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Evaluation of Liver Graft Donation After Euthanasia

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IMPORTANCE The option of donating organs after euthanasia is not well known. Assessment of the results of organ transplants with grafts donated after euthanasia is essential to justify the use of this type of organ donation.

OBJECTIVES To assess the outcomes of liver transplants (LTs) with grafts donated after euthanasia (donation after circulatory death type V [DCD-V]), and to compare them with the results of the more commonly performed LTs with grafts from donors with a circulatory arrest after the withdrawal of life-supporting treatment (type III [DCD-III]).

DESIGN, SETTING, AND PARTICIPANTS This retrospective multicenter cohort study analyzed medical records and LT data for most transplant centers in the Netherlands and Belgium. All LTs with DCD-V grafts performed from the start of the donation after euthanasia program (September 2012 for the Netherlands, and January 2005 for Belgium) through July 1, 2018, were included in the analysis. A comparative cohort of patients who received DCD-III grafts was also analyzed. All patients in both cohorts were followed up for at least 1 year. Data analysis was performed from September 2019 to December 2019.

EXPOSURES Liver transplant with either a DCD-V graft or DCD-III graft.

MAIN OUTCOMES AND MEASURES Primary outcomes were recipient and graft survival rates at years 1, 3, and 5 after the LT. Secondary outcomes included postoperative complications (early allograft dysfunction, hepatic artery thrombosis, and nonanastomotic biliary strictures) within the first year after the LT.

RESULTS Among the cohort of 47 LTs with DCD-V grafts, 25 organ donors (53%) were women and the median (interquartile range [IQR]) age was 51 (44-59) years. Among the cohort of 542 LTs with DCD-III grafts, 335 organ donors (62%) were men and the median (IQR) age was 49 (37-57) years. Median (IQR) follow-up was 3.8 (2.1-6.3) years. In the DCD-V cohort, 30 recipients (64%) were men, and the median (IQR) age was 56 (48-64) years. Recipient survival in the DCD-V cohort was 87% at 1 year, 73% at 3 years, and 66% at 5 years after LT. Graft survival among recipients was 74% at 1 year, 61% at 3 years, and 57% at 5 years after LT. These survival rates did not differ statistically significantly from those in the DCD-III cohort. Incidence of postoperative complications did not differ between the groups. For example, the occurrence of early allograft dysfunction after the LT was found to be 13 (31%) in the DCD-V cohort and 219 (45%) in the DCD-III cohort. The occurrence of nonanastomotic biliary strictures after the LT was found to be 7 (15%) in the DCD-V cohort and 83 (15%) in the DCD-III cohort.

CONCLUSIONS AND RELEVANCE The findings of this cohort study suggest that LTs with DCD-V grafts yield similar outcomes as LTs with DCD-III grafts; therefore, grafts donated after euthanasia may be a justifiable option for increasing the organ donor pool. However, grafts from these donations should be considered high-risk grafts that require an optimal donor selection process and logistics.

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Invited Commentary

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Few countries have accepted the possibility of euthanasia as an alternative to permanent, severe physical or mental illness. Currently, euthanasia is legalized under certain conditions in Belgium, Canada, Colombia, Luxembourg, and the Netherlands.[1] Euthanasia differs from physician-assisted suicide. During euthanasia, the physician administers medication to a patient to intentionally end their life, whereas in physician-assisted suicide, the patient self-administers the medication that has been prescribed by the physician.

Organ donation after euthanasia could help alleviate the current organ shortage. A retrospective study found that 10% of patients who underwent euthanasia in Belgium could have been a suitable organ donor.[2] Especially in patients for whom organ replacement therapy options are limited, including candidates for a liver transplant, the use of organs donated after euthanasia could reduce waiting-list mortality. At present, organ donation after euthanasia is allowed in Belgium and the Netherlands and has been decriminalized in Canada.[3,4] However, there is little awareness of the possibility to donate organs after euthanasia among both physicians and patients.

Although liver transplant (LT) with grafts donated after euthanasia has been shown feasible in several countries,[5,6] assessing the outcomes of LT with these grafts is essential to justify this type of organ donation to the general public. Recently, based on a single-center study, Gilbo et al[7] concluded that LT with grafts donated after euthanasia yielded similar survival rates as LT with grafts from donation after circulatory death (DCD) type III, defined as grafts from donors with a circulatory arrest after the withdrawal of life-supporting treatment.[8] However, the study by Gilbo et al[7] had a small sample size and did not report information on postoperative complications, such as posttransplant cholangiopathy.

