver transplant volume is associated with improved patient and graft survival.

#### **KEYWORDS**

allograft survival, donation after circulatory death liver transplantation, high volume liver transplantation, marginal allografts, waitlist mortality

# 1 | INTRODUCTION

In the United States, the supply of transplantable liver allografts is not keeping pace with demand.<sup>1</sup> In 2019, 12 767 new patients were added to the liver transplantation (LT) waiting list, which was higher than any

year previous.<sup>2</sup> To meet waitlist demand, donation after circulatory death (DCD) LT has become an acceptable and effective mechanism for expanding the donor pool and decreasing waitlist mortality.<sup>3-6</sup> Studies from high volume DCD LT centers have recently demonstrated noninferior outcomes for DCD LT when compared to donation after brain

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death (DBD) LT.<sup>7-12</sup> These contributions have led the transplant community to encourage broad adoption of the aggressive utilization of DCD LT to mitigate waitlist mortality. In an effort to disseminate best practices, the American Society of Transplant Surgeons has developed and implemented annual hands-on DCD workshop, covering all facets of DCD recovery and transplantation.

The volume-outcomes relationship for complex surgical procedures was first described in 1979 and found a 16% decrease in mortality when complex surgical procedures were performed at annual high-volume hospitals.<sup>13,14</sup> In an attempt to improve guality and encourage high volume care, annual hospital minimum volume recommendations have been established for certain high-risk surgical procedures.<sup>15</sup> However, in LT, transplant center volume has had an unclear relationship with outcomes.<sup>16-20</sup> In addition, DCD LT is a relatively uncommon procedure mainly performed by a few highutilization centers, and the risks associated with broad adoption remain unknown.<sup>21</sup> Furthermore, United Network for Organ Sharing (UNOS) new acuity circle policy for liver allocation replaced donation service area and regional boundaries previously used, prioritizing recipients up to 500 nautical miles away from the donor hospital for brain dead donors, but only 150 miles for DCD donors.<sup>22</sup> This shift in allocation may force some centers to increase their utilization of DCD LT as they no may no longer have access to local brain dead donors.

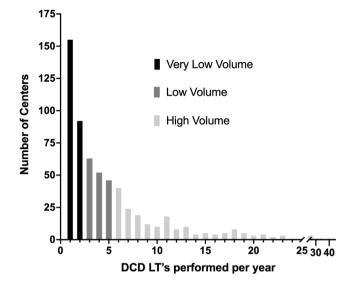
The objective of this study was to assess the relationship between annual transplant center volume and recipient outcomes in DCD LT. Furthermore, we aimed to identify an annual minimum threshold of DCD LTs that centers can strive for to ensure optimal outcomes for their patients. Our hypothesis was that increased annual center volume would be associated with improved outcomes for DCD LT recipients. The relationship between annual center volume and recipient outcomes for DCD LT is especially important for the transplant community as new policies and nationwide metrics are being implemented to encourage increased organ utilization.

### 2 | METHODS

#### 2.1 Data source and study population

The Organ Procurement and Transplantation Network (OPTN) Standard Transplant Analysis and Research (STAR) files were obtained which contain de-identified data on listed patients as well as donors and recipients for every transplant event since October 1987 in the United States.<sup>23</sup> Given that previous work has demonstrated a significant improvement in DCD LT outcomes over time, we chose to only evaluate the most recent era (since 2011) of DCD LT in this study.<sup>5</sup> 3273 DCD LTs were identified between 2011 and 2019 and included in the study. The University of Cincinnati Institutional Review Board (IRB) declared this investigation non-human subjects research and exempt from IRB approval (# 2021-0506).

# Distribution of donation after circulatory death liver transplants performed by center per year



**FIGURE 1** Histogram displaying the distribution of donation after circulatory death (DCD) liver transplant (LT) annual center volume from 2011 to 2019. The lowest tertile corresponds to very-low volume centers which perform 1–2 per year, the middle tertile represents low volume centers which perform 3–5 per year, and the highest tertile represents high volume centers which perform > 5 per year

#### 2.2 | Center volume

Prior to initiation of the analysis, the study team decided to define the volume-based cutoffs (tertiles) in an evidence-based fashion based on the distribution of each transplant centers number of DCD LTs performed in a given year, similar to previously published volumeoutcomes studies (Figure 1).<sup>19,24</sup> From 2011 to 2019, 33% of transplant centers performed 1–2 DCD LT's per year defined as "Very Low Volume" (VLV); 33% performed 3–5 DCD LT's per year defined as "Low Volume" (LV); and 33% of centers performed > 5 DCD LT's per year defined as "High Volume" (HV). Each year of the study period, a transplant center could be considered VLV, LV, or HV based on that individual year's DCD LT volume. Through evaluating center-volume on an annual basis, we attempt to isolate the volume effect, minimizing center-specific and historical confounding.

