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The Impact of Implantation Time During Liver Transplantation on Outcome: A Eurotransplant Cohort Study

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Background. The liver graft quickly rewarms during transplantation when the vascular anastomoses are being performed, potentially impacting on outcomes. **Methods.** We investigated the relationship between implantation time and outcome in 5223 recipients of deceased-donor livers transplanted in Eurotransplant (2004-2013). Cox regression analyses were corrected for donor, preservation, and recipient variables. Transplant loss represents all-cause graft failure. **Results.** Median implantation time was 41 minutes (interquartile range, 34-51). Implantation time independently associated with transplant loss (adjusted hazard ratio, 1.04 for every 10-minute increase; 95% confidence interval, 1.01-1.07; $P = 0.007$). The magnitude of the implantation time effect was comparable to the effect of each additional hour of cold ischemia (adjusted hazard ratio, 1.03; 95% confidence interval, 1.02-1.05; $P < 0.001$). The effect was most pronounced early posttransplant with no evidence of a significant effect beyond 3 months. A similar detrimental effect of implantation time was seen for graft and patient survivals. The increased risk for transplant loss in livers donated after circulatory determination of death could be attributed to donor warm ischemia time. **Conclusions.** Implantation time associates with inferior liver transplant outcome in a continuous way. These findings need confirmation and further study of confounding factors is needed so steps toward improving outcomes can be made.

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Ischemia-reperfusion injury is a major threat to the liver transplant. Prolonged cold ischemia time impairs graft function and survival.^{1,2} Additionally, donor warm ischemia before organ retrieval in donation after circulatory determination of death (DCD) impacts organ viability and increases the risk of ischemic biliary type strictures.^{3,4} However, as soon as the graft leaves the ice for implantation, the liver starts rewarming rapidly.⁵ This period of warm ischemia, called the anastomosis time or implantation time, may cause additional harm to the graft resulting in decreased graft and patient survival. In liver transplantation, implantation time has not been studied in detail.

Although it has been incorporated as a dichotomous factor in some outcome analyses where it was found to be a risk factor for patient death,^{6,7} a systematic literature search could not define a study that specifically investigated the effect of implantation time on outcome (SDC, **Materials and Methods**, <http://links.lww.com/TXD/A94>; SDC 12 - References - <http://links.lww.com/TXD/A95> and **Table S1, SDC**, <http://links.lww.com/TXD/A84>). It is unclear from the current literature how big the impact of implantation time on patient level might be, whether it affects all types of liver grafts, or if the effect of implantation time is constant over time.

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We aimed to further define the relation between implantation time and outcome using the Eurotransplant registry, the deceased donor organ allocation organization of 8 European countries.

MATERIALS AND METHODS

Study Population

Eurotransplant is an international nonprofit organization that manages patient-oriented allocation and cross-border exchange of deceased donor organs to achieve the best possible match between available donor organs and patients on the transplant waiting list in 8 countries: Austria, Belgium, Croatia, Germany, Hungary, Luxembourg, the Netherlands, and Slovenia. The Eurotransplant registry prospectively records data for all liver transplants performed in 38 liver transplant centers in its region. Data are collected on a voluntary basis to develop best practice recommendations and policies to improve organ allocation and transplant outcomes.⁸ We analyzed data submitted to this registry from all recipients of solitary liver transplants from deceased donors undertaken between January 1, 2004, and December 31, 2013. This study was approved by the Eurotransplant Liver and Intestinal Advisory Committee and the Organ Procurement Committee.

Implantation time was defined as the time between the graft leaving the ice and restoration of blood flow to the liver in the recipient. Donor warm ischemia time in DCD livers was defined as the time between circulatory arrest in the donor and cold flush of the liver. Cold ischemia time was defined as the time between the start of the cold flush in the donor and the start of graft implantation in the recipient when the liver leaves the ice and is placed inside the recipients body to start the first vascular anastomosis.

Transplant failure refers to all-cause graft failure and was taken as time from transplantation to graft failure or death of the patient. Graft failure was defined as relisting for liver transplantation or death of the patient due to liver failure and was therefore censored for death with a functioning graft. Survival of the patient was defined as time from transplantation until death.