As do grafts from DCD-III, organs donated after euthanasia undergo donor warm ischemia time (DWIT), which triggers the occurrence of posttransplant complications that could worsen long-term outcomes.[9,10] As such, according to the modified Maastricht criteria, grafts donated after euthanasia are considered the fifth subtype of DCD (DCD-V).[8]

In general, the use of DCD grafts in LT has rapidly increased. Within the Eurotransplant region, the number of DCD liver grafts used in LT increased from 42 in 2010 to 160 in 2019.[11] When compared with LT with grafts from donation after brain death, however, LT with DCD grafts tends to yield a higher incidence of graft failure and biliary complications, of which nonanastomotic strictures are the most harmful.[9,12,13]

In this multicenter cohort study, the outcomes of LTs with DCD-V grafts in Belgium and the Netherlands were examined. We aimed to assess these outcomes and to compare them with the results of the more commonly performed LTs with DCD-III grafts.

Key Points

Question What are the outcomes of liver transplants with grafts donated after euthanasia?

Findings In this cohort study of 47 liver transplants with grafts donated after euthanasia in the Netherlands and Belgium, recipient and graft survival rates were comparable with the survival rates in a comparative cohort of 542 recipients of liver grafts from donors with a circulatory arrest after the withdrawal of life-supporting treatment. The use of liver grafts donated after euthanasia can expand the pool of grafts donated after circulatory death by approximately 7%.

Meaning Findings from this study suggest that the use of liver grafts donated after euthanasia is justifiable and can expand the existing liver donor pool.

Legal and Practical Aspects of Euthanasia

Euthanasia was legalized in the Netherlands in 2001 and in Belgium in 2002. According to both the Dutch and Belgian law, patients who request euthanasia must be experiencing severe physical or mental distress with no chance for improvement and no reasonable alternative.[14,15] Furthermore, a patient's appeal for euthanasia must be well considered and completely voluntarily. In addition to the physician handling the euthanasia request, an independent physician must reassess whether the request is justified. Euthanasia is performed by a physician who administers a drug that induces a coma (preferably, thiopental sodium; in the Netherlands, propofol is used as an alternative) followed by a nondepolarizing neuromuscular blocking agent (eg, rocoronium bromide, atracurium besylate, or cistracurium besylate).[16,17]

Legal and Practical Aspects of Organ Donation After Euthanasia

In the Netherlands, the Erasmus MC University Medical Center and Maastricht University Medical Center developed a manual on organ donation after euthanasia, and the Dutch Transplant Society created a multidisciplinary national guideline for organ donation after euthanasia.[5,18] In Belgium, a national guideline on DCD-V is nonexistent, but all transplant centers across the country have a local protocol for this type of organ donation. The most important ethical aspect of facilitating DCD-V is that the organ donation and euthanasia should be handled as 2 separate, strictly regulated processes. Neither the patients and their relatives nor the physicians should experience any form of social pressure or conflict of interest.

The process of DCD-V is initiated by a voluntary request from a patient whose euthanasia request has already been granted. After this request, a physician (often a general practitioner) contacts a transplant coordinator. The transplant coordinator evaluates the patient's medical record to ascertain whether the patient is a suitable organ donor. Often, additional screening investigations, such as blood tests and imaging, must be performed before a final decision can be made. The contraindications for DCD-V are similar to the contraindications for the other types of deceased donation. Despite some previous cases in which the coma-inducing drug was administered to the patient at home, today the complete euthanasia procedure is highly recommended to take place in the hospital.[19]

Donation and Transplant Procedure

After circulatory arrest has been declared by the physician who performed the euthanasia, the DCD-V procedure commences

in a similar way as the DCD-III donation. To ascertain irreversible circulatory arrest, a 5-minute period of no touch is obligatory. In the Netherlands, transporting the donor to the operating theater during these 5 minutes is prohibited. In both Belgium and the Netherlands, a super-rapid sternolaparotomy is performed to procure donor organs. The implantation techniques are transplant center–specific but generally include the piggyback technique (or a variant of it) for the caval vein anastomosis, an end-to-end arterial and portal anastomosis, and a duct-to-duct biliary anastomosis.

