DOI: 10.1002/lt.26461

ORIGINAL ARTICLE



Donation after circulatory death transplant outcomes using livers recovered by local surgeons

Caroline C. Jadlowiec¹ | Elizabeth Macdonough² | Kylie Pont¹ | Kristi Valenti¹ | Blanca Lizaola-Mayo² | Abigail Brooks³ | Devika Das⁴ | Raymond Heilman⁵ | Amit K. Mathur¹ | Winston Hewitt¹ | Adyr Moss¹ | Bashar Aqel² | Kunam S. Reddy¹

¹Division of Transplant Surgery, Department of Surgery, Mayo Clinic, Phoenix, Arizona, USA

²Division of Gastroenterology and Hepatology, Mayo Clinic, Phoenix, Arizona, USA

³Tel Aviv University School of Medicine, Tel Aviv-Yafo, Israel

⁴Division of Internal Medicine, Mayo Clinic, Rochester, Minnesota, USA

⁵Division of Nephrology, Mayo Clinic, Phoenix, Arizona, USA

Earn MOC for this article: www. wileyhealthlearning.com/aasld.aspx

Correspondence

Caroline C. Jadlowiec, Division of Transplant Surgery, Mayo Clinic, 5777 East Mayo Boulevard, Phoenix, AZ 85054, USA. Email: Jadlowiec.Caroline@Mayo.edu Abstract

Donation after circulatory death (DCD) liver transplantation (LT) outcomes have been attributed to multiple variables, including procurement surgeon recovery techniques. Outcomes of 196 DCD LTs at Mayo Clinic Arizona were analyzed based on graft recovery by a surgeon from our center (transplant procurement team [TPT]) versus a local procurement surgeon (non-TPT [NTPT]). A standard recovery technique was used for all TPT livers. The recovery technique used by the NTPT was left to the discretion of that surgeon. A total of 129 (65.8%) grafts were recovered by our TPT, 67 (34.2%) by the NTPT. Recipient age (p = 0.43), Model for End-Stage Liver Disease score (median 17 vs. 18; p = 0.22), and donor warm ischemia time (median 21.0 vs. 21.5; p = 0.86) were similar between the TPT and NTPT groups. NTPT livers had longer cold ischemia times (6.5 vs. 5.0 median hours; p < 0.001). Early allograft dysfunction (80.6% vs. 76.1%; p = 0.42) and primary nonfunction (0.8% vs. 0.0%; p = 0.47) were similar. Ischemic cholangiopathy (IC) treated with endoscopy occurred in 18.6% and 11.9% of TPT and NTPT grafts (p = 0.23). At last follow-up, approximately half of those requiring endoscopy were undergoing a stent-free trial (58.3% TPT; 50.0% NTPT; p = 0.68). IC requiring re-LT in the first year occurred in 0.8% (n = 1) of TPT and 3.0% (n = 2) of NTPT grafts (p = 0.23). There were no differences in patient (hazard ratio [HR], 1.95; 95% confidence interval [CI], 0.76–5.03; p = 0.23) or graft (HR, 1.99; 95% CI, 0.98–4.09; p = 0.10) survival rates. Graft survival at 1 year was

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; CI, confidence interval; CIT, cold ischemia time; DCD, donation after circulatory death; DRI, donor risk index; DWIT, donor warm ischemia time; EAD, early allograft dysfunction; fDWIT, functional donor warm ischemia time; HA, hepatic artery; HAT, hepatic artery thrombosis; HCV, hepatitis C virus; HR, hazard ratio; HTK, histidine tryptophan ketoglutarate; IC, ischemic cholangiopathy; ICU, intensive care unit; INR, international normalized ratio; IQR, interquartile range; LOS, length of stay; LT, liver transplantation; MELD, Model for End-Stage Liver Disease; NASH, nonalcoholic steatohepatitis; NTPT, nontransplant procurement team; OPO, Organ Procurement Organization; OPTN, Organ Procurement and Transplantation Network; OR, operating room; PNF, primary nonfunction; PV, portal vein; TIPS, transjugular intrahepatic portosystemic shunt; TPT, transplant procurement team; UW, University of Wisconsin.

SEE EDITORIAL ON PAGE 1704

This is an open access article under the terms of the Creative Commons Attribution-NonCommercial License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited and is not used for commercial purposes. © 2022 The Authors. *Liver Transplantation* published by Wiley Periodicals LLC on behalf of American Association for the Study of Liver Diseases. 91.5% for TPT grafts and 95.5% for NTPT grafts. Excellent outcomes can be achieved using NTPT for the recovery of DCD livers. There may be an opportunity to expand the use of DCD livers in the United States by increasing the use of NTPT.

INTRODUCTION

Despite improving outcomes with donation after circulatory death (DCD) liver transplantations (LTs), liver allografts from DCD donors continue to be underused. Although contemporary data have demonstrated good outcomes with DCD grafts, concerns regarding decreased survival, ischemic cholangiopathy (IC), and primary nonfunction (PNF) continue to prevent wider use of DCD livers.^[1-7] In addition, the resource usage required to facilitate organ procurement and the lack of reliable indicators predicting donor progression to circulatory death and donor warm ischemia time (DWIT) continue to be barriers to DCD liver use in the United States.^[8–10] Some of the variability in DCD outcomes has been attributed to procurement events, the recovering surgeon, and center experience.^[2,11,12] In the United Kingdom and Eurotransplant, there is more uniformity in organ recovery techniques, and it is common for there to be a regional on-call procurement team. In the United States, however, there is considerable variability in recovery techniques, and most centers use their own team (transplant procurement team [TPT]) for liver allograft recovery, particularly for DCD donors. At our program, we initially started using livers procured by the local surgeon (nontransplant procurement team [NTPT]) when there were time constraints for the DCD recovery and our TPT was unable to travel within the allotted time. With increasing experience, we have begun to rely more on NTPT, particularly for out-of-state donors. The aim of this study was to analyze the outcomes of DCD livers procured by our TPT compared with those procured by the NTPT.

