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DCD Liver Grafts Can Safely Be Used for Recipients With Grade I–II Portal Vein Thrombosis: A Multicenter Analysis

Lydia A. Mercado, MD,[1] Harpreet K. Bhangu, MD,[1] Esteban Calderon, MD,[2] Amit K. Mathur, MD,[2] Bashar Aqel, MD,[3] Kaitlyn R. Musto, BSc,[1] Kymberly D. Watt, MD,[4] Charles B. Rosen, MD,[5] Candice Bolan, MD,[6] Jordan D. LeGout, MD,[6] C. Burcin Taner, MD,[1] Denise M. Harnois, DO,[1] and Kristopher P. Croome, MD, MS[1]

Background. With donation after circulatory death (DCD) liver transplantation (LT), the goal of the recipient implantation procedure is to minimize surgical complexity to avoid a tenuous environment for an already marginal graft. The presence of portal vein thrombosis (PVT) at the time of LT adds surgical complexity, yet, to date, no studies have investigated the utilization of DCD liver grafts for patients with PVT. **Methods.** All DCD LT performed at Mayo Clinic-Florida, Mayo Clinic-Arizona, and Mayo Clinic-Rochester from 2006 to 2020 were reviewed (N = 771). Patients with PVT at the time of transplant were graded using Yerdel classification. A 1:3 propensity match between patients with PVT and those without PVT was performed. **Results.** A total of 91 (11.8%) patients with PVT undergoing DCD LT were identified. Grade I PVT was present in 62.6% of patients, grade II PVT in 27.5%, grade III in 8.8%, and grade 4 in 1.1%. At the time of LT, thromboendovenectomy was performed in 89 cases (97.8%). There was no difference in the rates of early allograft dysfunction (43.2% versus 52.4%; $P = 0.13$) or primary nonfunction (1.1% versus 1.1%; $P = 0.41$) between the DCD PVT and DCD without PVT groups, respectively. The rate of ischemic cholangiopathy was not significantly different between the DCD PVT (11.0%) and DCD without PVT groups (10.6%; $P = 0.92$). Graft ($P = 0.58$) and patient survival ($P = 0.08$) were similar between the 2 groups. Graft survival at 1-, 3-, and 5-y was 89.9%, 84.5%, and 79.3% in the DCD PVT group. **Conclusions.** In appropriately selected recipients with grades I–II PVT, DCD liver grafts can be utilized safely with excellent outcomes.

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Recent changes to liver graft allocation in the United States have resulted in broader sharing of standard criteria donor donation after brain death (DBD) livers. Although these changes have resulted in improved access to DBD organs for the highest model for end-stage liver disease (MELD) patients, they have also led to decreased availability of DBD organs for many patients with MELD scores at or below the median within a respective area. Additionally, changes to hepatocellular carcinoma (HCC) exception pathways have made it more difficult to transplant HCC patients using DBD grafts.[1] In response to these developments, there has been a renewed interest in donation after circulatory death (DCD) liver grafts. This is clearly demonstrated by the continued increase in the number of DCD liver transplants (LT) performed annually.[2]

DCD liver grafts have by definition already undergone an ischemic insult through mandatory warm ischemia in the period between withdrawal of life support and cold perfusion in the donor. As such, it is generally accepted that the goal of the recipient implantation procedure should be to minimize surgical complexity and recipient instability as much as possible to avoid a tenuous environment for an already marginal graft.[2] Many transplant programs have become interested in broadening acceptable recipient selection for DCD liver allografts to help minimize waiting list mortality. The presence of portal vein thrombosis (PVT) at the time of LT adds an additional technical element to the transplant operation. The additional surgical complexity of PVT can vary dramatically depending on the extent of portal venous thrombosis. Indeed, previous studies looking cohorts of

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[1] Department of Transplant, Mayo Clinic Florida, Jacksonville, FL.

[2] Department of Surgery, Mayo Clinic Arizona, Phoenix, AZ.

[3] Division of Gastroenterology and Hepatology, Mayo Clinic Arizona, Phoenix, AZ.

[4] Division of Gastroenterology and Hepatology, Mayo Clinic Rochester, Rochester, MN.

[5] Department of Surgery, Mayo Clinic Rochester, Rochester, MN.

[6] Department of Radiology, Mayo Clinic Florida, Jacksonville, FL.