Methods

Most transplant centers in the Netherlands and Belgium (N = 8) participated in this population-based cohort study. This study was approved by the Medical Research Ethics Committee of the Erasmus MC University Medical Center Rotterdam, which waived the requirement to obtain informed consent because the study used only deidentified data.

Study Population

All LTs with DCD-V grafts performed in the Netherlands and Belgium from the start of the donation after euthanasia program (January 2012 for the Netherlands, and January 2005 for Belgium) through July 1, 2018, were included in this analysis. Liver grafts from DCD-V that were preserved with machine perfusion were excluded. We obtained LT data from prospectively collected databases maintained by many transplant centers. In case of missing data, we accessed individual medical records or the Donor Data application from Eurotransplant.

To compare the results of LTs with DCD-V grafts with LTs with DCD-III grafts (comparative cohort), we used a Dutch database that contains all adult LTs with DCD-III performed between January 1, 2006, and January 1, 2017. Liver grafts recovered on machine perfusion and liver graft retransplants were excluded from this database. This comparative cohort was extended to LTs with DCD-III performed in the same period in 3 Belgian transplant centers (in Leuven, Antwerp, and Liège) that performed most of the LTs with DCD-V.

Primary and Secondary Outcomes and Definitions

The primary outcomes of this study were the recipient and graft survival rates at years 1, 3, and 5 after the LT. *Patient loss* was defined as death with or without a functioning graft, whereas *graft loss* was defined as either a recipient death or a retransplant. Secondary outcomes were the occurrence of early allograft dysfunction, hepatic artery thrombosis, and nonanastomotic biliary strictures within the first year after the LT. As described, the DWIT can be divided into an agonal phase and an asystolic phase.[20] In an LT with DCD-V graft, the agonal phase was defined as the time between administration of euthanatics (coma-inducing drug and nondepolarizing neuromuscular blocking agent) and circulatory arrest. In an LT with DCD-III graft, the agonal phase was defined as the period between withdrawal of life-supporting treatment and circulatory arrest. The definition of the asystolic phase was the same for both LT with DCD-III graft and LT with DCD-V graft: the time between circulatory arrest and start of cold perfusion.

The cold ischemia time was described as the period between the start of cold perfusion in the donor and the removal of the liver graft from ice before implantation. The recipient warm ischemia time was the period between the removal of the liver graft from ice and the portal or arterial reperfusion, whichever came first. Regarding the secondary outcome parameters, early allograft dysfunction was classified according to the Olthoff criteria and was diagnosed only in patients who were alive and did not undergo a retransplant within week 1 after the LT.[21] Nonanastomotic biliary strictures were described as any stricture of the biliary tree other than those at the level of the anastomosis and in the absence of a hepatic artery thrombosis.

Statistical Analysis

Continuous variables are presented as median (interquartile range [IQR]), whereas categorical variables are presented as frequency (valid percentage). To compare the 2 groups, we used either an unpaired χ^2 test (categorical variables) or an unpaired Mann-Whitney test (continuous variables). Recipient and graft survival rates were calculated with the Kaplan-Meier method. A log-rank test was performed to assess the statistical differences in survival rates between the DCD-V and DCD-III cohorts.

All statistical analyses were performed in SPPS, version 25 (SPSS Inc). A 2-sided $P < .05$ was considered statistically significant. Data analysis was performed from September 2019 to December 2019.

Results

As of July 1, 2018, a total of 59 LTs with DCD-V grafts had been performed in Belgium and in the Netherlands. Between January 1, 2012, and December 31, 2017, approximately 7% of all LTs with DCD performed in both countries were with DCD-V grafts. In 12 cases, the liver graft underwent machine preservation, and these cases were excluded from further analysis. The final cohort comprised 47 LTs with DCD-V grafts. The comparative cohort consisted of 542 LTs with DCD-III grafts. The median (IQR) follow-up period of the complete cohort was 3.8 (2.1-6.3) years.