PATIENTS AND METHODS

This was a retrospective study of patients who underwent DCD LT at Mayo Clinic Arizona between January 2015 and December 2020. Multivisceral transplants were excluded. Two groups were defined: DCD liver grafts recovered by surgeons from our TPT and DCD liver grafts recovered by local surgeons (NTPT). Surgeons in the NTPT cohort included those from centers that do not routinely use DCD liver donors as well as fellows. This study was approved by the Mayo Clinic Institutional Review Board (no. 20-006586).

A standardized approach to recovery was used for DCD grafts recovered by our center during this period.^[3]

Our recovery approach consists of a rapid recovery technique in which the abdomen is incised to allow maximal exposure, a medial visceral rotation is performed, and the aorta is cannulated. We use a standardized instrument setup that we prepare prior to donor withdrawal of support. The aortic in situ flush is begun with histidine-tryptophan-ketoglutarate (HTK) preservation solution, and is followed by sequential clamping of the supraceliac aorta, venting of the inferior vena cava in the abdomen, placement of ice, opening of the sternum, and transection of the suprahepatic vena cava. Following these steps, the portal vein (PV) is identified at the level of the pancreas and cannulation of the superior mesenteric vein–splenic confluence is performed to allow for an additional portal venous in situ flush.

DCD organ donation protocols are widely variable in the United States, and determination of which donation protocols are used is decided by the donor hospital. The recovery technique and preservation solution used by the NTPT cohort was left to the discretion of the surgeon. Our center considers all DCD offers regardless of hospital-specific DCD donor protocol variability. Criteria used by our center to accept and use a DCD liver allograft include (1) donor age <65 years; (2) DWIT of <30 min; (3) gross appearance; and (4) when performed, satisfactory liver allograft biopsy findings confirmed by our center's pathology team.

DWIT was defined as the time from withdrawal of donor support to aortic flushing with a preservation solution. This is the definition we use in our clinical decision making. Functional DWIT (fDWIT) was defined as the time from donor systolic blood pressure <50 mm Hg to aortic flushing to align with the UK DCD score,^[13] although we do not use fDWIT as part of our organ acceptance decision-making process. The donor risk index (DRI) was calculated using the following donor variables: age, cause of death, race, DCD status, partial-liver or split-liver graft, height, organ location, and cold ischemia time (CIT).^[14,15] The UK DCD score was calculated as described by Schlegel et al.^[13] Our center does not use composite DCD risk index scores to make clinical decisions regarding DCD use.[13-15] Early allograft dysfunction (EAD) was defined as bilirubin >10 mg/dl on Day 7, international normalized ratio (INR) >1.6 on Day 7, or alanine aminotransferase (ALT) and/or aspartate aminotransferase (AST) >2000 IU/L within the first 7 days.^[16] PNF was defined as early graft failure requiring retransplantation in the absence of technical or immunologic problems.

IC was defined as presence of nonanastomotic extrahepatic or intrahepatic bile duct strictures in the absence of hepatic artery (HA) stenosis or HA thrombosis (HAT) identified with imaging.^[13] All cases of IC were confirmed with endoscopic cholangiography. Indications for first post-LT endoscopy include the presence of a normal liver ultrasound (no underlying vascular or technical issue) with either of the following: (1) cholesteric pattern of liver injury beyond the first posttransplant week or (2) failure for bilirubin to normalize by 3 weeks after transplant.^[3] IC patterns (minor form, confluence dominant, multifocal progressive, diffuse necrosis) were classified as recently published.^[17]

Patients received methylprednisolone for induction and were then started on triple drug immunosuppression (tacrolimus, prednisone, mycophenolate mofetil). Maintenance immunosuppression was reduced to tacrolimus monotherapy by 3–4 months after transplant unless otherwise indicated, with trough levels maintained at 4–7 ng/ml.

Statistical methods

Continuous variables were described using means and standard deviations, and categorical variables were described using count and percentage. Baseline and posttransplant characteristics were analyzed using *t*tests and chi-square analysis. Survival analysis was performed using the Kaplan–Meier curve method. Data were analyzed using GraphPad Prism 8.1.0 (GraphPad Software, Inc.). Multivariable regression analysis was completed looking at risk for DCD cholangiopathy at 1 year after LT.

RESULTS

During this period, 129 DCD LTs were recovered using our TPT (65.8%); 67 were procured by the NTPT (34.2%). In this series, our surgical team attempted 368 DCD LT recoveries, of which 129 (35.1%) were successful. A total of 20 local recovery surgeons without affiliations to our center were used for the 67 NTPT recoveries that occurred in 13 organ procurement organizations (OPOs) spanning Organ Procurement and Transplantation Network (OPTN) Regions 4, 5, 6, and 8. For these NTPTs, 60% (n = 12) of the surgeons were practicing transplant surgeons, all of whom had completed training at fellowships not affiliated with our center; 25% (n = 5) were organ recovery surgeons who only work for OPOs; 10% (n = 2) were fellows from nonaffiliated institutions; and one (n = 1, 5%) was a recovery technician (nonmedical doctor) who works for an OPO (Table 1).