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L.A.M., H.K.B., E.C., A.K.M., B.A., K.R.M., K.D.W., C.B.R., C.B., J.D.L., C.B.T., D.M.H., and K.P.C. participated in research design. L.A.M., D.M.H., and K.P.C. participated in data analysis. L.A.M., H.K.B., E.C., A.K.M., B.A., K.R.M., K.D.W., C.B.R., C.B., J.D.L., C.B.T., D.M.H., and K.P.C. participated in the performance of the research. L.A.M., D.M.H., and K.P.C. participated in the writing of the paper.

Correspondence: Kristopher P. Croome, MD, MS, Department of Transplant, Mayo Clinic Florida, 4500 San Pablo Rd, Jacksonville, FL 32224. (croome.kristopher@mayo.edu).

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patients with PVT at the time of LT have shown an association with risk of death within 30 d of transplant.[3]

The international liver transplant society recently published a consensus paper on donor and recipient selection for DCD LT.[4] One of the topics covered in that paper was the utilization of DCD liver grafts for recipients with PVT. To date, there are no studies that have investigated the utilization of DCD liver grafts for patients with PVT. The authors of that consensus document express that the number of reports of DCD liver grafts utilized for PVT is scarce. Given the elevated donor risk transferred with DCD liver grafts, additional technical or medical recipient risk factors should generally be limited. The conclusion of that consensus group was that The international liver transplant society does not recommend the routine use of DCD livers for recipients with known complex PVT.[4]

The present analysis sought to investigate the outcomes of using DCD liver grafts for recipients with PVT. In addition, we also sought to determine if the extent of PVT had a significant impact on outcome.

MATERIALS AND METHODS

This study was performed with the approval of the Mayo Clinic Institutional Review Board. The study population included all DCD LT performed at Mayo Clinic Florida, Mayo Clinic Arizona, and Mayo Clinic Rochester from January 1, 2006, to December 31, 2020. Data were acquired from patients' medical records, outside medical records, and from prospectively maintained transplant databases from each site. Data were also obtained and extracted from the United Network of Organ Sharing Standard Analysis and Research file from January 1, 2006, to December 31, 2020.

A 1:3 propensity match between recipients with a PVT undergoing DCD LT and recipients without a PVT undergoing DCD LT was performed. Matching was performed for the following variables: recipient age, calculated MELD at transplant, allocation MELD at transplant, secondary diagnosis of HCC, retransplantation status, simultaneous liver kidney transplant, recipient medical condition at the time of transplant, calendar year of transplantation, donor age, and donor warm ischemia time. Patients were matched 1:3 without replacement. Caliper matching on propensity score was performed. Propensity score matching was performed using Stata "*psmatch2*" functions. Graphic verification was used to check that covariates were balanced across treatment and comparison groups.

PVT was identified by radiologist review of the last cross-sectional imaging performed before LT. All cases were further verified by review of operative reports from the time of LT. PVT was classified by the reviewing radiologist according to the Yerdel classification: Grade I, thrombus at main portal vein (PV) affecting <50% of the lumen with or without minimal extension into superior mesenteric vein (SMV); grade II, thrombus at PV affecting more than 50%, including complete thrombosis, with or without minimal extension into the SMV; grade III, complete PVT plus thrombosis extending to the proximal SMV with patent distal SMV; grade IV, complete PVT plus complete thrombosis of the SMV (Figure 1).[5] For cases with PVT, cross-sectional imaging was updated every 3 mo while awaiting transplant. Patients with clinically significant PVT were treated with coumadin while on the waiting list unless contraindicated. Post-LT patients were routinely placed on acetylsalicylic acid 81 mg daily unless contraindicated.

Tissue plasminogen activator was not used in the 3 participating centers. None of the DCD LTs included in this study utilized machine perfusion. Postreperfusion syndrome (PRS) was defined as a decrease in mean arterial pressure >30% below the baseline value, for at least 1 min, occurring during the first 5 min after reperfusion of the liver graft, asystole or hemodynamically significant arrhythmias, or the need to start the infusion of vasopressors during the intraoperative period.[6,7] Early allograft dysfunction (EAD) was determined based on the previously validated definition of the presence of 1 or more of the following: bilirubin 10 mg/dL on day 7; international normalized ratio 1.6 on day 7; and alanine aminotransferase or aspartate aminotransferase >2000 IU/L within the first 7 d.[8,9] Ischemic cholangiopathy (IC) was defined using previously described methods and criteria.[10] IC was classified according to the following previously described radiologic patterns (diffuse necrosis, multifocal progressive, confluence dominant, and minor form).[10] PV flow was not routinely measured in any of the 3 centers.