Donor, Recipient, and Surgical Characteristics

In the DCD-V cohort, 25 organ donors (53%) were women and 22 (47%) were men, with a median (IQR) age of 51 (44-59) years (**Table 1**). This composition was statistically significantly different from the DCD-III cohort, which comprised 335 men (62%) and 207 women (38%; $P = .04$), with a median (IQR) age of 49 (37-57) years. In the DCD-V cohort, a neurodegenerative disease (eg, amyotrophic lateral sclerosis, multisystem atrophia, and Huntington disease) was the most common indication for euthanasia request (17 [36%]), followed by a psychiatric disorder (11 [23%]). Compared with donors in the DCD-III cohort, those in the DCD-V cohort had significantly lower levels of median (IQR) transaminase (aspartate aminotrans-

Table 1. Donor Demographic Characteristics

Characteristic	No. (%)[a] DCD-V cohort (n = 47)	DCD-III cohort (n = 542)	*P* value
Sex			
Men	22 (47)	335 (62)	.04
Women	25 (53)	207 (38)	
Age, median (IQR), y	51 (44-59)	49 (37-57)	.17
BMI, median (IQR)	23 (20-26)	24 (22-26)	.09
Indication for euthanasia			
Neurodegenerative diseases	17 (36)	NA	NA
Psychiatric disorders	11 (23)	NA	NA
Multiple sclerosis	8 (17)	NA	NA
Unbearable pain	3 (6)	NA	NA
Tetraplegia or quadriplegia	1 (2)	NA	NA
Locked-in syndrome	2 (4)	NA	NA
Cerebrovascular accident	1 (2)	NA	NA
Other	3 (6)	NA	NA
Unknown	1 (2)	NA	NA
Highest AST level, median (IQR), IU/L	26 (21-33)[b]	67 (36-140)	<.001
Highest ALT level, median (IQR), IU/L	25 (20-38)	52 (25-115)[c]	<.001
DWIT, median (IQR), min			
Agonal[d]	7 (5-9)	14 (9-20)[e]	<.001
Asystolic[f]	11 (8-14)	12 (9-17)[g]	.03

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); DCD, donation after circulatory death (type III or type V); DWIT, donor warm ischemia time; IQR, interquartile range.

SI conversion factors: To convert ALT and AST to microkatals per liter, multiply by 0.0167.

[a] Data are shown as frequency (valid percentages) unless noted otherwise. Percentages may not add to 100% because of rounding.

[b] Proportion of missing data for this variable was 2.1%.

[c] Proportion of missing data for this variable was 0.2%.

[d] Agonal DWIT is the time between administration of euthanatics (DCD-V) or withdrawal of life support (DCD-III) and circulatory arrest.

[e] Proportion of missing data for this variable was 14.4%.

[f] Asystolic DWIT is the time between circulatory arrest and cold perfusion.

[g] Proportion of missing data for this variable was 5.5%.

ferase: 26 [21-33] IU/L vs 67 [36-140] IU/L; alanine aminotransferase: 25 [20-38] IU/L vs 52 (25-115) IU/L; $P < .001$). (To convert aspartate aminotransferase and alanine aminotransferase to microkatals per liter, multiply by 0.0167.) The median (IQR) agonal DWIT was 7 (5-9) minutes, which was significantly shorter than that in the comparative cohort (14 [9-20] minutes) ($P < .001$). The median (IQR) asystolic DWIT was also significantly shorter in the DCD-V population (11 [8-14] vs 12 [9-17] minutes; $P = .03$) (Table 1).

In the DCD-V cohort, 30 recipients (64%) were men and 17 (36%) were women, with a median (IQR) age of 56 (48-64) years (**Table 2**). Median (IQR) recipient warm ischemia time was 39 (32-46) minutes and cold ischemia time was 356 (308-423) minutes. No statistically significant differences in recipient and surgical characteristics were observed between the DCD-V and DCD-III groups. For example, the median (IQR) body mass index (calculated as weight in kilograms divided by height in meters squared) for recipients was 25 (22-29) in the DCD-V cohort and 26 (23-29) in the DCD-III cohort ($P = .12$). Hepatocellular carcinoma was the most common indication for transplant in both groups (13 [28%] vs 177 [33%]; $P = .10$) (Table 2).

Postoperative Course

The peak median (IQR) serum levels of both aspartate aminotransferase (895 [606-2047] IU/L vs 1505 [837-3099] IU/L; $P = .003$) and alanine aminotransferase (674 [450-1223] IU/L vs 1063 [544-2136] IU/L; $P = .02$) within week 1 after the LT were statistically significantly lower in the DCD-V cohort than in the DCD-III cohort (**Table 3**). However, no significant difference was found in the occurrence of early allograft dysfunction after the LT (13 [31%] vs 219 [45%]; $P = .09$).