#### 2.3 Statistical analysis

Descriptive statistics were performed on baseline donor and recipient demographics and clinical characteristics. Data is described with mean  $\pm$  standard deviation if normally distributed, median [interquartile range] for non-parametric distributions, or frequency (percentages) as appropriate. Comparisons of normally distributed continuous variables were conducted with the analysis of variance (ANOVA) assessment, non-parametric distributions with the Wilcoxon-Rank

Sums test, and categorical variables with the Pearson's Chi Squared analysis. If a continuous distribution violated the principle of homogeneity of variances, Welch's ANOVA was conducted. Differences were considered statistically significant for P-values < .05. To best assess cumulative differences in donor characteristics between groups, we used the previously validated UK DCD Risk Score.<sup>25</sup> Patient and graft survival were assessed with multivariable cox-proportional hazards models. Graft survival was measured as a combined endpoint, defined as time from transplant until recipient mortality or allograft failure and re-transplantation. Variables were included in the multivariable model if their contribution was P < .10 in the bivariable analysis. The multivariable survival models adjusted for recipient age, recipient ethnicity, final model for end-stage liver disease (MELD) lab score at transplant, serum creatinine at transplant, serum sodium at transplant, dialysis in the week prior to transplant, intubated at the time of transplant, donor age, donor body mass index, cold ischemia time, warm ischemia time, total center liver transplant volume, and living donor liver transplant volume. To quantify the risk of undergoing DCD LT at a VLV or LV center for 1-year graft failure and patient mortality, bivariable and multivariable logistic regression models were constructed. Similarly, variables were included in the multivariable model if their contribution was significant on bivariable analysis. The multivariable logistic regression models adjusted for recipient age, ethnicity, final MELD lab score, serum creatinine, dialysis in the week prior to transplant, intubated at the time of transplant, donor age, donor body mass index, cold ischemia time, and warm ischemia time. Finally, a sensitivity analysis was conducted to assess the role of total annual center volume (DBD LT plus DCD LT) on recipient outcomes to ensure our analysis isolated the volume effect in DCD LT alone (Figure S1). All statistical analysis were conducted in JMP PRO version 15.0 (SAS Institute Inc., Cary, NC, USA, 1989-2019) and SAS version 9.4 (SAS Institute Inc., Cary, NC, USA, 1989-2019).

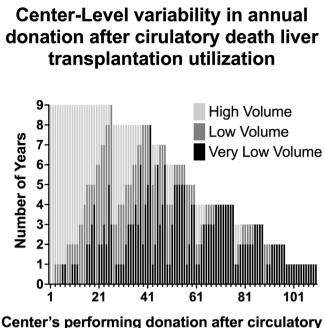
#### 3 | RESULTS

#### 3.1 | Study population

Over the course of the study period, 110 unique transplant centers (78.6% of all centers) performed DCD LT's and accounted for 3273 individual LTs (6.6% of all LTs). VLV centers accounted for 339 (10.4%) of all DCD LTs, LV centers performed 627 (19.2%), and HV centers performed 2307 (70.4%) of all LTs. There was no difference in recipient selection between VLV, LV, and HV centers with respect to recipient age, sex, body mass index, race/ethnicity, etiology of liver disease, final MELD lab score, or medical condition at the time of transplant. However, patients who underwent DCD LT at HV centers spent significantly less time on the waitlist (HV-105 days [29–265] vs. LV-168 days [42–376] vs. VLV-187 days [55–417], P < .01). With respect to donor selection, HV centers accepted older donors (HV-36 years [26–48] vs. LV-29 years [22–39] vs. VLV-28 years [21–38], P < .01), those with

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**FIGURE 2** Grouped bar graph depicting every center that performed donation after circulatory death (DCD) liver transplantation (LT) between 2011 and 2019. The y-axis is the number of years that an individual center was very low volume (VLV, 1–2 DCD LT's per year), low volume (LV, 3–5 DCD LT's per year), or high volume (HV, > 5 DCD LT's per year)

higher body mass indexes (HV-27.4  $\pm$  6.3, LV-26.2  $\pm$  5.7 vs. VLV-25.4  $\pm$  5.5, P < .01), and a higher proportion from a regional share (HV-32.0% vs. LV-12.4% vs. VLV-13.3%, P < .01). There was no difference in the UK DCD risk score, warm ischemia time, or cold ischemia time between groups (Table 1).