The Kidney Disease Improving Global Outcomes (KDIGO) criteria was utilized to stratify the severity of acute kidney injury.[11] For the KDIGO criteria classification, the following definitions were used: stage 1 = ↑ serum creatinine × 1.5–1.9 or ≥0.3 mg/dL increase (within 48 h), stage 2 = ↑ serum creatinine × 2–2.9, and stage 3 = ↑ serum creatinine × 3 or increase in Cr ≥ 4 or initiation of post-LT continuous renal replacement therapy. Patients on dialysis at the time of LT, patients receiving a SLK, and patients who died within the first 48 h were excluded.

All statistical analyses were performed using STATA 16 software (Stata Corp, College Station, TX). Results were presented as mean ± SD except in situations in which results were not normally distributed for which they were presented as median (range). Differences between groups were analyzed using the unpaired *t* test for continuous variables and by the χ^2 test or continuity correction method for categorical variables. Wilcoxon rank-sum was used for variables that did not display a normal distribution. Survival curves for patient or graft survival were generated using the Kaplan-Meier method and compared by the log-rank test. All statistical tests were 2-sided and differences were considered significant when $P < 0.05$.

RESULTS

Between January 2006 and December 2020, a total of 771 DCD LT were performed in the 3 participating centers (Mayo Clinic Florida N = 351, Mayo Clinic Arizona N = 306, Mayo Clinic Rochester N = 114). Median follow-up was 37 mo. All patients had a minimum of 1-y follow-up. A total of N = 91 (11.8%) recipients had a PVT at the time of LT. Using the Yerdel classification system, grade I PVT was present in 57 patients (62.6%), grade II PVT in 25 patients (27.5%), grade III PVT in 8 patients (8.8%), and grade IV PVT in 1 patient (1.1%). At the time of LT, thromboendovenectomy was performed in 89 cases (97.8%). None of the patients undergoing thromboendovenectomy alone had a PV-to-PV interposition graft. One patient with a grade III PVT had a thromboendovenectomy with PV to PV anastomosis and then had a SMV to PV jump graft using donor iliac vein performed to augment the flow. For the 1 patient with a grade IV PVT, a venous jump graft using donor iliac vein was performed off a varix. During that case, the venous

