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Variation in DCD Liver Transplant Protocols Among Transplant Centers in the United States

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Background. Variation in donation after circulatory death (DCD) organ recovery and liver transplant practices exist among transplant centers. This study aimed to evaluate these practices among centers in the United States. **Methods.** Scientific Registry of Transplant Recipients data were accessed to identify centers that performed liver transplantation in 2021 and 2022. Surveys were sent to transplant centers that consistently performed ≥ 5 DCD liver transplants per year. **Results.** DCD liver transplants were performed by 95 centers (65.1%) of the 146 liver transplant centers in the United States. Survey results were recorded from 42 centers that consistently performed ≥ 5 DCD liver transplants per year, with a 59.5% response rate. Withdrawal-to-asystole and agonal time were used to define donor warm ischemia time (WIT) in 16% and 84% centers, respectively. Fifty-six percent of the centers did not use oxygen saturation to define donor WIT. Systolic blood pressure cutoffs used to define agonal time varied between 50 and 80 mmHg, donor age cutoffs ranged between 55 and 75 y, and cold ischemia times varied between 4 and 10h. Seventy-six percent of centers used normothermic machine perfusion for DCD liver transplantation. **Conclusions.** This study highlights the wide variation in use, recovery, and definition of donor WIT. Using national data to rigorously define best practices will encourage greater utilization of this important donor resource.

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

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Encouraging outcomes and a steady increase in the national annual liver transplant volume from donation after circulatory death (DCD) donors have been observed in the United States.^{1,2} DCD liver transplantation also provides a survival benefit compared with remaining on the waitlist.³ There is wide variation in usage and recovery practices of DCD donors among organ procurement organizations and transplant centers.^{4,6} Despite recently issued American Society of Transplant Surgeons (ASTS) recommendations⁷ on best practices in DCD organ procurement, significant inconsistencies are found in the willingness to pursue, acceptance criteria, recipient selection, and implantation practices. This study aimed to evaluate DCD liver graft utilization and DCD liver transplant protocols among transplant centers in the US.

MATERIALS AND METHODS

Program-specific Reports maintained by the Scientific Registry of Transplant Recipients were accessed to identify transplant centers in the United States that performed liver transplantation in the years 2021 and 2022. Among these, centers that performed at least 1 DCD liver transplant in a calendar year were identified. Surveys were sent to transplant centers that consistently performed at least ≥ 5 DCD liver transplants per year in 2021 and 2022. Surveys were sent to both center directors and individual transplant surgeons, and only a single response was recorded at each center.

The survey included questions about centers' criteria for DCD liver graft acceptance, that is, whether centers used a withdrawal-to-asystole time or agonal time, definition of

agonal time, length of withdrawal-to-asystole time or agonal time, acceptable cold ischemia time (CIT), perioperative use of heparin and tissue plasminogen activator, personnel performing DCD recovery, use of liver grafts procured by local procurement surgeons, use of normothermic machine perfusion (NMP) or hypothermic machine perfusion (HMP), and acceptable recipient characteristics for the use of DCD liver grafts. The survey questionnaire is presented in the Supplemental Material and Methods (SDC, <http://links.lww.com/TXD/A660>). In the United States, DCD liver grafts are initially allocated to status 1A and 1B recipients registered at a transplant hospital that is within 500 nautical miles (NM) from the donor hospital. This is followed by the sequential allocation of organs to recipients registered at a transplant hospital within 150, 250, and 500 NM from the donor hospital and then nationally, according to a candidate's model for end-stage liver disease (MELD) score and donor/recipient blood group (<https://optn.transplant.hrsa.gov/professionals/by-organ/liver-intestine/>).

Data analyses were generated using Qualtrics software, Version (August–November 2023), Copyright© 2023 Qualtrics, Provo, UT, and for Program-specific Reports data using SAS software, version 9.4, Copyright© 2016, SAS Institute Inc, Cary, NC.

RESULTS

In 2021 and 2022, liver transplantation was performed by 146 transplant centers in the United States. Of these, 95 centers (65.1%) performed at least 1 DCD liver transplantation. Median center DCD liver transplant volume was 1 (interquartile range, 0–7; range, 0–74) in 2021 and 1 (interquartile range, 0–7; range, 0–129) in 2022. For each of the years 2021 and 2022, 50% of DCD liver transplants were performed by 14 transplant centers (9.6%; Figure 1). Ten or more DCD liver transplants per year were performed by 21 transplant centers, whereas ≥ 5 DCD liver transplants per year were performed by 42 transplant centers. Surveys sent to these 42 liver transplant centers were analyzed.