## 3.2 | Center-level characteristics

One hundred and ten LT centers performed DCD LTs in the study period and accounted for 603 independent center-years. Among these centers, the median number of years with a DCD LT was 6 [3–8]. Only 26 centers (23.6%) performed at least one DCD LT in every year. Nationwide, only 18 centers (16.4%) were HV centers (performed > 5 DCD LTs) more than 50% of time. However, 48 centers (43.6%) were LV or HV (performed > 2 DCD LTs) more than 50% of the time. In addition, 50 centers (45.5%) were defined as HV at least once throughout the study period. Figure 2 illustrates the significant annual center-level variability associated with DCD LT, with the majority of centers performing VLV DCD LTs annually. Figure 3 illustrates the significant regional variability in utilization of DCD LT: centers in region 10 and region 6 were more likely to perform HV DCD LT, in contrast to centers in regions 1, 3, 4, and 11.

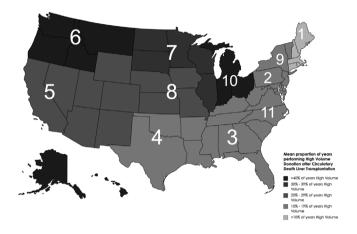
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### **TABLE 1** Donor and recipient baseline patient demographics and clinical characteristics stratified by annual center volume

Clinical characteristic	Very low volume ( <i>n</i> = 339)	Low volume ( <i>n</i> = 627)	High volume $(n = 2307)$	P-value
Recipient age, years, median [IQR]	58 [50-64]	58 [53-63]	58 [52-63]	.52
Recipient sex, Female, n (%)	111 (32.7%)	183 (29.2%)	713 (30.9%)	.50
Recipient BMI, mean ± SD	$28.1 \pm 5.7$	28.6 ± 5.5	28.6 ± 5.6	.29
Race/ethnicity, n (%)				.17
White	230 (67.9%)	472 (75.3%)	1733 (75.1%)	
Black	30 (8.9%)	39 (6.2%)	166 (7.2%)	
Hispanic	60 (17.7%)	79 (12.6%)	272 (11.8%)	
Other	18 (5.7%)	37 (5.9%)	136 (5.9%)	
Recipient MELD at transplant (lab), mean $\pm$ SD	19.5 <u>+</u> 9.3	19.4 <u>+</u> 9.3	19.4 <u>+</u> 8.9	.96
Primary etiology of liver disease, n (%)				.36
Viral hepatitis	59 (17.5%)	129 (20.6%)	445 (19.3%)	
Non-alcoholic steatohepatitis	39 (11.5%)	66 (10.5%)	325 (14.1%)	
Alcoholic cirrhosis	62 (18.3%)	122 (19.5%)	424 (18.4%)	
Malignancy	119 (35.2%)	201 (32.1%)	729 (31.6%)	
Primary sclerosing cholangitis	12 (3.6%)	20 (3.2%)	58 (2.5%)	
Primary biliary cirrhosis	6 (1.8%)	17 (2.7%)	55 (2.4%)	
Metabolic liver disease	7 (2.1%)	8 (1.3%)	60 (2.6%)	
Idiopathic / autoimmune	20 (5.9%)	35 (5.9%)	136 (5.9%)	
Other	14 (4.1%)	29 (4.6%)	75 (3.3%)	
Medical condition at transplant, <i>n</i> (%)				.31
Intensive care unit	24 (7.2%)	45 (7.2%)	124 (5.4%)	
Hospitalized, non-ICU	39 (11.7%)	80 (12.8%)	273 (11.8%)	
Home	271 (81.1%)	499 (80.0%)	1909 (82.8%)	
Hemodialysis prior to transplant, years, n (%)	30 (8.9%)	56 (8.9%)	164 (7.1%)	.22
Waitlist duration, days, median [IQR]	187 [55-417]	168 [42-376]	105 [29-265]	<.01
Length of Stay, days, median [IQR]	9[7-16]	9[7-16]	8[6-13]	<.01
Donor characteristics				
Donor age, years, median [IQR]	28[21-38]	29[22-39]	36[26-48]	<.01
Donor sex, Female, n (%)	105 (31.0%)	192 (30.6%)	772 (33.5%)	.32
Donor BMI, mean ± SD	$25.4 \pm 5.5$	26.2 ± 5.7	$27.4 \pm 6.3$	<.01
Donor race/ethnicity, n (%)				.27
White	267 (78.8%)	509 (81.2%)	1793 (77.7%)	
Black	28 (8.3%)	47 (7.5%)	232 (10.1%)	
Hispanic	36 (10.6%)	52 (8.3%)	218 (9.5%)	
Other	7 (2.4%)	19 (3.0%)	64 (2.8%)	
Donor share, n (%)	, (_, , , , , , , , , , , , , , , , , ,	17 (01070)	0 1 (21070)	<.01
Local	285 (84.1%)	530 (84.5%)	1406 (60.9%)	2.01
Regional	45 (13.3%)	78 (12.4%)	738 (32.0%)	
National	9 (2.7%)	19 (3.0%)	163 (7.1%)	
Cause of death, n (%)		27 (0.070)	100 (	<.01
Anoxia	146 (43.1%)	281 (44.8%)	1175 (50.9%)	1.01
Cerebrovascular Accident	47 (13.9%)	70 (11.2%)	399 (17.3%)	
Head Trauma	136 (40.1%)	255 (40.7%)	646 (28.0%)	
Other	10 (3.0%)	21 (3.3%)	87 (3.8%)	