Donor and recipient variables for the two groups are shown in Table 1. The overall median Model for

End-Stage Liver Disease (MELD) score in both groups was 18 (TPT 17 vs. NTPT 18; p = 0.22). Alcohol and nonalcoholic steatohepatitis (NASH) were the most common indications for LT (p = 0.56), and most patients did not have hepatocellular carcinoma (72.4%; n = 142). A small number of recipients had either a transjugular intrahepatic portosystemic shunt (TIPS) 16.3%, n = 32) or PV thrombosis (17.9%, n = 35) at the time of transplant. The majority of recipients were not hospitalized at the time of liver offer (93.9%, n = 184).

Liver allografts recovered using an NTPT were more likely to be regional (76.1% vs. 61.2%) or national (17.9% vs. 12.4%) offers (p = 0.003); 10.4% (n = 7) of these allografts were post–cross clamp offers (Table S4). Both groups had a similar DRI score (p = 0.79) and a similar number of high-risk grafts compared with the TPT group, as calculated through the UK DCD score (34.9% vs. 40.0%; p = 0.14); 4.6% (n = 3) of grafts in the NTPT cohort had a futile UK DCD score. Travel distance (median 609 vs. 370 miles; p < 0.001) and CITs (6.4 ± 1.3 vs. 5.2 ± 0.9 h; p < 0.001) were longer for livers recovered by an NTPT.

Donor withdrawal of support occurred in the operating room (OR) for 45.7% of livers recovered by our TPT and 52.2% of livers recovered by the NTPT (p = 0.13). Withdraw locations outside the OR included the intensive care unit (ICU) and the preoperative anesthesia care unit. There were no time differences between the teams when assessing donor withdrawal of support to declaration of death (p = 0.41), donor declaration of death to aortic flush (p = 0.71), fDWIT (11.9 ± 4.5 vs. 11.4 ± 3.7 min; p = 0.45), or DWIT (p = 0.86). HTK was more commonly used by our TPT (p < 0.001; Table 1).

There were no differences in overall hospital length of stay (LOS) between TPT and NTPT groups (median 6.0 vs. 6.0; p = 0.71). Median ICU LOS was 1.0 day for DCD grafts recovered by our TPT compared with 2.0 days for DCD grafts recovered by an NTPT (p = 0.50; Table 2). Both groups had a similar rate of EAD (TPT 80.6% vs. NTPT 76.1%; p = 0.46), with AST and/or ALT greater than or equal to 2000 U/L in the first week post-LT being the most common criterion observed. No allografts in either group met all three EAD criteria. PNF rates were low (TPT 0.8% vs. NTPT 0.0%; p = 0.47), with only one observed event that occurred in a liver allograft recovered by our TPT. There were no differences in liver function tests (total bilirubin, AST, ALT, alkaline phosphatase, INR) at 1 week, 1 month, 4 months, and 1 year after LT when comparing TPT and NTPT groups (Table S4).

Biliary anastomotic strictures occurred in similar frequency between groups (p = 0.90; Table 3). The median time to endoscopy for an anastomotic stricture for both groups was 1.8 months. The median number of endoscopies required for those with anastomotic strictures was lower compared with that observed for IC (median 4.0 vs. 7.0; p = 0.008). The majority of patients

TABLE 1 Recipient and donor variables and recovering surgeon characteristics

	TPT (<i>n</i> = 129)	NTPT (<i>n</i> = 67)	p value
Recipient			
Age, years	57.9 ± 9.3	59.0 ± 8.7	0.43
Female	51 (39.5)	15 (22.4)	0.02
Hispanic	18 (14.0)	12 (17.9)	0.47
			0.37
White	103 (79.8)	51 (76.1)	
Black	1 (0.8)	2 (3.0)	
Other	7 (5.4)	2 (3.0)	
Biologic MELD score ^a	17.5 ± 6.6 (17.0)	18.8 ± 6.8 (18.0)	0.22
Diagnosis			0.56
Alcohol	29 (22.5)	21 (31.3)	
NASH	39 (30.2)	22 (32.8)	
HCV	22 (17.1)	12 (17.9)	
Cholestatic	12 (9.3)	4 (6.0)	
Cryptogenic	10 (7.8)	2 (3.0)	
Other	17 (13.2)	7 (10.4)	
Hepatocellular carcinoma	35 (27.1)	19 (28.4)	0.18
Prior LT	0 (0.0)	0 (0.0)	_
TIPS	22 (17.1)	10 (14.9)	0.70
PV thrombosis	25 (19.4)	10 (14.9)	0.45
Donor			
Age, years	50.3 ± 10.1	47.9 ± 10.7	0.12
Female	39 (30.2)	18 (26.9)	0.62
BMI, kg/m ²	28.6 ± 6.9	29.2 ± 7.0	0.59
DRI	2.3 ± 0.4 (2.3)	2.3 ± 0.4 (2.4)	0.79
UK DCD score, points ^a			0.14
Low risk, 0–5	83 (64.3)	36 (55.4)	
High risk, 6–10	45 (34.9)	26 (40.0)	
Futile, >10	1 (0.8)	3 (4.6)	
Offer			0.003
Local	34 (26.4)	4 (6.0)	
Regional	79 (61.2)	51 (76.1)	
National	16 (12.4)	12 (17.9)	
CIT, h	5.2 ± 0.9 (5.0)	6.4 ± 1.3 (6.5)	<0.001
Recovering surgeon			-
Practicing transplant surgeon	129 (100.0)	12 (60.0)	
Organ recovery surgeon	-	5 (25.0)	
Abdominal transplant fellow	-	2 (10.0)	
Organ recovery technician	-	1 (5.0)	
Distance from donor hospital to our center, miles	370.0 (138.0–412.0)	609.0 (363.0–775.0)	<0.001
Local	49.9 ± 55.6 (19.1)	92.5 ± 92.8 (76.0)	0.19
Regional	414.2 ± 135.6 (385.0)	534.4 ± 202 (414.0)	<0.001
National	903.5 ± 165.3 (842.0)	1080 ± 247 (1125.0)	0.03