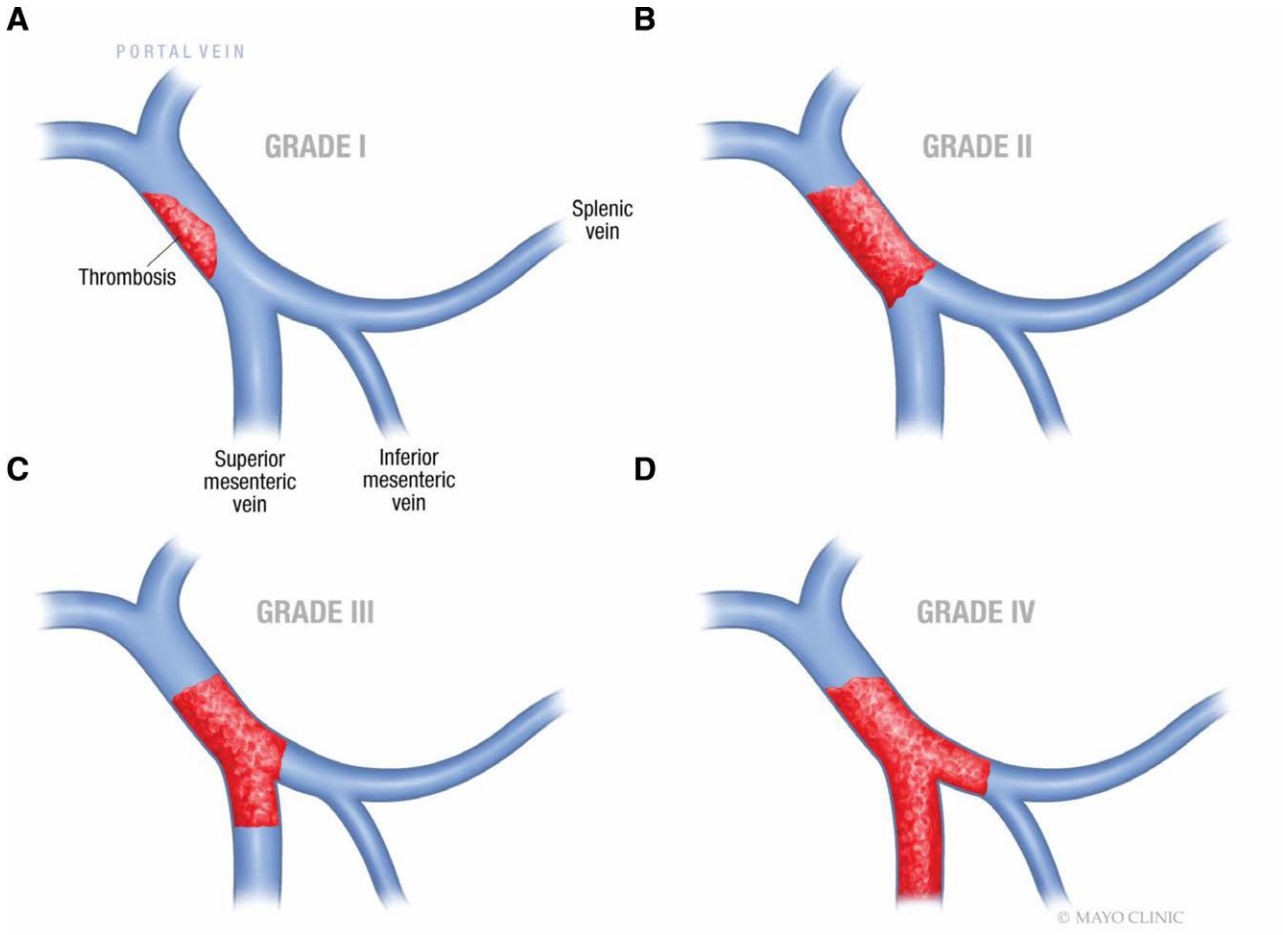

FIGURE 1. Yerdel classification of PVT for LT. A, Grade I: thrombus at main PV affecting less than 50% of the lumen with or without minimal extension into SMV; (B) grade II: thrombus at PV affecting more than 50%, including complete thrombosis, with or without minimal extension into the SMV; (C) grade III: complete PVT plus thrombosis extending to the proximal SMV with patent distal SMV; (D) grade IV: complete PVT plus complete thrombosis of the SMV (proximal and distal). LT, liver transplant; PV, portal vein; PVT, PV thrombosis; SMV, superior mesenteric vein.

TABLE 1.

Recipient characteristics in the DCD PVT and DCD no-PVT groups

	DCD with PVT	DCD without PVT (propensity match)	
Recipient characteristics	**N = 91**	**N = 273**	***P***
Age at transplant (y)	59.9 ± 8.7	59.7 ± 8.5	0.83
Body mass index	29.2 ± 6.0	28.5 ± 5.9	0.31
HCC exception	17 (18.7%)	43 (15.8%)	0.51
Disease etiology			
HCV	34 (37.4%)	91 (33.3%)	0.48
Alcohol	12 (13.2%)	47 (17.2%)	0.37
NASH	17 (18.7%)	54 (19.8%)	0.82
Cholestatic	4 (4.4%)	15 (5.5%)	0.68
Calculated MELD score	18.0 ± 5.4	18.5 ± 7.5	0.51
Match MELD score	23.1 ± 4.9	22.4 ± 6.1	0.35
Retransplant	1 (1.1%)	1 (0.4%)	0.41
SLK	3 (4.3%)	12 (3.3%)	0.65
Ventilated at transplant	0 (0%)	0 (0%)	NA

DCD, donation after circulatory death; HCC, hepatocellular carcinoma; HCV, hepatitis C virus; MELD, model for end-stage liver disease; NASH, nonalcoholic steatohepatitis; PVT, portal vein thrombus; SLK, simultaneous liver kidney.

graft clotted on several occasions requiring revision. That patient ultimately had a primary nonfunction (PNF) and passed away in the intensive care unit within 24 h of LT.

A 1:3 propensity match was performed to generate a DCD without PVT control cohort. Recipient characteristics for the DCD PVT and DCD with no-PVT groups can be seen

TABLE 2.

Donor and graft characteristics in the DCD PVT and DCD no-PVT groups

	DCD with PVT	DCD without PVT (propensity match)	
Donor characteristics	**N = 91**	**N = 273**	***P***
Age (y)	40.2 ± 13.6	41.2 ± 14.5	0.59
Body mass index (kg/m^2)	26.9 ± 7.5	27.9 ± 6.8	0.24
DWIT (WDLS to CC min)	23.0 ± 7.6	21.8 ± 6.1	0.14
fDWIT (<sBP 50 mm Hg to CC min)	11.1 ± 4.5	11.5 ± 4.6	0.46
Cold ischemia time (h)	5.6 ± 1.3	5.8 ± 2.1	0.23

CC, cross clamp; DCD, donation after circulatory death; DWIT, donor warm ischemia time; fDWIT, functional DWIT; PVT, portal vein thrombus; sBP, systolic blood pressure; WDLS, withdrawal of life support.

in Table 1. Given that patients were propensity matched, no significant differences were seen between the groups. Donor characteristics for the 2 groups can be seen in Table 2.