#### TABLE 1 (Continued)

Recipient characteristics							
Clinical characteristic	Very low volume (n = 339)	Low volume (n = 627)	High volume (n = 2307)	P-value			
Donor microsteatosis, %, mean $\pm$ SD	6.1 ± 9.3	$7.3 \pm 13.5$	7.7 ± 14.7	.73			
Donor macrosteatosis, %, mean $\pm$ SD	$8.4 \pm 16.2$	$4.3 \pm 5.0$	$7.1 \pm 11.4$	.57			
UK DCD risk score, mean $\pm$ SD	$4.7 \pm 3.2$	$4.7 \pm 3.1$	4.9 ± 2.9	.17			
Warm ischemia time, min, median [IQR]	16.5 [11-23]	17[11-22]	18 [11-22]	.34			
Cold ischemia time, hours, median [IQR]	5.7 [4.5-6.8]	5.4 [4.5-6.9]	5.4 [4.4-6.4]	.12			



**FIGURE 3** Map of the United States illustrating the significant regional level variation in utilization of donation after circulatory death (DCD) liver transplantation (LT). Centers in regions 6 and 10 were significantly more likely to perform annual HV DCD LT than centers in regions 1, 3, 4, 11

# 3.3 | Graft survival

Recipients of DCD LTs at HV centers had improved 30-day (HV-95.8% vs. LV- 94.1% vs. VLV- 92.3%, P = .02), 90-day (HV- 93.5% vs. LV-91.2% vs. VLV- 89.2%, P < .01), and 1-year (HV- 85.2% vs. LV- 83.2% vs. VLV- 78.8%, P = .03) graft survival when compared to those at LV and VLV centers (Figure 4). On multivariable logistic regression for 1-year graft failure, undergoing a DCD LT at a VLV center (OR: 1.86 [1.31-2.64], P < .01) and a LV center (OR: 1.31 [.99 – 1.74] P = .06) was associated with an increased odds ratio of graft failure when compared to HV centers (Table 2). Similarly, on multivariable cox-proportional hazards survival modeling, undergoing a DCD LT at a VLV center (HR: 1.66 [1.23 – 2.25], P < .01) and a LV center (HR: 1.18 [.93 – 1.50], P = .16) was associated with an increased risk of long-term graft failure when compared to HV centers (Figure 5A).