DCD Recovery Practices

Twenty-five transplant centers responded to our survey with a 59.5% overall response rate. Four centers (16%) use

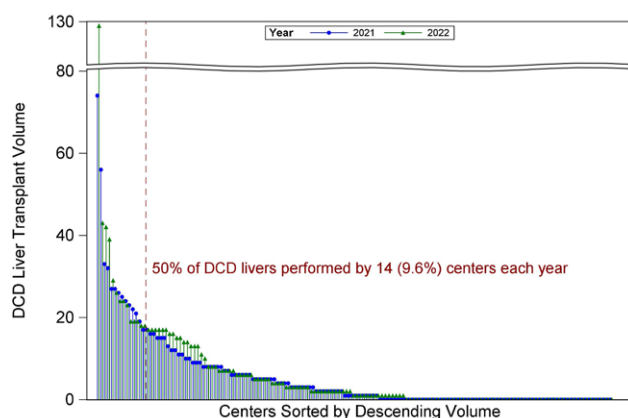


FIGURE 1. Needle plot for center volumes in the years 2021 and 2022. Needle plots of DCD transplant volume in the years 2021 (blue dot) and 2022 (green arrow). Y-axis—DCD liver transplant volume per year; X-axis—transplant centers sorted by descending volume. DCD, donation after circulatory death.

withdrawal to asystole as the time criteria for DCD liver acceptance (Table 1). Two of these centers use 30 min as the limit and 1 center has a 45-min limit, whereas another center has a time limit of 40 min for donors 40 y or younger and 30 min for donors older than 40 y. Twenty-one centers (84%) used functional warm ischemia time as the criteria for DCD liver acceptance. The definition of agonal time is variable among centers. Ten centers (47.6%) do not use oxygen saturation in the definition of agonal time, whereas 9 centers (42.8%) use an oxygen saturation of 80% and 2 centers (9.5%) use an oxygen saturation of 70% to define agonal time. Blood pressure criteria to define agonal time is also variable. Three centers (14.2%) use mean arterial pressure (MAP), with 2 centers using MAP of 50 mmHg and another center using MAP of 60 mmHg. Eighteen centers (85.8%) use systolic blood pressure (SBP) as criteria to define agonal time. Nine centers (42.8%) use an SBP of 80 mmHg, 2 centers (9.5%) use an SBP of 70 mmHg, and 7 centers (33.3%) use an SBP of 50 mmHg to define agonal time. The most common combination of SBP of 80 mmHg and 80% oxygen saturation to define agonal time is used by 7 centers (33.3%).

The donor age cutoff for DCD liver graft acceptance is 55 y or younger in 2 centers (8%), 60 y or younger in 3 centers (12%), 65 y or younger in 10 centers (40%), 70 y or younger in 4 centers (16%), 75 y or younger in 1 center (4%), and 5 centers (20%) have no cut off for donor age. One center omits a donor age cutoff only with the use of NMP.

In 12 transplant centers (48%), attending transplant surgeons from the recipient transplant center routinely recover DCD liver grafts. Eight transplant centers (32%) have their fellows recover DCD liver grafts. Four centers (16%) had dedicated donor procurement surgeons for DCD recovery, and 1 center (4%) routinely has DCD liver grafts procured by the organ procurement organization surgeon. Nine centers (36%) do not accept DCD liver grafts procured by local recovery surgeons, whereas 16 centers (64%) accept DCD liver grafts procured by local recovery surgeons. Of them, 1 center only uses DCD liver grafts procured by local recovery surgeons after assessing the liver on NMP.

DCD Liver Graft Perfusion Practices

Sixteen centers (64%) use University of Wisconsin perfusate for in situ flush post aortic cross-clamp, whereas 9 centers (36%) use histidine-tryptophan-ketoglutarate solution (Table 2). Response to the amount of fluid used for in situ flush was received from 18 centers (72% response rate). The amount of University of Wisconsin used for in situ flush varied from 3 to 6L and was not reported by 6 centers. The amount of histidine-tryptophan-ketoglutarate used for in situ flushing varied from 5 to 10L, and no response was recorded from 3 centers (33.3%).

Heparin was not used in the in situ perfusion fluid by 15 centers (60%), whereas 10 centers (40%) routinely added heparin to the flush. Tissue plasminogen activator was not used at all by 17 centers (68%), used during implantation by 6 centers (24%), used in the in situ flush at the donor recovery by 1 center (4%), and used both at donor recovery and during implantation by 1 center (4%).