Perioperative outcomes for the 2 groups can be seen in Table 3. There was no difference in the rate of PNF between the 2 groups. PRS, EAD, number of units of red blood cells and fresh frozen plasma were also not different between the 2 groups. KDIGO classification of post-LT acute kidney injury was no different between the groups, nor was return to operating room within 30 d of LT. The overall rate of any severity of IC was not significantly different between the DCD PVT (11.0%) and DCD without PVT groups (10.6%; P = 0.92). Additionally, when looking at the more severe form of IC (diffuse necrosis and multifocal progressive), there was no difference between the groups. Recurrent partial PVT was demonstrated in 5 patients in the DCD PVT group. One patient in the DCD PVT group developed recurrent complete PVT 1 y after LT. That patient was treated with systemic anticoagulation and the thrombosis ultimately resolved without additional intervention.

TABLE 3.

Perioperative outcomes for the DCD PVT and DCD no-PVT groups

	DCD with PVT	DCD without PVT (propensity match)	
Perioperative variable	**N = 91**	**N = 273**	***P***
PNF	1 (1.1%)	3 (1.1%)	0.41
PRS	29 (31.9%)	76 (27.8%)	0.46
EAD[a]	38 (43.2%)	140 (52.4%)	0.13
RBC (units) during LT	7 (3–11)	6 (3–10)	0.84
FFP (units) during LT	6 (2–9)	4 (2–8)	0.06
KDIGO classification for AKI[b]			
Stage 1	16 (19.0%)	21 (19.1%)	0.99
Stage 2	9 (10.7%)	21 (8.2%)	0.48
Stage 3	3 (3.6%)	10 (3.9%)	0.89
Return to OR within 30 d	21 (23.1%)	60 (22.0%)	0.83
Ischemic cholangiopathy	10 (11.0%)	29 (10.6%)	0.92
Diffuse necrosis	3 (3.3%)	4 (1.5%)	0.27
Multifocal progressive	3 (3.3%)	10 (3.7%)	0.87
Confluence dominant	3 (3.3%)	10 (3.7%)	0.87
Minor form	1 (1.1%)	5 (1.8%)	0.63

[a]Patients who died or were retransplanted before day 7 blood work were excluded.
[b]Patients on dialysis at the time of LT, patients receiving a SLK and patients who died within the first 48 h were excluded.
AKI, acute kidney injury; DCD, donation after circulatory death; EAD, early allograft dysfunction; FFP, fresh frozen plasma; KDIGO, Kidney Disease Improving Global Outcomes; LT, liver transplant; OR, operating room; PNF, primary nonfunction; PRS, postreperfusion syndrome; PVT, portal vein thrombosis; RBC, red blood cells; SLK, simultaneous liver kidney.

Patient survival for the 2 groups can be seen in Figure 2. Patient survival was not statistically different between the 2 groups (P = 0.08). Patient survival at 1, 3, and 5 y was 92.1%, 90.7%, and 85.1% in the DCD PVT group and 96.1%, 86.8%, and 78.7% in the DCD without PVT group. Graft survival for the 2 groups can be seen in Figure 3. Graft survival was not statistically different between the 2 groups (P = 0.59). Graft survival at 1, 3, and 5 y was 89.9%, 84.5%, and 79.3% in the DCD PVT group and 92.0%, 83.1%, and 72.1% in the DCD without PVT group.

A sensitivity analysis was performed investigating graft survival based on grade of PVT. There was not a statistically significant difference on graft survival between the grade I, grade II, and grade III groups (P = 0.87). Graft Survival in the DCD PVT group based on grade of PVT can be seen in Figure 4.

In addition to the above multicenter analysis, we sought to investigate the impact of documented PVT at the time of transplant on outcome of DCD LT using SRTR data. Although SRTR data does code PV thrombus at the time of transplant (variable *PORTAL_VEIN_TRR*), it does not provide granular detail on grade or what extent of thrombus was present. Graft survival for the patients undergoing DCD LT with documented PVT or without documented PVT using the SRTR dataset can be seen in Figure 5. Graft survival was not statistically different between the 2 groups (P = 0.32).