We calculated the Donor Risk Index (DRI) for all transplants as a measure of graft quality.⁹ Because the Eurotransplant registry entails no data on donor ethnicity, we considered all donors to be non-African American. As sharing schemes are different in Eurotransplant compared the United States of America,⁸ we did not take the parameters on regional or national sharing into account.

Statistical Analysis

Follow-up analysis of the study population included all data submitted to Eurotransplant by May 3, 2016. Only recipients for whom data for both implantation time and outcome data were available were included in the study. Continuous variables are presented as median (interquartile range), categorical variables as number (%).

Multivariable Cox regression models were used to evaluate the relation of implantation time with transplant, graft, and patient survival. Variables in the multivariable models were included if they were shown to affect transplant outcome in scientific literature and available in the Eurotransplant Registry. In addition, possible confounders that might affect the association between implantation time and outcome were

considered (Table 1). A multivariate imputation was performed for variables with missing data (SDC, **Materials and Methods**, <http://links.lww.com/TXD/A94>). Once the set of confounders was determined based on the backward stepwise selection with multiple imputation, the model was extended with implantation time. Furthermore, a random effect for center was added to model the correlation between the survival times of patients within the same center, as the recipient center can have an impact on outcome.¹⁰ As simultaneous correction for 2 random effects in Cox regressions was not feasible in this data set, separate analyses were performed including donor and recipient center as a random effect separately. These analyses indicated that the impact of recipient center on outcome was more important than the effect of donor center (data not shown); therefore, results from the analyses correcting for recipient center are reported. By including a random effect for recipient center, the interpretation of the effect of implantation time refers to differences in risk between patients within the same center having a different duration of implantation time.¹¹ Centers were anonymized in the analyses.

When the Cox model was tested to ascertain whether the effect of implantation time was constant over time, we found this was not the case (data not shown).¹² To handle the nonproportional hazards in the multivariable model, implantation time was used as a time-varying variable, allowing it to have a different effect in the following periods: <3 months, 3 to 6 months, 6 to 12 months, and >12 months (SDC, **Materials and Methods**, <http://links.lww.com/TXD/A94>). Restricted cubic splines were used to allow nonlinearity in the relation between implantation time and the log-hazard.¹³

The effect of implantation time on early outcome was visualized based on a multivariable Cox regression model restricting the follow-up time to 3 months, and centering the implantation time on the mean of the center to mimic the correction for the random center effect. These figures give the mean survival function for varying values of anastomosis time, adjusted for all other covariates in the Cox model.¹⁴

We performed interaction analyses to determine whether implantation time had more effect on survival in recipients of DCD livers than in recipients of donation after brain death (DBD) livers, livers from donors with a higher DRI, livers with longer cold ischemia times, and whether the effect of implantation time was modified by type of the graft (whole graft versus split graft).

All reported results involving variables with missing values were based on multiple imputations. *P* values less than 0.050 were considered significant. All analyses were performed using SAS software (v 9.4 for Windows).

The STROBE guidelines were followed in reporting this study.

RESULTS

Characteristics of the Study Population

Fifteen thousand one hundred thirty-six deceased-donor liver transplants were performed in the Eurotransplant region between January 1, 2004, and December 31, 2013. Data on implantation time were available in 5461 cases from which we excluded 80 transplants in which implantation times were reported to be extremely short (<10 minutes) or long (>200 minutes) as well as 118 cases because of missing

TABLE 1.
Donor and recipient demographics (n = 5223)