	TPT (<i>n</i> = 129)	NTPT (<i>n</i> = 67)	<i>p</i> value
Donor withdrawal of support location			0.13
Outside the OR	61 (47.3)	23 (34.3)	
In the OR	59 (45.7)	35 (52.2)	
Data unavailable/missing	9 (7.0)	9 (13.4)	
Donor withdrawal of support to declaration of death time, min	16.6 ± 5.8	17.3 ± 4.5	0.41
DWIT, min	21.6 ± 6.7 (21.0)	21.7 ± 4.8 (21.5)	0.86
fDWIT, min ^a	11.9 ± 4.5 (11.0)	11.4 ± 3.7 (11.0)	0.45
Declaration of death-to-aortic flush, min	4.6 ± 2.6 (4.0)	4.5 ± 3.0 (3.0)	0.71
Preservation fluid used for aortic flush			<0.001
НТК	113 (87.6)	5 (7.8)	
UW	16 (12.4)	59 (92.2)	
Volume of aortic flush fluid, L	7.4 ± 2.1 (7.0)	4.4 ± 1.2 (4.0)	<0.001

TABLE 1 (Continued)

Note: Data are provided as *n* (%), mean ± standard deviation, mean ± standard deviation (median), or median (range).

Abbreviations: BMI, body mass index; CIT, cold ischemia time; DCD, donation after circulatory death; DRI, donor risk index; DWIT, donor warm ischemia time; fDWIT, functional donor warm ischemia time; HCV, hepatitis C virus; HTK, histidine tryptophan ketoglutarate; LT, liver transplantation; MELD, Model for End-Stage Liver Disease; NASH, nonalcoholic steatohepatitis; NTPT, nontransplant procurement team; OR, operating room; PV, portal vein; TIPS, transjugular intrahepatic portosystemic shunt; TPT, transplant procurement team; UW, University of Wisconsin.

^aThere were two donors with data missing to calculate the UK DCD score and fDWIT.

TABLE 2 Post-LT outcomes

	TPT (<i>n</i> = 129)	NTPT (<i>n</i> = 67)	p value
ICU LOS, days	1.0	2.0	0.50
Hospital LOS, days	6.0	6.0	0.71
EAD	104 (80.6)	51 (76.1)	0.46
EAD			0.69
0 criteria	25 (19.4)	16 (23.9)	
1 criterion	96 (74.4)	46 (68.7)	
2 criteria	8 (6.2)	5 (7.5)	
Day 7 total bilirubin ≥10 mg/dl	5 (3.9)	5 (7.5)	0.28
Day 7 INR ≥1.6	3 (2.3)	1 (1.5)	0.70
AST/ALT ≥2000 U/L first week	104 (80.6)	50 (74.6)	0.33
Peak post-LT AST, U/L	4824 ± 2375	4217 ± 2616	0.86
PNF	1 (0.8)	0 (0.0)	0.47
HAT	1 (0.8)	1 (1.5)	0.64
HA stenosis	15 (11.6)	2 (3.0)	0.04

Note: Data are provided as median, *n* (%), or mean ± standard deviation. Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; EAD, early allograft dysfunction; HA, hepatic artery; HAT, hepatic artery thrombosis; ICU, intensive care unit; INR, international normalized ratio; LOS, length of stay; LT, liver transplantation; NTPT, nontransplant procurement team; PNF, primary nonfunction; TPT, transplant procurement team.

with an anastomotic stricture were stent free as of last follow-up (TPT 82.2%, NTPT 95.8%; p = 0.11).

IC treated with endoscopic intervention occurred in 18.6% of DCD grafts recovered by our TPT and

TABLE 3 Biliary outcomes

	TPT (<i>n</i> = 129)	NTPT (<i>n</i> = 67)	<i>p</i> value
Biliary anastomotic stricture	45 (34.9)	24 (35.8)	0.90
IC requiring endoscopy	24 (18.6)	8 (11.9)	0.23
Time from LT to first endoscopy, months	2.4 (1.4–3.7)	4.1 (1.9–6.6)	0.63
Number of endoscopies	8.8 ± 4.7 (9.0)	6.6 ± 6.0 (4.5)	0.30
Percentage stent free	14 (58.3)	4 (50.0)	0.68
IC patterns			0.83
Minor form	3 (12.5)	1 (12.5)	
Confluence dominant	10 (41.7)	2 (25.0)	
Multifocal progressive	8 (33.3)	4 (50.0)	
Diffuse necrosis	3 (12.5)	1 (12.5)	
IC requiring re-LT ^a	1 (0.8)	2 (3.0)	0.23

Note: Data are provided as n (%), mean ± standard deviation (median), or median (range).