DISCUSSION

Outcomes with DCD LT have continued to improve over time.[12] Many single-center reports have demonstrated that equivalent graft and patient survival rates can be achieved between DCD and DBD LT with careful donor and recipient selection.[13-18] One underlying principle with DCD recipient selection is to avoid cases where increased surgical complexity is anticipated. This has raised the question as to what impact a recipient with PVT may have on outcomes following DCD LT.[4]

In the present analysis, we demonstrate equivalent graft and patient survival in patients with PVT compared with a propensity matched group of patients without PVT undergoing DCD LT. Additionally, when we looked more specifically at perioperative outcomes between the 2 groups, we found no difference in the rates of PNF, PRS, EAD, or postoperative renal dysfunction. Perhaps one of the most concerning outcomes when discussing DCD LT is IC. No significant difference in total rate of IC was seen between the 2 groups, nor was there any difference in the rates of more severe forms of IC (diffuse necrosis and multifocal progressive).

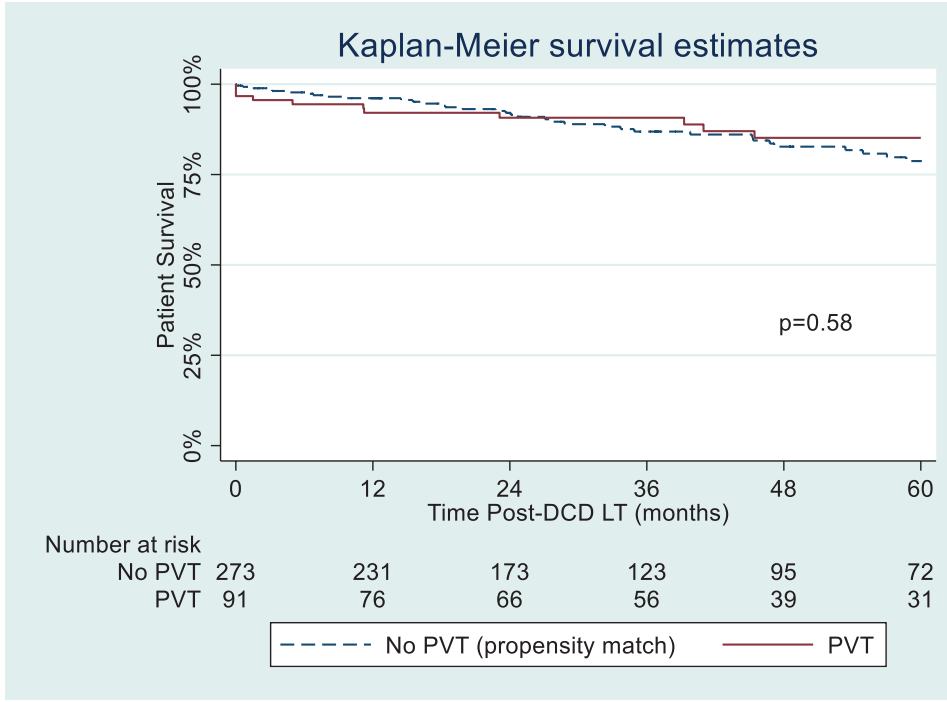

FIGURE 2. Patient Survival in the DCD PVT group and propensity matched DCD without PVT groups. DCD, donation after circulatory death; LT, liver transplant; PVT, portal vein thrombosis.