Response to the CIT that was considered acceptable for DCD liver transplant was received from 24 centers (96%

TABLE 1.**DCD recovery practices among centers in the United States**

2021 volume	2022 volume	Center time criteria	Agonal time SBP/MAP, mm Hg	Agonal time sat, %	Time criteria Agonal time/ withdrawal to asystole	DCD donor age, y	Use local recovery	Recovery surgeon
74	129	Withdrawal to asystole	NA	NA	45	70	Yes	Dedicated procurement surgeon
32	43	Agonal time	50	No	90 (≤55 y) 60 (>55 y)	None with NMP/NRP	Yes	Attending
56	42	Agonal time	80	No	30	65	Yes, after NMP	Fellow
27	39	Agonal time	80	80	30	70	Yes	Fellow
33	29	Agonal time	80 ^a or (50 MAP)	80	30–45	No cutoff	No	Attending
9	24	Agonal time	70	70	45	70	No	Fellow
25	24	Agonal time	50	No	60	75	No	Attending
6	23	Withdrawal to asystole	NA	NA	40 (≤40 y) 30 (41–65 y)	65	Yes	Attending
23	19	Agonal time	60 MAP	80	45	65	Yes	Fellow ^b or procurement specialist
9	19	Agonal time	80	80	30	65	Yes	Fellow
8	18	Agonal time	50	No	20	65	No	Attending
11	18	Agonal time	50	No	45	No cutoff	Yes	Attending
15	17	Agonal time	50	No	30	65	Yes	Fellow
27	17	Agonal time	50 ^a or (50 MAP)	No	Age dependent	65	Yes	Attending
5	16	Agonal time	80	No	30	70	No	Fellow
12	15	Withdrawal to asystole	NA	NA	30	60	Yes	Attending
7	14	Agonal time	50	No	30	65	Yes	Fellow
6	13	Agonal time	80	80	45	None	Yes	Dedicated procurement surgeon
12	10	Agonal time	70	No	30	65	Yes	Dedicated procurement surgeon
6	8	Agonal time	50	70	30	60	No	Attending
5	8	Agonal time	80	80	27	55	No	Attending
10	7	Agonal time	80	80	30	60	Yes	Attending
8	6	Withdrawal to asystole	NA	NA	30	65	Yes	OPO
17	6	Agonal time	50 MAP	80	30	No cutoff	No	Dedicated procurement surgeon
7	6	Agonal time	80	80	30	55	No	Attending

Centers arranged according to 2022 DCD volume.

^aUsed SBP data for analysis.^bUsed fellow for analysis.

DCD, donation after circulatory death; MAP, mean arterial pressure; NA, not applicable; NMP, normothermic machine perfusion; NRP, normothermic regional perfusion; OPO, Organ Procurement Organization; SBP, systolic blood pressure.

response rate). DCD liver grafts were considered for transplant when the CIT did not exceed 10, 8, 7, 6, 5, and 4 h by 1 center (4%), 4 centers (16.6%), 1 center (4%), 12 centers (50%), 2 centers (8%), and 1 center (4%), respectively. Three centers (12.5%) do not have a threshold for CIT with the use of NMP pumps. All centers responded to whether they use machine perfusion for DCD liver grafts. Six centers (24%) did not use any kind of machine perfusion, whereas NMP was used by 18 centers (72%), and a combination of HMP and NMP was used by 1 center (4%). Among the 19 centers that used NMP for DCD liver grafts, 10 centers (53%) routinely used NMP for all their DCD liver grafts, and 9 centers (47%) performed a proportion of their DCD liver transplants even without NMP.

Criteria for Recipient Selection for the Use of DCD Liver Grafts

Responses about the use of DCD liver grafts in patients for redo liver transplantation, high MELD recipients, and patients with prior upper abdominal surgery were received from 22 centers (88% response rate; Table 2). DCD liver grafts were not used for redo liver transplantation by 11 centers (50%), not used in recipients with high MELD in 6 centers (27%), and not used in recipients with prior abdominal surgery in 2 centers (9%). Redo liver transplantation, high MELD status, and prior upper abdominal surgery in a recipient did not preclude 2 centers (9%) from using DCD liver grafts with or without NMP, but these criteria did not preclude 6 centers (27%) from using DCD liver grafts only when NMP was used.