Characteristics	Results	% Missing
Donor		
Age, y	49 (37-61)	0
Sex		0
Male	2751 (53%)	
Female	2472 (47%)	
Body mass index, kg/m ²	24.7 (22.7-27.5)	0.02
Cause of death		0
Trauma	1198 (23%)	
CVA	3159 (60.5%)	
Anoxia	599 (11.5%)	
Other	267 (5%)	
Donor cardiac arrest		52
Yes	570 (23%)	
No	1962 (77%)	
Donor type		0
DBD	5015 (96%)	
DCD	208 (4%)	
Donor warm ischemia time, min		
In DCD transplants	15 (11-18)	23
DRI	1.5 (1.3-1.8)	41
AST, U/L		
Highest	55 (33-112)	1.2
Terminal	45 (28-81)	1.3
Bilirubin, mg/dL		
Highest	0.6 (0.4-1.0)	2.8
Terminal	0.5 (0.3-0.9)	2.8
Sodium, mmol/L		
Highest	149 (144-155)	0.2
Terminal	147 (142-152)	0.2
Other organs donated		0
Heart	2225 (43%)	
Lungs	1561 (30%)	
Heart and lungs	1058 (20%)	
Pancreas	1710 (33%)	
Kidney	4924 (94%)	
Recipient		
Age, y	53 (43-60)	0
Sex		0
Male	3371 (65%)	
Female	1852 (35%)	
Body mass index, kg/m ²	24.7 (21.6-28.0)	0.08
Laboratory MELD	18 (11-31)	22
Indication for transplant		0
Acute liver failure	465 (8.9%)	
Cholestatic disease	613 (11.7%)	
Hepatocellular carcinoma	667 (12.8%)	
Post alcoholic cirrhosis	664 (12.7%)	
Viral hepatitis	706 (13.5%)	
Retransplant	779 (14.9%)	
Other	1329 (25.5%)	
Process		
Preservation fluid		3.5
HTK	3286 (64.7%)	
UW	1755 (34.5%)	
Other	39 (0.8%)	
Type of graft		0

Continued next page

TABLE 1. (Continued)

Characteristics	Results	% Missing
Whole	4732 (91%)	
Split	491 (9%)	
Arterial anatomy ^a		57.8
Normal	1562 (71%)	
Abnormal	643 (29%)	
Cold ischemia time, h	9.1 (7.4-11.0)	2.4
Implantation time, min	41 (34-51)	0

Values are presented as median (interquartile range) or number (%).

^a As reported by donor surgeon.

AST, aspartate aminotransferase; CVA, cerebrovascular accident; HTK, histidine-tryptophan-ketoglutarate solution; UW, University of Wisconsin solution.

outcome data. Transplant characteristics were comparable between the 5223 transplants included and the 9913 transplants excluded from this study (Table S2, SDC, <http://links.lww.com/TXD/A85>). The variability in reporting rates of implantation times is shown in Table S3 (SDC, <http://links.lww.com/TXD/A86>), the correlation between average implantation time and reporting rates was weak ($\rho = 0.06$).

All patients without an event have a minimal follow-up of at least 1 year. Median follow-up after transplantation was 4.5 years (2.4-6.8 years). Table 1 shows the donor and recipient characteristics at the time of transplantation. Median cold ischemia time was 9.1 hours (7.4-11.0 hours), and median implantation time was 41 minutes (34-51 minutes) (Figure 1).

Implantation Time Independently Impairs Outcome

Implantation time was independently associated with an increased overall transplant failure rate for all deceased-donor livers (adjusted hazard ratio [HR], 1.04; 95% confidence interval [CI], 1.01-1.07; $P = 0.007$) (Table 2 and Table S4, SDC, <http://links.lww.com/TXD/A87>). The magnitude of the effect of every 10-minute increase in implantation time was comparable to the effect of each hour of additional cold ischemia time (adjusted HR, 1.03; 95% CI, 1.02-1.05; $P < 0.001$). Implantation time was also an independent risk factor for graft loss (adjusted HR, 1.04; 95% CI, 1.01-1.09, $P = 0.03$) and patient death (adjusted HR 1.03, 95% CI 1.00-1.06, $P = 0.048$) (Tables S5-S6, SDC, <http://links.lww.com/TXD/A88>, <http://links.lww.com/TXD/A89>).

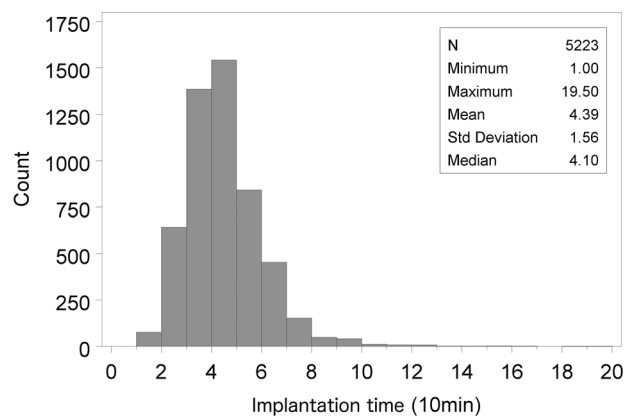


FIGURE 1. Histogram of implantation time per 10 minutes.