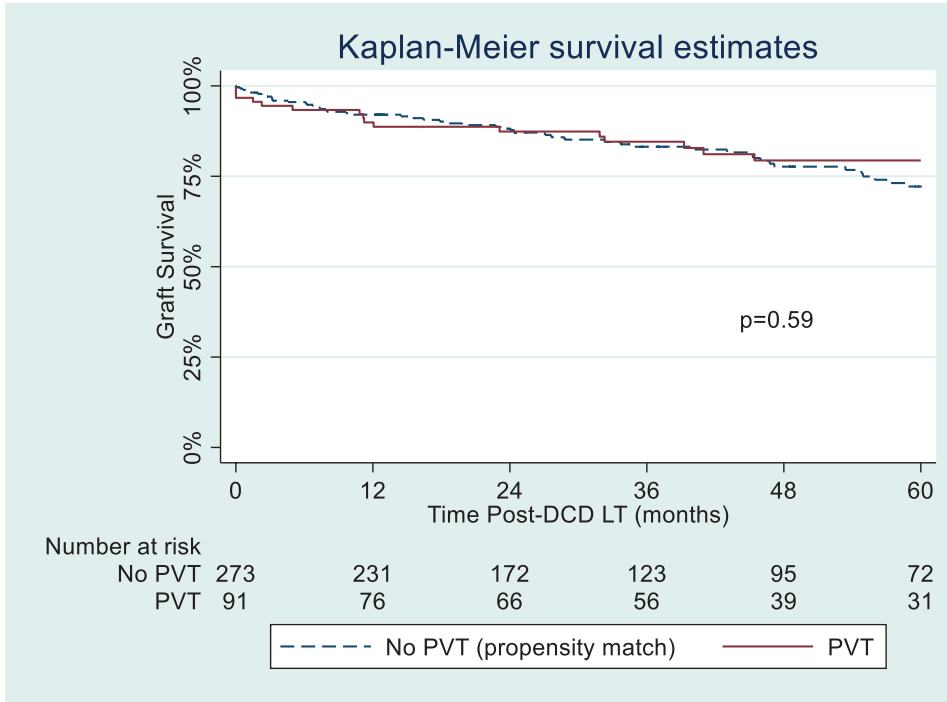

FIGURE 3. Graft Survival in the DCD PVT group and propensity matched DCD without PVT groups. DCD, donation after circulatory death; LT, liver transplant; PVT, portal vein thrombosis.

These data are highly encouraging; however, it is important to highlight that all except for 1 patient in the current cohort had grades I–III PVT. The majority of the patients comprising the cohort had grade I–II PVT (90.1%). Additionally, in 97.8% of the cases, the PVT was removed through thromboendovenectomy allowing for a PV–PV anastomosis. Indeed, previous publication looking at PVT in DBD cohorts have demonstrated that results similar to patients without PVT can be achieved when an end-to-end porto-portal anastomosis can be performed.[19] Achieving physiologic inflow to the liver is a key factor impacting post-LT outcomes. A nonphysiological reconstruction has been shown to be associated with a significantly higher risk of PV rethrombosis, gastrointestinal bleeding, and small bowel obstruction.[20] More complex techniques such as venous jump grafts, reniportal anastomoses, and cavoportal hemitransposition result in increased morbidity in

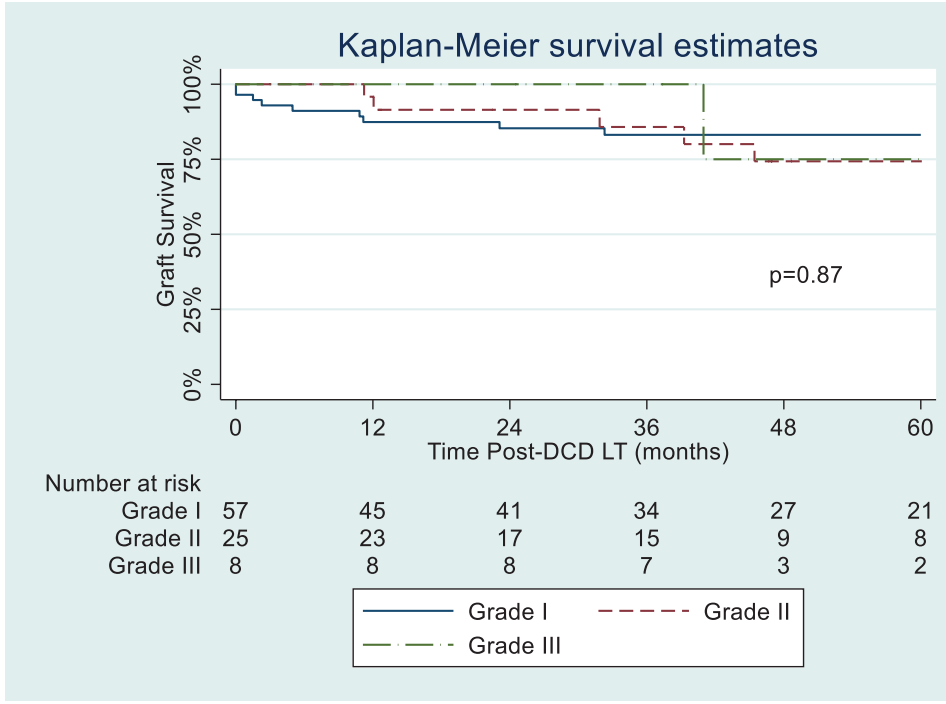

FIGURE 4. Graft survival in the DCD LT with PVT group based on grade of PVT. DCD, donation after circulatory death; LT, liver transplant; PVT, portal vein thrombosis.