TABLE 2.**DCD liver graft perfusion practices and recipient criteria for the use of DCD liver grafts among centers in the United States**

2021 volume	2022 volume	Perfusion fluid	Perfusate volume, L	Heparin in fluid	tPA	CIT, h	NMP/HMP	Routine use of NMP/HMP for all DCD liver grafts	Machine used	Recipient criteria for the use of DCD liver graft
74	129	HTK	5	No	No	8	Yes	No	TransMedics	NR
32	43	UW	4-aorta	Yes	No	10	Yes	No	TransMedics	No criteria with NMP
			3-portal 1-artery back table							
56	42	HTK	10	No	Recipient surgery	6	Yes	No	OrganOx	No criteria
27	39	HTK	5	No	No	8	Yes	Yes	OrganOx	No criteria with NMP ^a
33	29	HTK	7	No	Perfusion fluid	6	Yes	No	NA	Redo
9	24	UW	3	Yes	No	No limit with NMP	Yes	Yes	TransMedics	No criteria with NMP
25	24	HTK	NR	Yes	No	6	No	NA	NA	Redo
6	23	UW	4	No	No	6	Yes	Yes	TransMedics	No criteria with NMP
23	19	UW	5	No	Perfusion fluid + recipient surgery	8	Yes	No	TransMedics	No criteria with NMP
9	19	HTK	NR	Yes	Recipient surgery	NR	Yes	No	TransMedics + LifePort	High MELD
8	18	UW	NR	Yes	No	6	Yes	Yes	OrganOx	Redo
11	18	UW	6	No	No	5	Yes	No	OrganOx	No criteria
15	17	HTK	NR	No	No	No limit with NMP	Yes	Yes	TransMedics	Redo
27	17	HTK	6	No	Recipient surgery	6	Yes	Yes	OrganOx + TransMedics	NR
5	16	UW	4	Yes	No	6	Yes	Yes	OrganOx + TransMedics	NR
12	15	UW	N/R	Yes	No	6	No	NA	NA	All (redo; high MELD; prior upper abdominal surgery)
7	14	UW	6	Yes	No	6	Yes	Yes	OrganOx	Redo
6	13	UW	6	No	No	No limit with NMP	Yes	Yes	TransMedics	No criteria with NMP
12	10	UW	6	Yes	No	6	Yes	Yes	OrganOx	High MELD
6	8	UW	NR	Yes	No	6	Yes	No	TransMedics	High MELD
5	8	HTK	8	Yes	No	7	No	NA	NA	Redo; high Meld
10	7	UW	5	No	Recipient surgery	5	No	NA	NA	Redo
8	6	UW	6	No	Recipient surgery	6	Yes	No	OrganOx	Redo
17	6	UW	6	No	Recipient surgery	4	No	NA	NA	All (redo; high MELD; prior upper abdominal surgery)
7	6	UW	NR	Yes	No	8	No	NA	NA	Redo

^aCenter does not use DCD for redo liver transplantation if the cause of liver failure is ischemic cholangiopathy.

CIT, cold ischemia time; DCD, donation after circulatory death; HMP, hypothermic machine perfusion; HTK, histidine-tryptophan-ketoglutarate; MELD, model for end-stage liver disease; NA, not applicable; NMP, normothermic machine perfusion; NR, no response; tPA, tissue plasminogen activator; UW, University of Wisconsin.

DISCUSSION

DCD liver grafts are used by 65.1% of centers in the United States, with 34.9% of the centers not performing any DCD liver transplants. A majority of DCD liver transplants are performed by a select few centers, where 14 (9.6%) centers perform 50% of the DCD liver transplants. Only 21 centers performed ≥ 10 DCD liver transplants consistently in the calendar year 2021 and 2022. DCD organ recovery practices, DCD liver graft perfusion practices, and criteria for recipient selection widely differ among transplant centers. Fifty-six

percent of the centers do not use oxygen saturation in the evaluation of DCD liver grafts. Seventy-six percent of the transplant centers have adopted the use of NMP for DCD liver transplantation, with 40% of the centers routinely using NMP for all their DCD liver transplants.