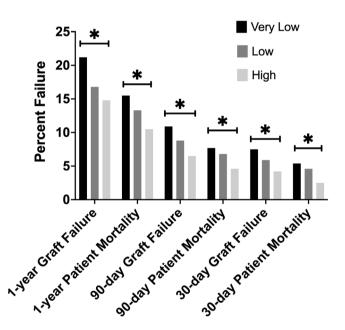
#### 3.4 | Patient survival

Recipients of DCD LTs at HV centers had improved 30-day (HV-97.5% vs. LV- 95.4% vs. VLV- 94.7%, P < .01), 90-day (HV- 95.4% vs.

DCD Liver Outcomes by Annual Center Volume

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**FIGURE 4** Comparison of patient and graft survival outcomes at Very Low Volume (VLV), Low Volume (LV), and High Volume (HV) centers for donation after circulatory death (DCD) liver transplantation. \* = P < .05

LV- 93.2% vs. VLV-92.3%, P = .02), and 1-year (HV- 89.5% vs. LV-86.7% vs. VLV- 84.6%, P = .04) patient survival when compared to those at LV and VLV centers (Figure 4). On multivariable logistic regression for 1-year patient mortality, undergoing a DCD LT at a VLV center (OR: 1.74, [1.12-2.69], P = .01) and at a LV center (OR: 1.42, [1.01-2.00], P = .04) were associated with increased 1-year patient mortality versus HV centers (Table 2). On multivariable coxproportional hazards survival modeling, undergoing a DCD LT at a VLV center (HR: 1.52 [1.07-2.16], P = .02), and at a LV center (HR: 1.22 [.94-1.58], P = .14) were associated with an increased risk of long-term mortality when compared to HV centers (Figure 5B).

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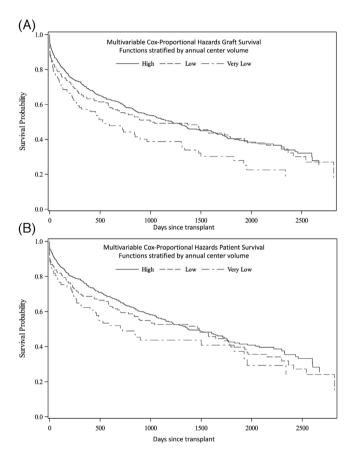
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**TABLE 2** Odds ratios from multivariable logistic regression for 1-year patient and allograft failure, as well as hazard ratios from multivariable cox-proportional hazards models for patient and allograft survival for donation after circulatory death liver transplants between 2011 and 2019

Annual center volume	1-year graft failure (OR: 95% Cl)ª	1-year patient mortality (OR: 95% CI) <sup>a</sup>	Graft survival (HR: 95% Cl) <sup>b</sup>	Patient survival (HR: 95% CI) <sup>b</sup>
Very-low volume	1.86 (1.31–2.64)	1.74 (1.12–2.69)	1.66 (1.23–2.25)	1.52 (1.07–2.16)
Low volume	1.31 (.99–1.74)	1.42 (1.01-2.00)	1.18 (.93–1.50)	1.22 (.94–1.58)
High volume	Reference	Reference	Reference	Reference

<sup>a</sup>Multivariable logistic regression analysis adjusted for: recipient age, ethnicity, final MELD lab score, serum creatinine, dialysis in the week prior to transplant, intubated at the time of transplant, donor age, donor body mass index, cold ischemia time, and warm ischemia time.

<sup>b</sup>Multivariable cox-proportional hazards models were adjusted for: recipient age, recipient ethnicity, final model for end-stage liver disease (MELD) lab score at transplant, serum creatinine at transplant, serum sodium at transplant, dialysis in the week prior to transplant, intubated at the time of transplant, donor age, donor body mass index, cold ischemia time, warm ischemia time, total center liver transplant volume, and living donor liver transplant volume.



**FIGURE 5** (A) Multivariable Cox-Proportional hazards modeling for graft survival functions stratified by annual center volume. In this analysis, high volume centers (> 5/year) had improved survival versus low and very low volume centers. B: Multivariable Cox-Proportional hazards modeling for long-term patient survival functions stratified by annual center volume demonstrating improved survival for recipients of donation after circulatory death liver transplantation at a high-volume center

# 4 DISCUSSION

In this analysis of donation after circulatory death liver transplantation we found that an annual center volume > 5 DCD LTs per year was associated with improved patient and graft survival, independent of total center liver transplant volume. Furthermore, undergoing a DCD LT at a VLV center was independently associated with increased odds of 1year mortality and graft failure. Similarly, undergoing a DCD LT at a LV center was independently associated with 1-year mortality, when compared to recipients who undergo DCD LT at HV center. In addition, there was significant regional and center-based variability in the utilization of DCD LTs nationwide.