Abbreviations: IC, ischemic cholangiopathy; LT, liver transplantation; NTPT, nontransplant procurement team; TPT, transplant procurement team. ^aWithin 1 year of LT.

11.9% of DCD grafts recovered by an NTPT (p = 0.23; Table 3). The median time from LT to first endoscopy for IC was 2.4 months in the TPT group compared with 4.1 months in the NTPT group (p = 0.63). Overall, the

median number of endoscopies performed was 7.0 between the two groups (TPT 9.0, NTPT 4.5; p = 0.30). At the time of last follow-up, approximately half of those requiring endoscopy had been successfully treated and were undergoing a stent-free trial (58.3% TPT; 50.0% NTPT; p = 0.68). There were no differences in IC patterns between the two groups (p = 0.83). IC requiring retransplantation in the first year occurred in 0.8% (n = 1) of grafts recovered by our TPT versus 3.0% (n = 2) for those recovered by the NTPT (p = 0.23). Four additional patients required retransplantation within a year as a result of cholestatic allograft failure in the setting of hepatic arterial issues. These allografts were all recovered by our TPT. In looking beyond the first posttransplant year, 2.0% of patients required retransplantation for IC (3.1% TPT vs. 1.5% NTPT; p = 0.69). Those with a diffuse necrosis IC pattern were more likely to fail endoscopic interventions and need re-LT (Table 3).

There were no differences in patient survival (hazard ratio [HR], 1.95; 95% confidence interval [CI], 0.76–5.03; p = 0.23), graft survival (HR, 1.99; 95% CI, 0.98-4.09; p = 0.10), or death-censored graft loss (HR, 1.77; 95% CI, 0.66–4.79; p = 0.31; Figure 1). Median follow-up was 3.5 years (interguartile range [IQR], 2.4-5.3 years) for DCD grafts recovered by our TPT and 3.5 years (IQR, 2.1-5.6 years) for DCD grafts recovered by NTPT surgeons. The 1-year patient and graft survival rates were 95.3% and 91.5%, respectively, in the TPT group compared with 98.5% and 95.5%, respectively, in the NTPT group. In a multivariate model, after accounting for differences in CIT and national offers, the surgeon was not associated with the development of IC within 1 year after LT (odds ratio, 1.46; 95%) CI, 0.57-4.08).

In the NTPT group, there were seven grafts accepted as post-cross clamp offers (10.4%; Table S5). The majority of these offers were nonlocal (71.4%). The median distance from the donor hospital to our center was 775 miles. Median CIT was 7.32 h and hospital LOS (median) was 5 days. Two recipients required endoscopy after LT. One recipient developed IC, which was managed endoscopically. There have been no grafts losses or patient deaths observed for this subset of NTPT grafts.

DISCUSSION

Livers from DCD donors are underused for a variety of factors including the risk and fear of IC, PNF, inferior graft survival, and increased clinical resource utilization.^[1–10] Successful use of DCD allografts requires more resource expenditure before, during, and after transplant.^[3,8–10] Significant center-to-center variability has been described in DCD LT outcomes. In the United Kingdom and Eurotransplant, there is more uniformity in DCD recovery techniques, and it is

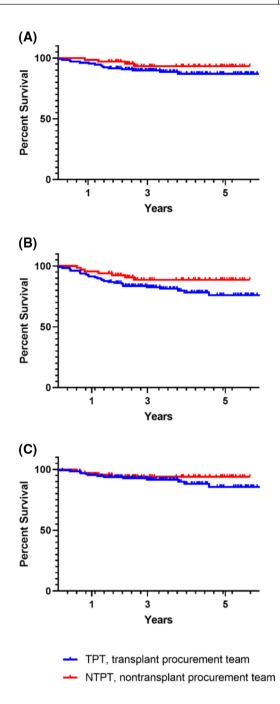


FIGURE 1 Patient and liver allograft survival. (A) Patient survival (HR, 1.95; 95% CI, 0.76–5.03; p = 0.23). (B) Liver allograft survival (HR, 1.99; 95% CI, 0.98–4.09; p = 0.10). (C) Death-censored graft loss (HR, 1.77; 95% CI, 0.66–4.79; p = 0.31)