The main strength of our study is that we look at center-level utilization of DCD liver grafts, DCD transplant protocols, and practices among centers in the United States. This study highlights the wide variation in use, recovery, and description of agonal time. Our study also lists the high-volume DCD liver

transplant centers and their transplant practices. We believe that our findings would encourage centers to learn from each other's transplant practices and further boost DCD liver utilization. We acknowledge that our study provides a snapshot of current DCD transplant protocols and liver graft utilization at a time when many centers are adopting NMP/normothermic regional perfusion and expanding their DCD liver graft acceptance criteria and DCD liver transplant volume. One of the limitations of our study is that we do not look at DCD liver graft survival. The relationship between a center's DCD liver transplant volume, transplant protocols, and liver graft survival was not explored in this study. However, the main outcome of interest in DCD liver transplant, ischemic cholangiopathy (IC) or nonanastomotic stricture (NAS), is not explored. It is challenging to get accurate rates of IC/NAS among different centers at the national level because of diagnostic and reporting biases. Another limitation of our study is that our survey did not include any questions about the use of normothermic regional perfusion in DCD liver transplantation in the United States.

In a DCD donor recovery, donor warm ischemia time (DWIT), which starts after withdrawal of life-sustaining therapy, is very critical. There is a general consensus that longer DWIT leads to worse outcomes, but the criteria to define DWIT are widely variable. Some centers use withdrawal of life-sustaining therapy to cross-clamp to define DWIT, whereas most centers use agonal time. Again, the criteria to define agonal time is widely variable, with some centers using a combination of SBP/MAP measurements and oxygen saturation and other centers just using SBP/MAP measurements.⁸ One study suggests that the amount of time a liver graft spends, beyond 16 min, on oxygen saturation of <80% does not affect graft survival.⁹ The latest ASTS recommendations suggest using time from SBP <50 mmHg until cross-clamp to define agonal time.⁷

ASTS recommendations also suggest that DCD procurements should be performed by experienced teams familiar with protocols and techniques specific to DCD rapid organ recovery.⁷ 36% of transplant centers in our study did not accept liver grafts procured by local recovery surgeons. Donor recovery techniques that prolong the nonperfusion period, such as time from asystole to cross-clamp, and hepatectomy time have been attributed to increased risk of IC/NAS and primary nonfunction.^{10,11} Growing center experience and standardization of donor recovery techniques would encourage transplant centers to use liver grafts procured by other teams while achieving good patient and graft outcomes.¹²

The International Liver Transplantation Society (ILTS) recommends routine use of DCD donors up to 60 y or younger and selective utilization of DCD donors older than 60 y with consideration of other donor risk factors. It also recommends using DCD liver grafts with a CIT <8 h and not using liver grafts with a CIT >12 h. It also advises selective utilization of DCD liver grafts with CIT >8 h but <12 h with consideration of other donor risk factors.¹³ We have observed in our study that only 20% of the centers had a hard cutoff of donor age at 60 y or younger. Interestingly, we have also observed that 60% of the centers have a threshold for CIT at ≤6 h.

Organ Procurement and Transplantation Network website shows that national annual DCD liver transplant volumes have increased from 915 in 2021 to 1696 in 2023 (<https://optn.transplant.hrsa.gov/data/view-data-reports/national-data/>).

It is interesting to see that centers in the United States have adopted the use of NMP, especially for DCD liver transplants. Seventy-six percent of the transplant centers in this study used NMP for DCD liver transplantation, with 40% of the centers routinely using NMP for all their DCD liver transplants. NMP has allowed centers to expand their donor criteria, such as age, use of local recovery, and CIT. Interestingly, HMP is not widely used in the United States yet, with only 1 center using it, also in conjunction with NMP. Normothermic perfusion has also allowed centers to expand their recipient criteria for DCD liver transplantation. The ILTS recommends routine use of DCD livers for recipients with an MELD score of ≤25 and careful selection of DCD liver grafts for recipients with MELD score >25. Using NMP to mitigate the risk of ischemia/reperfusion injury has enabled at least 10 centers to use DCD liver grafts for high MELD recipients. The ILTS also recommends selective use of DCD liver grafts for redo liver transplantation and for recipients with prior abdominal surgery. NMP and its ability to extend CIT has enabled at least 6 centers to use DCD liver grafts for redo liver transplantation and for recipients with prior abdominal surgery.

In conclusion, the majority of the DCD liver transplants were performed by a select few centers. DCD recovery practices and transplant protocols widely vary among centers. The wide variation may challenge the widespread adoption of DCD and/or NMP, as centers that are looking to get into the DCD space would not know where to start. NMP has enabled centers to expand their donor criteria and also use these grafts for recipients with risk factors. Using national data to rigorously define best practices will encourage greater utilization of this important donor resource.

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