A total of 7 patients (15%) who underwent an LT with DCD-V graft had a diagnosis of nonanastomotic stricture of the biliary tree within the first year after the LT. This number was not statistically significant, compared with 83 patients (15%) in the comparative DCD-III cohort. Rates of primary nonfunction (2 [4%] vs 9 [2%]) and hepatic artery thrombosis (3 [6%] vs 23 [4%]) did not differ between the DCD-V and DCD-III cohorts (Table 3).

Recipient and Graft Survival

Recipient survival in the DCD-V cohort was 87% at 1 year, 73% at 3 years, and 66% at 5 years after LT. These rates did not differ significantly from the survival rates in the comparative cohort: 90% at 1 year, 81% at 3 years, and 77% at 5 years after transplant (log-rank $P = .18$) (**Figure 1**). Graft survival among DCD-V recipients was 74% at 1 year, 61% at 3 years, and 57% at 5 years. In the DCD-III cohort, graft survival was 83% at 1 year, 72% at 3 years, and 68% at 5 years after LT (**Figure 2**). This difference in survival was not statistically significant (log-rank $P = .11$).

Table 2. Recipient and Surgical Demographic Characteristics

Characteristic	No. (%)[a] DCD-V cohort (n = 47)	DCD-III cohort (n = 542)	*P* value
Sex			
Men	30 (64)	401 (74)	.13
Women	17 (36)	141 (26)	
Gender mismatch			
No mismatch	31 (66)	334 (62)	.66
Male donor to female recipient	4 (9)	71 (13)	
Female donor to male recipient	12 (26)	137 (25)	
Age, median (IQR), y	56 (48-64)	58 (51-64)	.35
BMI, median (IQR)	25 (22-29)	26 (23-29)[b]	.12
Indication for transplant			
Hepatocellular carcinoma	13 (28)	177 (33)	.10
Alcoholic liver cirrhosis	9 (19)	129 (24)	
Cholestatic diseases (PBC/PSC)	6 (13)	56 (10)	
Cirrhosis due to viral hepatitis	2 (4)	45 (8)	
Cryptogenic cirrhosis	1 (2)	23 (4)	
Acute liver failure	3 (6)	6 (1)	
NASH	1 (2)	15 (3)	
Other	12 (26)	91 (17)	
Laboratory MELD score	16 (11-23)	15 (10-20)[c]	.19
Surgical procedure duration, median (IQR), min			
RWIT	39 (32-46)	39 (31-46)[d]	.48
CIT	356 (308-423)	373 (295-461)[d]	.38

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); CIT, cold ischemia time; DCD, donation after circulatory death (type III or type V); IQR, interquartile range; MELD, Model for End-stage Liver Disease; NASH, nonalcoholic steatohepatitis; PBC, primary biliary cirrhosis; PSC, primary sclerosing cholangitis; RWIT, recipient warm ischemia time.

[a] Data are shown as frequency (valid percentages) unless noted otherwise. Percentages may not add to 100% because of rounding.

[b] Proportion of missing data for this variable is 20.7%.

[c] Proportion of missing data for this variable is 1.3%.

[d] Proportion of missing data for this variable is 0.2%.

Table 3. Postoperative Demographic Characteristics and Complications

Postoperative outcome	No. (%)[a] DCD-V cohort (n = 47)	DCD-III cohort (n = 542)	*P* value
Length of stay, median (IQR), d			
ICU	3 (2-6)	3 (2-6)	.82
Hospital	17 (14-31)	18 (13-26)	.73
Peak level in week 1, median (IQR), IU/L[b]			
AST	895 (606-2047)[c]	1505 (837-3099)[d]	.003
ALT	674 (450-1223)[c]	1063 (544-2136)[d]	.02
Bilirubin level on day 7, median (IQR), μmol/L[b]	44 (20-100)[c]	29 (16-72)[e]	.16
Complications			
Primary nonfunction	2 (4)	9 (2)	.22
Early allograft dysfunction[b]	13 (31)[c]	219 (45)[d]	.09
Hepatic artery thrombosis[f]	3 (6)	23 (4)	.45
Nonanastomotic strictures[f]	7 (15)	83 (15)	.94

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; DCD, donation after circulatory death (type III or type V); ICU, intensive care unit; IQR, interquartile range.