Edwards and colleagues first investigated the volume-outcomes relationship for all LT's, not exclusively DCD LT, in 1999 and found centers who performed < 20 LT per year had increased rates of 1-year mortality.<sup>20</sup> Their data was based on the LT's performed between 1992 and 1994, and subsequently Northup et al. re-evaluated the relationship in 2006 using the same cutoff and found that although on unadjusted analysis 1-year mortality was higher at low-volume centers, on multivariable analysis this difference disappeared.<sup>16</sup> This led Northup and colleagues to conclude that LT center volume is no longer an independent predictor of posttransplant survival likely due to improved surgical technique, better immunosuppression, dissemination of best practices, and improved management of complications; signaling significant improvement in nationwide posttransplant management.<sup>16</sup> Similarly, Reese et al. found that center volume over a 10-year period (1996-2005) was not associated with improved outcomes in liver retransplantation.<sup>26</sup> In contrast to these studies, Ozhathil et al. in 2011 demonstrated improved patient and allograft survival with of marginal allografts and Macomber et al. in 2012 demonstrated improved in hospital mortality at high volume centers.<sup>18,19</sup> Our investigation, the first to exclusively evaluate the volume-outcomes relationship in DCD LT, suggest the significant center experience generated from DBD LT may not translate to DCD LT. In fact, on multivariable survival analysis, we found that high total LT volume centers and high living-donor liver transplant centers were not associated with improved DCD LT outcomes; and only, annual DCD LT volume was associated with prolonged patient and graft survival. Despite the similarities in the recipient procedure, the complexities and technical demands of donor retrieval, appropriate matching of donor and recipient to maximize recipient outcomes, and posttransplant management are unique to DCD LT, placing it in a category similar to other complex surgical procedures which benefit from annual minimum thresholds.

The impact of annual center volume on DCD LT recipient outcomes is of particular importance when considering the broader improvements and increasing utilization of marginal grafts nationwide. Zhang and colleagues recently showed patient and graft survival for recipients of marginal allografts has significantly improved from 2002 to 2016 and approach those of benchmark allografts.<sup>1</sup> Similarly, Scalea et al. used the UNOS database to show DCD LT donors < 50 years of age had superior outcomes to DBD LT donors > 60 years old.<sup>27</sup> In the United States and Europe, the recent literature has continued to support the findings that DCD LT is a safe procedure with noninferior survival outcomes when compared to DBD LT.<sup>28-30</sup> However, the majority of these findings are driven by select high-utilization centers.<sup>21</sup> Our study adds to this literature by highlighting the independent significance of annual DCD center volume for achieving high quality recipient outcomes. The lack of a protective effect of annual total transplant center volume (DBD plus DCD) or living donor liver transplant volume, further emphasizes the unique role center volume plays in achieving the best outcomes for DCD LT recipients. Furthermore, as we encourage continued aggressive utilization of DCD donors, preference towards high volume centers in allocation should be a consideration. Another significant intervention may be holding annual DCD LT conferences, where representatives from HV centers disseminate best practices nationwide.

Two recent policy changes in organ allocation have the potential to increase utilization of DCD liver allografts by very-low volume and low volume centers. First, the updated OPTN Final Rule includes larger acuity circles for distribution of DBD liver allografts and has led to a decrease in DBD LT in certain previously low volume regions.<sup>31</sup> This redistribution of allografts will force some centers who have traditionally had their pick of local DBD allografts to increase their utilization of marginal allografts. DCD LT may become a means to supplement the lost LT volume as the acuity circle for DCD LT remains at only 150 miles (in contrast to 500 miles for DBD donors). The second major change, further encouraging the utilization of DCD liver allografts, is the Center for Medicare and Medicaid Services (CMS) reliance on a national metric for determining the denominator for Organ Procurement Organization (OPO) determination of eligible donors.<sup>32</sup> Previously, DCD potential donors were not counted in the denominator of eligible donors; while after this change in policy, all DCD donors will be considered eligible donors, and count towards OPO utilization metrics. This national shift incentivizes OPOs to pursue every possible donor within their region, and likely will significantly increase the availability of DCD liver allografts.<sup>33</sup> As these policies encourage the aggressive utilization of DCD donors, the impact of annual center volume on outcomes becomes even more impactful.