common for there to be a regional on-call procurement team. In the United States, however, there is considerable variability in recovery techniques. Variation in recovery technique is related to clinical DCD experience during surgeon training and in practice. As a result, recovering surgeon experience is an important component influencing DCD LT outcomes.^[11,12] Our center historically relied exclusively on our own surgical team for DCD allograft recovery. However, there is often reluctance to mobilize a surgical team and resources due to the inability to predict DWIT and uncertainty regarding the ability to recover a transplantable liver allograft.^[7,8,11] There is also a pervasive lack of trust of procurement teams unaffiliated with the transplant program as they may not have a vested clinical interest in the recipient outcomes. We began incorporating the help of local procurement surgeons into our practice as our program grew and logistical constraints led to missed DCD liver opportunities. The aim of this study was to assess whether this shift in practice resulted in differences in DCD LT outcomes as this is a significant problem generalizable to the LT community. In a cohort of 196 DCD LTs, we found no significant differences in DCD LT outcomes based on procurement surgeon affiliation. Of these grafts, 34% were recovered by NTPTs, most of which were related to regional or national import offers, as reflected by longer median travel distances and longer CITs (median 6.5 vs. 5.0 h). Both groups had similar rates of early allograft dysfunction, ICU and hospital LOS, PNF, HAT, and IC. At the time of last follow-up, approximately half of those requiring endoscopy for IC had been successfully treated and were undergoing a stent-free trial (58.3% TPT, 50.0% NTPT; p = 0.68). Graft losses attributed to IC were low for both groups (TPT n = 1, NTPT n = 2). Patient and allografts survival rates were excellent and were similar between the two cohorts. The 1-year graft survival rate for livers recovered by our TPT was 91.5% compared with 95.5% for grafts recovered by an NTPT (Figure 1).

These data are notable for many reasons. First, despite inherent variability in recovering surgeon technique with DCD procurement across 20 different NTPT surgeons, 13 OPOs, and 4 OPTN regions, there were no significant differences with DCD LT outcomes when using grafts recovered by NTPT surgeons (n = 67) versus TPT surgeons (n = 129). The lack of difference in outcomes and good outcomes overall are noteworthy, as the majority of recovery surgeons comprising the NTPT cohort were located in low DCD use OPOs. In assessing for organ acceptance, DWIT of less than 30 min and gross appearance of the liver allograft were the primary factors used by our center to determine organ acceptance and proceed with transplantation. In an era of broader sharing, these data suggest that LT programs can safely pursue DCD LT with allografts recovered by other teams. Fears of poor outcomes can be mitigated with strict organ acceptance protocols and more liberal approaches to the personnel involved.

During this study period, our surgical team participated in 368 DCD LT attempts, of which 35.1% were successful. For our center, a DCD conversion rate of approximately 35% is representative of both recovery attempts by our TPT and the NTPT. The low percentage yield underscores the significant resource expenditure needed to maximize the use of DCD livers and the need to be creative in how to use these livers, which are good

quality but farther away. It also underscores the potential impact NTPT can make in helping to improve the use of DCD donors. Similar to our experience, Montgomery et al. described an average increase of 218 miles for each successful DCD liver procurement compared with each successful DBD liver procurement.^[9] In this study, there was a median difference of 239 miles when comparing the TPT and NTPT teams (p < 0.001). The ability to use local procurement surgeons without compromising outcomes allows for flexibility in logistics as well as minimization of workplace risk associated with procurement travel.^[13] In addition, there is risk of surgeon burnout with increased travel demands. Wider acceptance of NTPTs has the potential to increase the use of DCD donors across the transplant community. In an analysis of the Scientific Registry of Transplant Recipients data, Serrano et al. reported similar graft failure rates for livers procured by TPTs and NTPTs, but lower death-censored graft failure rates in the TPT cohort (HR, 0.96; 95% CI, 0.84-0.99). However, DCD donors compromised only a small proportion in both cohorts (4.9% and 4.5%, respectively). In addition, the difference in death-censored graft survival was small and not clinically significant.^[18] To our knowledge, this is the first study looking specifically at the role of the recovering surgeon on DCD LT outcomes.

The coordination of transplant logistics can become more complex when using NTPT surgeons over larger geographic distances. Our center's nurse-led procurement team is responsible for facilitating the coordination of all transplant logistics during initial organ offers and throughout the organ recovery process and final delivery to our center. Some of their many responsibilities include complex dynamic communication between multiple groups, including patients, the local recovering team (NTPT), the recipient surgical team and the OPO; organ transportation logistics; and scheduling the recipient's surgery. Given the longer geographic distances and inherent increases in CIT, we plan the recipient surgical time so as to minimize delays between liver allograft arrival and reperfusion. This most often results in the start of the hepatectomy prior to organ arrival, inspection, and backable preparation. The decision to do so is based on communication relayed from the NTPT.

Among the LTs in the NTPT group, there were 7 LTs accepted as post–cross clamp offers (10.4%; Table S4). These grafts are typically at very high risk for discard. Recipients of these grafts were not hospitalized at the time of organ offer, and the median door-to-door logistical travel time was 3.0 h. Clinically, this resulted in a median CIT of 7.32 h and a hospital LOS of 5 days. Recipients of these post–cross clamp DCD grafts recovered by NTPT surgeons did well. One recipient developed IC, which was managed endoscopically. There have been no grafts losses or patient deaths observed for this subset of NTPT grafts. The successful use of

post–cross clamp DCD grafts illustrates another area where broader acceptance of NTPT surgeons can lead to increased organ availability for those on the waiting list. Similarly, many of the grafts used in this study came from regional and national offers. Although the overall distribution of regional and national offers was similar between the TPT and NTPT groups, the geographic distances were longer in the NTPT cohort for both regional (median 414.0 vs. 385.0 miles; p < 0.001) and national offers (1125.0 vs. 842.0; p = 0.03). The majority of these liver offers came to our center as a result of local–regional decline. Despite the challenge of coordinating over a larger geographic area, we were able to successfully use these grafts with good outcomes.