SI conversion factors: To convert ALT and AST from units per liter to microkatals per liter, multiply by 0.0167.

[a] Data are shown as frequency (valid percentages) unless noted otherwise. Percentages may not add to 100% because of rounding.

[b] Patients who died or underwent retransplant within 7 days after liver transplant were excluded.

[c] Proportion of missing data for this variable is 4.5%.

[d] Proportion of missing data for this variable is 4.8%.

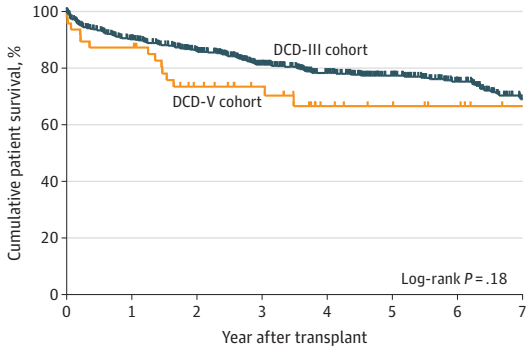
[e] Proportion of missing data for this variable is 7.5%.

[f] Development of complication within the first year after transplant.

Discussion

To our knowledge, this study is the largest research thus far into the outcome of LT with grafts donated after euthanasia. The results show that LTs with DCD-V liver grafts have recipient and graft survival rates that are similar to those of the more commonly performed LTs with DCD-III grafts. Accordingly, DCD-V liver grafts can be used to enlarge the DCD donor pool by approximately 7%. However, because both the experience with this type of graft is limited and the results are not superior to those of LT with DCD-III, liver

Figure 1. Kaplan-Meier Curve of Recipient Survival From Liver Graft Donation After Circulatory Death Type V (DCD-V) vs Type III (DCD-III)

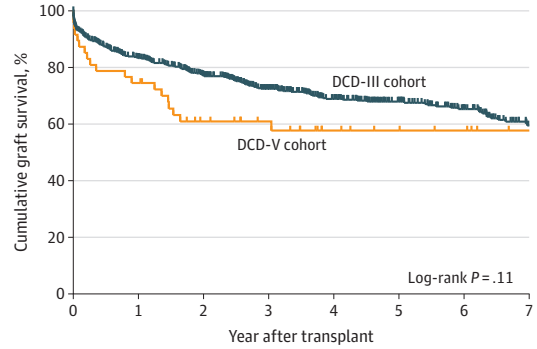


No. at risk

DCD-V cohort	47	41	29	23	13	10	7	3
DCD-III cohort	542	480	427	340	274	206	159	104

DCD-III liver grafts were donated after a planned withdrawal of life-supporting treatments. DCD-V liver grafts were donated after euthanasia.

Figure 2. Kaplan-Meier Curve of Graft Survival in Recipients of Liver Graft Donation After Circulatory Death Type V (DCD-V) vs Type III (DCD-III)



No. at risk

DCD-V cohort	47	35	24	19	11	8	6	2
DCD-III cohort	542	441	383	304	236	174	135	88

DCD-III liver grafts were donated after a planned withdrawal of life-supporting treatments. DCD-V liver grafts were donated after euthanasia.

grafts donated after euthanasia should be considered extended-criteria grafts.

The results of the present study are not in line with our hypothesis that LTs with DCD-V grafts have superior outcomes compared with LTs with DCD-III grafts and that these outcomes may even be similar to outcomes of LTs with grafts donated after brain death, which had a 5-year recipient survival rate of 80% and graft survival rate of 70%.[22]

This finding could be associated with a number of factors. First, patients who request euthanasia are often physically weakened. Because of their medical condition, patients can develop muscle atrophia, sarcopenia, and malnutrition. These conditions could have detrimental implications for the liver graft. Donors in the DCD-III cohort, especially those with trauma, often had a blank medical history. Second, the association between euthanatics and the DCD-V liver grafts is unclear. The nondepolarizing neuromuscular blocking agent is given in a relatively high dose and could therefore be hepatotoxic, especially given that this medication is eliminated mainly by the liver (through bile) and kidneys.[23] Furthermore, the postmortal effects of these medications as well as their effect during the first minutes of the cold flush of the graft is unknown. Further research into the effect of euthanatics on liver grafts is recommended. Meanwhile, the use of normothermic machine perfusion or normothermic regional perfusion to test the viability of DCD-V liver grafts may be helpful.