This analysis has several limitations. First, the data source was the UNOS dataset in which all transplant centers enter patient data prospectively but is subject to variability and data missingness. In particular, we were unable to evaluate surgeon-specific annual volumes, and only able to consider volume at the center level. For this analysis, we chose to assess center volume on an annual basis, in contrast to over a ten-year period, and allow individual centers to be classified as VLV, LV, or HV on an annual basis. This methodology allowed us to determine an annual volume threshold but limits our ability to identify HV centerlevel characteristics, because of the fluid nature of the classification. In **Clinical** TRANSPLANTATION

addition, a major issue with DCD LT is ischemic cholangiopathy, and this complication is not well captured in the UNOS dataset.

In conclusion, 1-year and long-term survival outcomes for recipients of donation after circulatory death liver transplantation at annual high-volume centers are better than those at very low volume and low volume centers. These findings suggest that the transplant centers should either commit to the aggressive utilization of DCD LTs or avoid accepting less than 5 DCD LTs every year. In addition, the OPTN could consider annual center volume in DCD LT allocation. As the transplant community strives for improved access, equity, and quality in allocation, the discourse should move towards developing a system that stresses allocating the right allograft, for the right patient, at the right time, and in the case of DCD, at the right center.

#### CONFLICTS OF INTEREST

No conflicts of interest or funding to disclose.

#### DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the Organ Procurement and Transplantation Network. Restrictions apply to the availability of these data, which were used under license for this study. Data are available from https://optn.transplant.hrsa.gov/data/view-data-reports/request-data/ with the permission of The Organ Procurement and Transplantation Network.

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#### REFERENCES

- Zhang T, Dunson J, Kanwal F, et al. Trends in outcomes for marginal allografts in liver transplant. JAMA Surg. 2020;155(10):926-932. https: //doi.org/10.1001/jamasurg.2020.2484
- Kwong AJ, Kim WR, Lake JR, et al. OPTN/SRTR 2019 annual data report: liver annual data report: liver. *Am J Transplant*. 2021;21 Suppl 2:208-315.
- Busuttil RW, Tanaka K. The utility of marginal donors in liver transplantation. *Liver Transpl*. 2003;9(7):651-663.
- Tector AJ, Mangus RS, Chestovich P, et al. Use of extended criteria livers decreases wait time for liver transplantation without adversely impacting posttransplant survival. *Ann Surg.* 2006;244(3):439-450.
- Croome KP, Lee DD, Keaveny AP, Taner CB. Improving national results in liver transplantation using grafts from donation after cardiac death donors. *Transplantation*. 2016;100(12):2640-2647.
- Mihaylov P, Mangus R, Ekser B, et al. Expanding the donor pool with the use of extended criteria donation after circulatory death livers. *Liver Transpl.* 2019;25(8):1198-1208.
- 7. Doyle MB, Collins K, Vachharajani N, et al. Outcomes using grafts from donors after cardiac death. J Am Coll Surg. 2015;221(1):142-152.
- Vanatta JM, Dean AG, Hathaway DK, et al. Liver transplant using donors after cardiac death: a single-center approach providing outcomes comparable to donation after brain death. *Exp Clin Transplant*. 2013;11(2):154-163.
- Taner CB, Bulatao IG, Willingham DL, et al. Events in procurement as risk factors for ischemic cholangiopathy in liver transplantation using donation after cardiac death donors. *Liver Transpl.* 2012;18(1):100-111.
- 10. Croome KP, Lee DD, Perry DK, et al. Comparison of longterm outcomes and quality of life in recipients of donation after cardiac

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death liver grafts with a propensity-matched cohort. *Liver Transpl.* 2017:23(3):342-351.