With the known organ shortage, there is an ongoing trend toward increased use of so-called "extended criteria" donors, and what is considered acceptable continues to be redefined. In this cohort, 46.3% of liver allografts had a DRI score greater than 2.5, with 4.3% having a score greater than 3. Overall, between the TPT and NTPT groups, 71 successful transplants (36.2%) were achieved using high-risk grafts, with four (2.0%) transplants using grafts with futile UK DCD scores. The majority of allografts in this study had EAD (79.1%), and the percentage of observed EAD in this study was higher than has previously been reported.^[19-21] Yet, despite these higher risk characteristics, we did not observe any impact of this on ICU or hospital LOS or patient and graft survival rates.^[16,20-22] Although EAD continues to be regarded as an intermediate outcome associated with poor outcomes, in our experience, EAD is a normal posttransplant finding for DCD allografts that does not portend adverse outcomes and should be managed expectantly.[16,20-22]

The similar outcomes between TPT and NTPT groups have to be considered in the context of the approach to posttransplant complication management. As previously reported, we believe that center experience in managing DCD liver allografts postoperatively plays a critical role in long-term outcomes.^[3] Abnormalities in hepatic function tests can persist for more than 1 week after transplant and should be monitored. In this series, 48.0% of patients required an endoscopy (IC, anastomotic stricture, other indication) within a year of LT, with the majority requiring more than one procedure (median 4.0). Overall, the median number of endoscopies performed was 7.0 between the two groups (TPT 9.0, NTPT 5.0; p = 0.30). At the time of last follow-up, approximately half of those requiring endoscopy had been successfully treated and were undergoing a stent-free trial (58.3% TPT, 50.0% NTPT; p = 0.68). IC was observed in 16.3% of LT recipients in this study, and the majority (90.6%) were managed endoscopically. In our experience, the majority of IC becomes clinically apparent within the first 2 months after LT, and it is very rare to develop new IC DCD-related complications beyond 6 months. When treating IC endoscopically, we

perform frequent stent exchanges for several reasons. There is considerable ability for the biliary tree to remodel in the setting of IC, and this occurs as a result of good biliary drainage, balloon dilation, and stenting. It is also common to see stents become clogged with biliary casts and debris. Frequent exchanges minimize this risk and help circumvent cholangitis, sepsis, and hospital admissions. We routinely perform these as outpatient procedures. IC unresponsive to endoscopic intervention and requiring retransplant within a year occurred in 1.5% (n = 3) of allografts in this series. In looking beyond the first posttransplant year, 2.0% of patients required retransplantation for IC (3.1% TPT vs. 1.5% NTPT; p = 0.69). Overall, 16.3% (n = 32) of patients went on to develop IC, and eight (4.1% of total cohort) ultimately required retransplantation. Those with a diffuse necrosis IC pattern were more likely to fail endoscopic interventions and needed re-LT (Table 3).^[17] As shown in our outcomes, the majority of IC responds to aggressive endoscopic intervention, and the need for retransplantation is an infrequent event.

This is a single-center study, so there are inherent limitations to generalizability. DCD LT represents a small percentage of all US LT volume. As a single-center result, there is risk for Type II error related to statistical power. However, these data originate from the largest single center for DCD LT by volume for adult patients at present, and the numbers shown (TPT, n = 129; NTPT, 67) represent a significant proportion of the entire US DCD LT case volume during this time period. In addition, we recognize that our experience and clinical practice, particularly with regard to post-LT endoscopy, may not be reflective of practice patterns across the United States. As a result, individual center experiences and outcomes with DCD allografts are not universal. However, given the significant need for liver allografts and the lack of availability of other alternatives, DCD LT represents one of the best opportunities to reduce waitlist mortality in the United States. We hope that by sharing our experience we can help improve DCD use by demonstrating that recovery of these allografts can safely be facilitated through the use of NTPTs.

In summary, excellent outcomes can be achieved with the use of NTPTs for DCD liver donors. The ability to use procurement surgeons unaffiliated with the transplant program without compromising outcomes allows for flexibility in logistics and minimization of workplace risk associated with procurement travel. There is a potential opportunity to increase the use of DCD livers by expanding the use of local recovery surgeons.

ACKNOWLEDGMENTS

The outcomes shown here would not have been possible without the hard work of our nurse-led procurement team. Thank you, Leanne Davidson (January 8, 1988–August 29, 2021), for your dedication and leadership. We will miss you greatly.

CONFLICT OF INTEREST

Amit K. Mathur advises CareDx.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ORCID

Caroline C. Jadlowiec D https://orcid.

org/0000-0001-7860-9519

Elizabeth Macdonough D https://orcid.

org/0000-0001-9762-3615

Kylie Pont https://orcid.org/0000-0002-1133-8766 *Kristi Valenti* https://orcid.org/0000-0003-4592-1885 *Blanca Lizaola-Mayo* https://orcid.

org/0000-0003-0130-0091

Abigail Brooks https://orcid.org/0000-0001-5257-4143 Devika Das https://orcid.org/0000-0003-0959-5656 Raymond Heilman https://orcid.

org/0000-0003-0367-2008

Amit K. Mathur https://orcid.org/0000-0002-9215-2014 Winston Hewitt https://orcid.org/0000-0001-8221-9521 Adyr Moss https://orcid.org/0000-0002-5617-3037 Bashar Aqel https://orcid.org/0000-0002-9671-9575 Kunam S. Reddy https://orcid.org/0000-0001-8912-2108