Optimal logistics is mandatory in the field of organ transplantation, especially when using high-risk grafts, which may describe DCD-V liver grafts. Therefore, a local allocation policy of DCD-V grafts, as used in the study by Gilbo et al,[7] could facilitate optimal recipient selection. Furthermore, the cold ischemia time can be kept as short as possible given that both organ procurement and transplant are performed by a single team.

As we hypothesized, the agonal phase of the DWIT was significantly shorter among donors in the DCD-V cohort compared with donors in the DCD-III group. However, this shorter agonal phase did not seem to be associated with superior survival rates among recipients of DCD-V grafts compared with recipients in the DCD-III group. We were unable to calculate the functional DWIT in this study. Research has shown that an oxygen saturation of less than 80% should be considered as the start of the functional DWIT.[20] However, in LTs with DCD-V grafts, the donor oxygen saturation and blood pressure levels are often not measured. In the few cases in which these parameters were measured, it was done noninvasively to minimize harm to the patient. This measurement cannot be compared with the typically invasive measurement method (ie, venous or arterial catheter) used in patients in the DCD-III cohort. Therefore, we chose the time of administration of euthanatics as the starting point of DWIT.

Significantly lower levels of alanine aminotransferase and aspartate aminotransferase were found in donors in the DCD-V cohort, which probably were associated with the lower posttransplant peak of aminotransferase levels. This finding may seem contradictory to our earlier statement that patients in the DCD-V cohort are physically weakened. However, donors in the DCD-III cohort, rather than those in the DCD-V group, are prone to having elevated transaminase levels associated with their traumatic or nontraumatic brain injury or cardiovascular event with possible resuscitation.[24-27] The absolute difference in transaminase levels between the two groups may be too small to have altered the outcome.

The DCD-V cohort comprised a substantially higher proportion of women. Although this finding was statistically nonsignificant in the current research, a higher risk of gender mismatch may be present among recipients of DCD-V liver grafts, especially woman-to-man transplant. Research has shown that this type of gender mismatch is associated with lower survival rates.[28,29]

When we compared the present study with the literature, we observed that recipient and graft survival rates at 3 years after LTs with DCD-V grafts were substantially higher in the single-center analysis of Gilbo et al[7] than in this multicenter

study. This difference may be associated with both logistic and allocation policy differences between the Dutch and Belgian DCD cohorts.

Strengths and Limitations

This study has some strengths. First, the study has a multicenter and international design, which enabled the inclusion of, to our knowledge, the largest population of donors and recipients of LTs with DCD-V grafts reported in the literature. Second, we believe this study has the ability to create awareness about donation after euthanasia among the medical community and the general public.

According to the Dutch guideline, the conversation regarding the possibility of organ donation after euthanasia must be initiated by the patient and not by the physician.[18] The implementation of the new Donor Act in the Netherlands has revived the debate on whether this recommendation is ethical.[30,31] On one hand, informing a patient about organ donation after euthanasia may put social pressure on the patient, which could potentially lead to a breach of trust. This conversation could be seen as a violation of a basic ethical principle in medical practice: *primum non nocere* (first, do no harm). On the other hand, withholding this information violates another important medical principle: patient autonomy. In both euthanasia and organ donation, the ability of patients to make their own choice using all available information is fundamental. Especially if the patient is registered as an organ donor, autonomy could be hampered if the physician does not inform the patient.

This study has some limitations. First, the sample size of the DCD-V group was relatively small. This limited size prevented us from performing more robust statistical analyses, such as regression analysis, to identify independent risk factors for inferior outcome of LTs with DCD-V grafts. Second, even though many Dutch and Belgian transplant centers prospectively collect data on LTs performed in their centers, the study design was retrospective and therefore prone to bias.

Conclusions

This cohort study found that LTs with DCD-V liver grafts achieved results comparable to those in LTs with DCD-III grafts. This finding suggests that DCD-V is a valuable source for increasing the organ donor pool. However, liver grafts from these types of organ donations should still be considered high-risk grafts that require an optimal donor selection process and favorable logistics.

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