TABLE 2.
Cox regression models for transplant failure after liver transplantation

	Unadjusted		Adjusted	
	HR (95% CI)	P	HR (95% CI)	P
Implantation time (fixed effect) ^{a,b}	1.03 (1.00-1.05)	0.02	1.04 (1.01-1.07)	0.007
Implantation time (time varying effect) ^a		—		<0.001
< 3 mo	1.06 (1.03-1.10)	<0.001	1.08 (1.05-1.12)	<0.001
3-6 mo	0.96 (0.88-1.04)	0.29	0.97 (0.90-1.06)	0.53
6-12 mo	0.93 (0.86-1.01)	0.10	0.95 (0.87-1.03)	0.18
> 12 mo	1.02 (0.98-1.07)	0.23	1.01 (0.97-1.06)	0.59

^a 10 minutes.

^b HR and P values of the other variables considered in the model are provided in Table S4 (SDC, <http://links.lww.com/TXD/A87>).

Donor and recipient age, year of transplant, and indication for transplantation were also independent risk factor for worse outcome (Table S4, SDC, <http://links.lww.com/TXD/A87>; Table S5, SDC, <http://links.lww.com/TXD/A88>; Table S6, SDC, <http://links.lww.com/TXD/A89>). Cold ischemia time and DCD donation were independent risk factors for graft and transplant failure but not for patient death (Table S4, SDC, <http://links.lww.com/TXD/A87>; Table S5, SDC, <http://links.lww.com/TXD/A88>; Table S6, SDC, <http://links.lww.com/TXD/A89>). Laboratory Model of End-Stage Liver Disease (MELD) at the time of transplantation was a risk factor for transplant failure and patient death but not for graft loss (Table S4, SDC, <http://links.lww.com/TXD/A87>; Table S5, SDC, <http://links.lww.com/TXD/A88>; Table S6, SDC, <http://links.lww.com/TXD/A89>).

Body mass index of neither donor nor recipient associated with outcome in the multivariable models. Type of preservation fluid had no independent effect on outcome, neither had the arterial anatomy as reported by the donor surgeon. Information on arterial reconstruction at time of transplantation is not available in the Eurotransplant Registry.

Because there is variability in reporting rates of implantation time by centers (Table S3, SDC, <http://links.lww.com/TXD/A86>), we repeated the analysis of implantation time on transplant survival only including centers with reporting rates of 50% or greater. Implantation time remained an independent risk factor for transplant loss with an HR of 1.05 (1.01-1.09; $P = 0.026$).

An exploratory analysis (Table S7, SDC, <http://links.lww.com/TXD/A90>) suggests that donor and recipient body mass index, recipient sex, abnormal arterial anatomy as reported by the donor surgeon, the indication for transplantation, and the transplant center volume seem associated with the duration of implantation time.

The Detrimental Effect of Implantation Time Impacts on Early Outcome

We next investigated whether the effect of implantation time is constant over time or whether the strength of the effect weakens as time evolves. Indeed, univariable models showed evidence of nonproportional hazards (data not shown). Therefore, assuming a similar magnitude of the detrimental effect of implantation time over time would be overly simplistic. When implantation time was used as a time-varying variable, distinguishing between outcome periods less than 3 months, 3 to 6 months, 6 to 12 months, and more than

12 months, the detrimental effect of implantation time was stronger early after transplantation (HR, 1.08; 95% CI, 1.05-1.12; $P < 0.001$). Beyond 3 months, there was no longer evidence for an effect of implantation time on transplant outcome (Table 2 and Table S8, SDC, <http://links.lww.com/TXD/A91>).

This short-term effect of implantation time on transplant outcome is visualized in Figure 2, illustrating the impact on patient level. In this data set, the average probability of transplant loss at 3 months for an implantation time of 30 minutes is 14.5%, whereas an implantation time of 60 and 90 minutes resulted in a 18.4% and 23.2% probability of graft loss, respectively. Figure 3 shows the expected survival function during the first 3 months for selected values of implantation time and visualizes the early effect of implantation time on transplant loss.