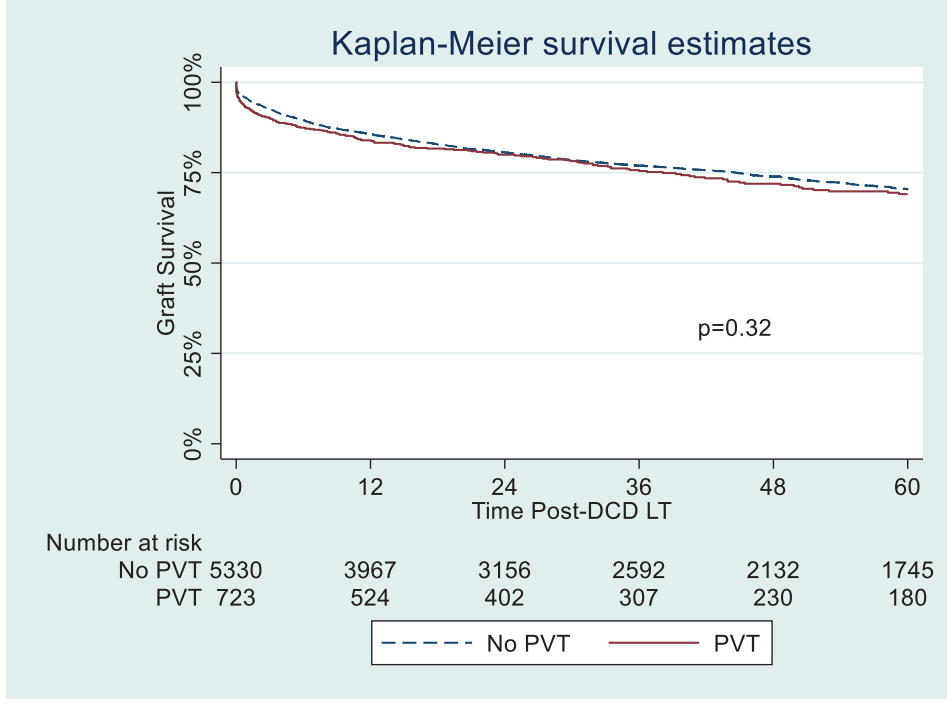

FIGURE 5. National Scientific Registry of Transplant Recipients data: graft survival in patients undergoing DCD LT with PVT at transplant vs those with no PVT. DCD, donation after circulatory death; LT, liver transplant; PVT, portal vein thrombosis.

even the most ideal scenarios and should be avoided when using DCD grafts. This is clearly highlighted by the 1 patient from the present cohort with grade 4 PVT requiring a venous jump graft who died from PNF shortly after transplant. With the more widespread availability of machine perfusion technologies such as normothermic machine perfusion and hypothermic machine perfusion, utilizing DCD grafts for patients with more complicated grade III–IV PVT requiring venous jump grafts may become a possibility. These machine perfusion technologies may facilitate the utilization of DCD livers for recipients with various technical challenges in which prolonged hepatectomy is anticipated.[21-24]

Data from the SRTR looking at PVT demonstrate no difference in graft survival between patients with PVT and patients without PVT undergoing DCD LT. SRTR data lack the granularity to determine the grade of PVT; therefore, it

is possible that many of the cases in this cohort represented uncomplicated low-grade PVT. One should therefore be cautious in interpreting that data to suggest that DCD grafts can be safely used for more complicated, higher grade PVT cases.

Given the inevitable possibility of discovering more extensive PVT than anticipated at the time of LT, we would strongly recommend having updated reliable imaging in all patients with PVT in whom a DCD liver graft is being considered. If uncertainty exists as to whether the PVT may not be able to be removed through thromboendovenectomy allowing for a PV–PV anastomosis, then a DCD liver graft should likely be avoided unless significantly elevated risk is warranted. Additionally, we would recommend evaluating portal flow following thromboendovenectomy in all recipients with PVT and performing ligation of collateral circulation (such as coronary veins or splenoreanal shunts) if necessary.

Limitation to the present study is inherent to its retrospective study design. Also, it should be stressed that these recipients were selected for cases in which it was anticipated that a PV–PV anastomosis would be possible following thromboendovenectomy. These results should not be generalized to apply to recipients with PVT requiring more extensive reconstructions. None of the patients in the present cohort underwent machine perfusion techniques and therefore what impact this may have in either donor or recipient selection when using DCD liver grafts cannot be addressed by the present study.

In conclusion, the present study demonstrates that in appropriately selected patients with grade I–II PVT, DCD liver grafts can be safely used. In patients in whom reliable updated imaging is available or in whom there is uncertainty as to whether physiological flow can be achieved through thromboendovenectomy, DCD liver grafts should likely be avoided.

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