REFERENCES

- Croome KP, Lee DD, Keaveny AP, Taner CB. Improving national results in liver transplantation using grafts from donation after cardiac death donors. Transplantation. 2016;100:2640–47.
- Croome KP, Mao S, Yang L, Pungpapong S, Wadei HM, Taner CB. Improved national results with simultaneous liver-kidney transplantation using donation after circulatory death donors. Liver Transpl. 2020;26:397–407.
- Nunez-Nateras R, Reddy KS, Aqel BA, Heilman R, Morgan P, Mathur AK, et al. Simultaneous liver-kidney transplantation from donation after cardiac death donors: an updated perspective. Am J Transplant. 2020;20:3582–9.
- Jadlowiec CC, Taner T. Liver transplantation: current status and challenges. World J Gastroenterol. 2016;22:4438–45.
- Foley DP, Fernandez LA, Leverson G, Chin LT, Krieger N, Cooper JT, et al. Donation after cardiac death: the University of Wisconsin experience with liver transplantation. Ann Surg. 2005;242:724–31.
- Abt PL, Desai NM, Crawford MD, Forman LM, Markmann JW, Olthoff KM, et al. Survival following liver transplantation from non-heart-beating donors. Ann Surg. 2004;239:87–92.
- Abt PL, Fisher CA, Singhal AK. Donation after cardiac death in the US: history and use. J Am Coll Surg. 2006;203:208–25.
- Pine JK, Goldsmith PJ, Ridgway DM, Pollard SG, Menon KV, Attia M, et al. Predicting donor asystole following withdrawal of treatment in donation after cardiac death. Transplant Proc. 2010;42:3949–50.
- Montgomery JR, Highet A, Hobeika MJ, Englesbe MJ, McElroy LM. Going the distance for procurement of donation after circulatory death livers for transplantation-does reimbursement reflect reality? Clin Transplant. 2020;34:e13780.
- Lindemann J, Dageforde LA, Vachharajani N, Stahlschmidt E, Brockmeier D, Wellen JR, et al. Cost evaluation of a donation

after cardiac death program: how cost per organ compares to other donor types. J Am Coll Surg. 2018;226:909–16.

- Taner CB, Bulatao IG, Willingham DL, Perry DK, Sibulesky L, Pungpapong S, et al. Events in procurement as risk factors for ischemic cholangiopathy in liver transplantation using donation after cardiac death donors. Liver Transpl. 2012;18:100–11.
- Chadha RM, Croome KP, Aniskevich S, Pai S-L, Nguyen J, Burns J, et al. Intraoperative events in liver transplantation using donation after circulatory death donors. Liver Transpl. 2019;25:1833–40.
- Schlegel A, Kalisvaart M, Scalera I, Laing RW, Mergental H, Mirza DF, et al. The UK DCD Risk Score: a new proposal to define futility in donation-after-circulatory-death liver transplantation. J Hepatol. 2018;68:456–64.
- Feng S, Goodrich NP, Bragg-Gresham JL, Dykstra DM, Punch JD, DebRoy MA, et al. Characteristics associated with liver graft failure: the concept of a donor risk index. Am J Transplant. 2006;6:783–90.
- Bates MD. Donor risk index for liver transplantation calculator; 2021 [cited 2021 Jan 12]. Available from: https://gastro.cchmc. org/calculators/donor-risk-index/
- Olthoff KM, Kulik L, Samstein B, Kaminski M, Abecassis M, Emond J, et al. Validation of a current definition of early allograft dysfunction in liver transplant recipients and analysis of risk factors. Liver Transpl. 2010;16:943–49.
- Croome KP, Mathur AK, Aqel B, Yang L, Taner T, Heimbach JK, et al. Classification of distinct patterns of ischemic cholangiopathy following DCD liver transplantation: distinct clinical courses and long-term outcomes from a multicenter cohort. Transplantation. 2022;106:1206–14.
- Serrano OK, Vock DM, Snyder JJ, Chinnakotla S, Kandaswamy R, Pruett TL, et al. Influence of the procurement surgeon on transplanted abdominal organ outcomes: an SRTR analysis to evaluate regional organ procurement collaboration. Am J Transplant. 2019;19:2219–31.
- Englesbe MJ, Merion RM. The riskiest job in medicine: transplant surgeons and organ procurement travel. Am J Transplant. 2009;10:2406–15.
- Lee DD, Croome KP, Shalev JA, Musto KR, Sharma M, Keaveny AP, et al. Early allograft dysfunction after liver transplantation: an intermediate outcomes measure for targeted improvements. Ann Hepatol. 2016;15:53–60.
- Lee DD, Singh A, Burns JM, Perry DK, Nguyen JH, Taner CB. Early allograft dysfunction in liver transplantation with donation after cardiac death donors results in inferior survival. Liver Transpl. 2014;20:1447–53.
- 22. Wadei HM, Lee DD, Croome KP, Mai ML, Golan E, Brotman R, et al. Early allograft dysfunction with short- and long-term kidney function impairment. AJT. 2016;16:850–9.

SUPPORTING INFORMATION

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

How to cite this article: Jadlowiec CC, Macdonough E, Pont K, Valenti K, Lizaola-Mayo B, Brooks A, et al. Donation after circulatory death transplant outcomes using livers recovered by local surgeons. Liver Transpl. 2022;28:1726– 1734. <u>https://doi.org/10.1002/lt.26461</u>