In an additional exploratory analysis, we observed a stronger effect of implantation time in their higher range pointing toward a clinically more important effect but this differential effect was not significant (Figure 4).

Higher-risk Organs Do Not Seem More Susceptible to the Detrimental Effect of Implantation Time

Table S9 (SDC, <http://links.lww.com/TXD/A92>) shows demographics of DCD versus DBD transplants. The DCD donors were younger with a lower body mass index and died more frequently after trauma or anoxia compared with DBD donors. Donor sodium levels were also lower in DCD.

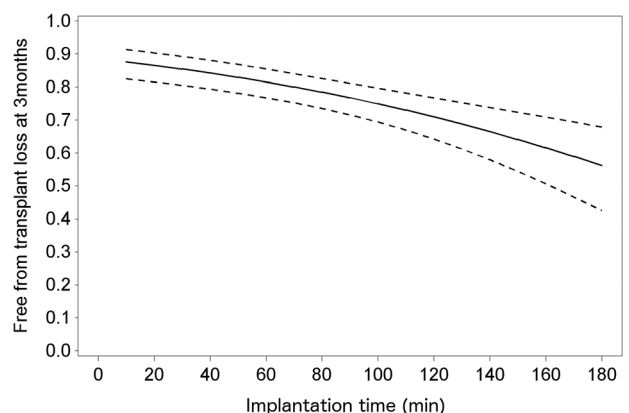


FIGURE 2. Probability of transplant survival at 3 months posttransplant with varying values for implantation time and adjusted for all other covariables in the Cox model. The dashed lines represent the 95% pointwise interval of the estimate.

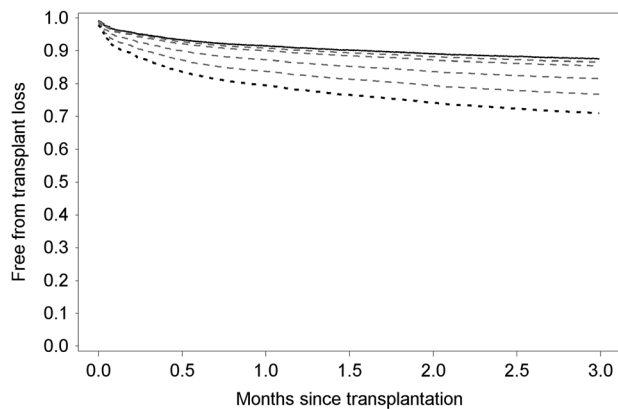


FIGURE 3. Expected transplant survival function during the first 3 months posttransplant for selected values for implantation time (ie, 10 minutes [black line], 120 minutes [dashed black line], and intermediate values of 20, 30, 60, and 90 minutes [dashed grey lines]), adjusted for all other covariables in the Cox model.

Histidine-tryptophan-ketoglutarate was more often used as preservation solution. Recipients were younger and had lower laboratory MELDs. DCD livers were rarely used for recipients with acute liver failure or in need of a retransplantation.

DCD donation was an independent predictor of transplant loss (adjusted HR, 1.54; 95% CI, 1.24-1.89; $P < 0.001$) and graft failure (adjusted HR, 2.13; 95% CI, 1.60-2.83; $P < 0.001$) but not of patient survival. When donor warm ischemia time was added as a predictor to the multivariable models for graft failure and transplant loss, DCD status was no longer a significant risk factor (Table 3). This shows that the increased risk of loss for DCD grafts is (even completely) due to the additional donor warm ischemia time.

We next assessed whether the detrimental effect of implantation time was more pronounced in DCD compared to DBD livers. This was not the case, there was no interaction effect between implantation time and donor type for transplant survival (Table S10, SDC, <http://links.lww.com/TXD/A93>).