- 11. Laing RW, Scalera I, Isaac J, et al. Liver transplantation using grafts from donors after circulatory death: a propensity score-matched study from a single center. *Am J Transplant*. 2016;16(6):1795-1804. https://doi.org/10.1111/ajt.13699
- Bohorquez H, Seal JB, Cohen AJ, et al. Safety and outcomes in 100 consecutive donation after circulatory death liver transplants using a protocol that includes thrombolytic therapy. *Am J Transplant*. 2017;17(8):2155-2164.
- Luft HS, Bunker JP, Enthoven AC. Should operations be regionalized? The empirical relation between surgical volume and mortality. N Engl J Med. 1979;301(25):1364-1369.
- 14. Luft HS. The relation between surgical volume and mortality: an exploration of causal factors and alternative models. *Med Care*. 1980;18(9):940-959.
- Birkmeyer JD, Dimick JB. Potential benefits of the new Leapfrog standards: effect of process and outcomes measures. *Surgery*. 2004;135(6):569-575.
- 16. Northup PG, Pruett TL, Stukenborg GJ, Berg CL. Survival after adult liver transplantation does not correlate with transplant center case volume in the MELD era. *Am J Transplant*. 2006;6(10):2455-2462.
- Axelrod DA, Guidinger MK, McCullough KP, Leichtman AB, Punch JD, Merion RM. Association of center volume with outcome after liver and kidney transplantation. *Am J Transplant*. 2004;4(6):920-927.
- Macomber CW, Shaw JJ, Santry H, et al. Centre volume and resource consumption in liver transplantation. *HPB* (Oxford). 2012;14(8):554-559.
- Ozhathil DK, Li YF, Smith JK, et al. Impact of center volume on outcomes of increased-risk liver transplants. *Liver Transpl.* 2011;17(10):1191-1199.
- Edwards EB, Roberts JP, McBride MA, Schulak JA, Hunsicker LG. The effect of the volume of procedures at transplantation centers on mortality after liver transplantation. *N Engl J Med.* 1999;341(27):2049-2053.
- 21. Hobeika MJ, Menser T, Nguyen DT, Beal LL, Zajac S, Graviss EA. United States donation after circulatory death liver transplantation is driven by a few high-utilization transplant centers. *Am J Transplant*. 2020;20(1):320-321.
- 22. Liver and Intestine Distribution Using Distance from Donor Hospital. Accessed: 06/23/2021, 2021. https://optn.transplant.hrsa.gov/media/ 2766/liver\_boardreport\_201812.pdf
- Network OPaT. Data. 2021. https://optn.transplant.hrsa.gov/data/ about-data/
- Singla A, Simons J, Li Y, et al. Admission volume determines outcome for patients with acute pancreatitis. *Gastroenterology*. 2009;137(6):1995-2001.

- 25. Schlegel A, Kalisvaart M, Scalera I, et al. The UK DCD risk score: a new proposal to define futility in donation-after-circulatory-death liver transplantation. *J Hepatol.* 2018;68(3):456-464.
- Reese PP, Yeh H, Thomasson AM, Shults J, Markmann JF. Transplant center volume and outcomes after liver retransplantation. *Am J Transplant*. 2009;9(2):309-317.
- Scalea JR, Redfield RR, Foley DP. Liver transplant outcomes using ideal donation after circulatory death livers are superior to using older donation after brain death donor livers. *Liver Transpl*. 2016;22(9):1197-1204.
- Taylor R, Allen E, Richards JA, et al. Survival advantage for patients accepting the offer of a circulatory death liver transplant. J Hepatol. 2019;70(5):855-865.
- 29. Schlegel A, Scalera I, Perera M, et al. Impact of donor age in donation after circulatory death liver transplantation: Is the cutoff "60" still of relevance?*Liver Transpl.* 2018;24(3):352-362.
- Croome KP, Mathur AK, Lee DD, et al. Outcomes of donation after circulatory death liver grafts from donors 50 years or older: a multicenter analysis. *Transplantation*. 2018;102(7):1108-1114.
- Chyou D, Karp S, Shah MB, Lynch R, Goldberg DS. A 6-month report on the impact of the organ procurement and transplantation network/united network for organ sharing acuity circles policy change. *Liver Transpl.* 2021;27(5):756-759.
- Goldberg D, Karp S, Shah MB, Dubay D, Lynch R. Importance of incorporating standardized, verifiable, objective metrics of organ procurement organization performance into discussions about organ allocation. *Am J Transplant*. 2019;19(11):2973-2978.
- Goldberg D, Kallan MJ, Fu L, et al. Changing metrics of organ procurement organization performance in order to increase organ donation rates in the United States. *Am J Transplant.* 2017;17(12):3183-3192.

#### SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

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