We next evaluated whether prolonged cold ischemia time, graft quality (assessed by DRI) or type of graft (whole vs split) might affect the susceptibility of the graft to increased implantation time. Interaction effects between implantation cold ischemia time, DRI, and type of graft were investigated

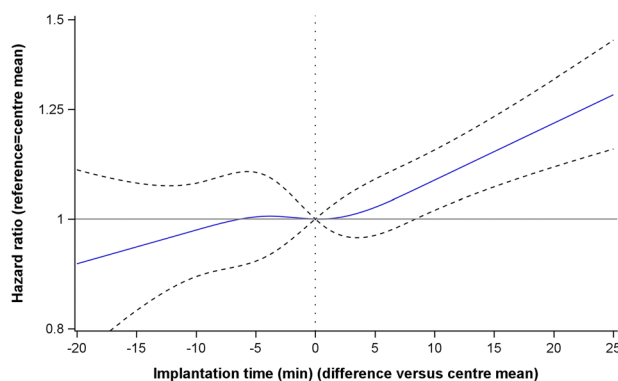


FIGURE 4. Hazard ratio and pointwise 95% CI comparing each value of implantation time with the center specific mean implantation time (therefore, the HR equals 1 at the center-specific mean). The result is obtained from a Cox regression allowing nonlinearity (on the log-scale) using restricted cubic splines and illustrates that the effect of increasing implantation time is more important in the higher range.

TABLE 3.

Cox regression models for graft failure and transplant failure after liver transplantation obtained after backward stepwise selection based on multiple imputation with the addition of donor warm ischemia time to the model

Factors	Graft survival		Transplant survival	
	HR (95% CI)	<i>P</i>	HR (95% CI)	<i>P</i>
Implantation time ^a	1.05 (1.01-1.09)	0.02	1.04 (1.01-1.07)	0.006
DCD status	0.68 (0.27-1.73)	0.42	0.82 (0.42-2.38)	0.56
Donor warm ischemia time ^a	2.09 (1.23-3.57)	0.007	1.58 (1.04-2.38)	0.03

^a 10 minutes, analysis based on 5175 cases as donor warm ischemia time was missing in 48 cases.

Other variables considered in the model are those mentioned in Table S3 (SDC, <http://links.lww.com/TXD/A86>) and Table S4 (SDC, <http://links.lww.com/TXD/A87>). HR and *P* values of these variables are not shown.

separately in the multivariate model. Although cold ischemia time, DRI, and type of graft were independently associated with transplant survival, the unfavourable effect of prolonged implantation time on graft survival was not influenced by either in any of the multivariable models (data not shown).

DISCUSSION

This analysis of 5223 deceased donor liver transplants captured in the Eurotransplant registry shows that implantation time is an independent risk factor of transplant loss, graft loss, and patient death. Every 10-minute increase in implantation time had a detrimental effect on outcome similar to that of every hour increase in cold ischemia time. We could also show that the effect of implantation time on outcome is time dependent and that the effect is clearest in the first 3 months posttransplant.

Although the association between implantation time and outcome might seem evident, so far, there has been limited interest in exploring the effect of implantation time during which the graft is rapidly rewarming. We studied the clinical importance of the effect of implantation time further. In this cohort—after correction for all other covariables in the Cox model—the probability to suffer transplant loss within the first 3 months after transplantation increased above 20% for implantation times above 70 minutes. This time correlates well with a previous study performed by Rana et al.⁶ While devising the “survival outcomes after liver transplantation score,” these authors describe that an implantation time above 70 minutes was an independent risk factor for patient death at 3 months posttransplant. Implantation times above 70 minutes are infrequent, but the detrimental effect of implantation time is continuous. Even with shorter implantation times, the risk of transplant loss is increased. The clinical relevance of that effect should be placed into context. By correcting the analyses for recipient center, the interpretation of the effect of implantation time refers to differences in risk between patients within the same center, having a different duration of implantation. Exploratory analyses show that when implantation time stays within a 10-minute interval from the average implantation time within a given center (Figure 4), the clinical impact of implantation time seems minimal. In other words, our results show that keeping the implantation time as close to and preferably below the average implantation time within a given center are likely to reduce the risk of graft loss and patient death.

Liver implantation should be both diligent—to reduce the risk of vascular complications—and swift—to reduce the impact of implantation time—stressing the importance of well-trained and experienced surgeons performing liver transplantations. The implantation technique might also reduce the time to reperfusion. Shorter implantation times for piggyback compared with classical caval replacement have been described,¹⁵⁻¹⁷ and this might contribute to the reported improved perioperative outcome after piggyback.¹⁸ Although long term outcome between the 2 techniques in the reported study was the same, our results suggests that further studies looking at implantation technique as a potential confounder are worthwhile.

The sequence by which the anastomosis are constructed and the liver is reperfused (portal vein first, hepatic artery first, or simultaneous reperfusion of portal vein and hepatic artery) might also play a role. Because Eurotransplant does not collect detailed information on portal and arterial reperfusion, we were unable to investigate this further. The reported implantation times in this article reflect the wide variety of surgical technique used in the different Eurotransplant liver transplant centers. Indeed, preliminary findings of a recent survey conducted within Eurotransplant, Swisstransplant, Scandiatransplant, and the British Transplantation Society showed that the portal vein is reperfused first in 61% of cases, simultaneous portal vein and hepatic artery in 19% of cases.¹⁹ Despite this limitation, a detrimental effect of implantation time was found, stressing the importance of more detailed investigation in other large data sets that capture the sequence of reperfusion. These will likely provide important insights that might help improve surgical technique and outcome after liver transplantation in the absence of randomized controlled trials.

Keeping the graft cold during implantation might improve outcome. Technical modalities to keep the liver cold during implantation need to be thought of. Surface cooling might not be very straightforward or effective for a large organ, such as the liver. Some centers rinse the liver during implantation to remove the preservation solution.^{20,21} Keeping this rinse solution cold might reduce rewarming and, therefore, the effect of longer implantation times on outcome.

Our results did not show an increased vulnerability of DCD livers to implantation time. DCD donation was an independent risk factor for worse outcome, and that effect was entirely caused by the donor warm ischemia time. However, there was no interaction between donor type and implantation time suggesting that DCD livers were not more susceptible to the deleterious effect of implantation time. Most likely, any potential effect remained undetected because there were only 208 DCD livers in our study. It is, therefore, warranted to repeat these analyses in a larger DCD series. Alternatively, and perhaps counterintuitively, one could hypothesize that the significant changes at the cellular and subcellular levels caused by the withdrawal phase and warm ischemia time in DCDs²² result in masking the effect of a second hit of warm ischemia time because most of the damage is already done (ie, the magnitude of the effect of implantation time is reduced in DCDs, whereas DCD-status still negatively impacts outcome).

The strength of our analysis is the use of a large cohort of transplant recipients in the Eurotransplant region. A limitation inherent to every registry study based on data from many different centers and countries is the lack of detailed

information regarding donor and recipient characteristics and incomplete data registration. In contrast to the US and UK transplant registries, data submission to the Eurotransplant registry is not compulsory, explaining the high frequency of missing data in this registry. However, even with mandatory data submission, the final cohort of a recent study looking at implantation time in kidney transplantation, using the United Network of Organ Sharing registry, represented only 57.7% of the eligible cohort.²³ Also, as baseline characteristics of transplants excluded because of missing data were comparable to the transplants included, we do not suspect that our results were importantly confounded. Although multiple imputations were used, a recognized strategy to reduce the concerns related to missing data, our findings should be confirmed using other large data sets.

Although this large cohort study allowed us to perform survival analyses, no in depth analysis on other transplant outcome variables was possible. We also cannot exclude that implantation time is a surrogate for other confounding factors that may impact outcome because the Eurotransplant Registry does not contain detailed information on possible determinants of the duration of implantation time during liver transplantation. Furthermore, a detailed analysis looking at an association of implantation time with early outcome such as primary nonfunction and early allograft dysfunction and the development of biliary complications—not captured by the Eurotransplant Registry—would be very valuable. In addition, now that the detrimental effect of longer implantation time has been demonstrated, additional confounding factors, such as surgical technique (piggyback vs caval replacement; reperfusion of the artery before portal vein, use of a cold rinse during implantation), the number and nature of the arterial reconstruction, the presence of portal vein thrombosis, and so on, that are not detailed in the Eurotransplant registry need to be teased out in other data sets that do contain this information.

In conclusion, implantation time is a risk factor for liver transplant outcome, especially in the first months after transplantation. This finding identifies the need for better understanding of confounding factors as well as the need to limit perioperative warm ischemic injury to improve outcome after liver transplantation. Validation of these findings and exploration of uncaptured confounders in other large data sets are needed.

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