Research Article

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A comprehensive risk assessment of mortality following donation after cardiac death liver transplant – An analysis of the national registry

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Background & Aims: Organ scarcity has resulted in increased utilization of donation after cardiac death (DCD) donors. Prior analysis of patient survival following DCD liver transplantation has been restricted to single institution cohorts and a limited national experience. We compared the current national experience with DCD and DBD livers to better understand survival after transplantation.

Methods: We compared 1113 DCD and 42,254 DBD recipients from the Scientific Registry of Transplant Recipients database between 1996 and 2007. Patient survival was analyzed using the Kaplan–Meier methodology and Cox regression.

Results: DCD recipients experienced worse patient survival compared to DBD recipients (p <0.001). One and 3 year survival was 82% and 71% for DCD compared to 86% and 77% for DBD recipients. Moreover, DCD recipients required re-transplantation more frequently (DCD 14.7% *vs.* DBD 6.8%, p <0.001), and re-transplantation survival was markedly inferior to survival after primary transplant irrespective of graft type. Amplification of mortality risk was observed when DCD was combined with cold ischemia time >12 h (HR = 1.81), shared organs (HR = 1.69), recipient hepatocellular carcinoma (HR = 1.80), recipient age >60 years (HR = 1.92), and recipient renal insufficiency (HR = 1.82).

Conclusions: DCD recipients experience significantly worse patient survival after transplantation. This increased risk of mortality is comparable in magnitude to, but often exacerbated by other well-established risk predictors. Utilization decisions should carefully consider DCD graft risks in combination with these other factors.

Keywords: Liver transplantation; Donation after cardiac death; Donation after brain death; Patient survival.

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Abbreviations: DCD, donation after cardiac death; US, United States; DBD, donation after brain death; CMS, centers for medicare and medicaid services; SRTR, scientific registry of transplant recipients; OPTN, organ procurement and transplantation network; BMI, body mass index; WIT, warm ischemia time; CIT, cold ischemia time; MELD, model for end-stage liver disease; HCV, hepatitis C virus; HCC, hepatocellular carcinoma; ICU, intensive care unit; RI, renal insufficiency; HR, hazard ratios; CI, confidence intervals.

Introduction

Dramatic improvements in patient survival since the introduction of liver transplantation have led to transplantation of "sicker" patients and increasing utilization of expanded criteria grafts [1,2]. These trends are a clear indication of the increasing discrepancy between organ supply and demand [1,3]. One example of increasing use of high risk grafts is the dramatic increase in donation after cardiac death (DCD) liver transplants in the United States (US), rising over the past decade from <1% to 6.4% of all deceased donor liver transplants [1].

However, DCD liver transplantation has been associated with inferior outcomes including higher rates of graft failure and biliary complications compared with donation after brain death (DBD) transplants [4–7]. While it has been established that DCD recipients experience worse graft survival [4,7–13], previous reports [4,5,8] have generally failed to identify a significant difference in patient survival between DCD and DBD recipients save for a select few single institution reports [12]. However, these analyses were restricted to small cohorts from single institution reports and a limited national experience.

Recently, the Centers for Medicare and Medicaid Services (CMS) published conditions of participation enforcing mandatory reporting of transplant center performance. In addition to quality improvement, the policy fosters transparency in communicating risk to better inform decision making by patients, clinicians, payers, and policy makers. As such, an enhanced understanding of the risks and outcomes associated with DCD grafts is of great importance.

This paper, using current national data, compares patient survival after DCD and DBD liver transplantation and examines

differences in survival in the context of other well-established donor and recipient risk predictors.

Material and methods

Data source and study population

We performed a retrospective analysis using data from the Scientific Registry of Transplant Recipients (SRTR) database. The SRTR contains information submitted by members of the Organ Procurement and Transplantation Network (OPTN) on all wait-listed and transplanted patients and is supplemented by the Social Security Death Master File. The study population includes all deceased donor liver transplant recipients performed in the US from April 1, 1996 to October 1, 2007 representing 1113 DCD and 42,254 DBD recipients. Pediatric (age <18 years), multi-organ transplants (except simultaneous liver–kidney transplants), and recipients with a previous liver transplant were excluded. There were no partial DCD transplants in this cohort; as such, only whole DBD liver transplants were included in the analysis. Recipients without follow-up ($n = 336$, 0.6%) were also excluded.

Data analysis

The primary outcome measure was patient mortality. Patient survival was calculated from date of transplant to death or last known follow-up. Potentially confounding donor and recipient factors were examined. Donor factors included age, race, gender, body mass index (BMI), cause of death, utilization of vasopressors, terminal serum creatinine, warm (WIT) and cold ischemia time (CIT), and rates of regional and national sharing. Recipient factors at time of transplant included age, race, gender, BMI, liver disease etiology, calculated Model for End-stage Liver Disease (MELD) score, hepatitis C virus (HCV), hepatocellular carcinoma (HCC), mechanical, ventilated or organ perfusion support, medical condition (at home, in the hospital, in the intensive care unit [ICU]), prior abdominal surgery, renal insufficiency (defined as terminal serum creatinine >1.5, hemodialysis, or simultaneous liver–kidney transplant), international normalized ratio, total bilirubin, and albumin were examined. Recipients were also dichotomized according to year of transplant (1996–2001 *vs.* 2002–2007) for comparison of survival outcomes.

Student's *t* tests and chi-square tests were used for comparison of continuous and categorical variables, respectively. Patient survival analysis was performed using the Kaplan–Meier methods and compared according to the log-rank test. Cox proportional hazards regression was used to analyze adjusted patient survival and evaluate risk predictors. DCD and DBD survival were compared after adjusting for all donor and recipient differences identified in Table 1. Stratified analyses were performed to examine binary interactions between the DCD graft type and other identified important covariates. Hazard ratios (HR) with 95% confidence intervals (CI) are reported. Additionally, the synergy index was calculated to examine evidence of interaction [14,15]. A synergy index of one is equivalent to no interaction. A p value <0.05 was considered statistically significant. Data was analyzed using StataSE10 (Stata Corp, College Station, TX). This study was deemed exempt by the Northwestern University Institutional Review Board.

Results

Study population

Recipients of DCD and DBD transplants differed in several important aspects (Table 1). While DCD recipients were older (DCD 53.5 ± 9.5 years *vs.* DBD 51.6 ± 10.1 years, p <0.001), they generally displayed lower risk characteristics compared with DBD recipients. They had lower MELD scores (DCD 18.8 ± 8.2 *vs.* DBD 20.2 ± 9.1, p <0.001), were less likely to be on life support (DCD 5% *vs.* DBD 7%, $p = 0.004$), and were less likely to be admitted to a hospital ward (DCD 13% *vs.* DBD 16%) or ICU (DCD 10% *vs.* DBD 15%) at transplant (p <0.001). There was, however, a greater proportion of HCC recipients in the DCD cohort (DCD 20% *vs.* DBD 13%, p <0.001). Additionally, DCD transplantation was associated

Table 1. Donor and recipient characteristics for DCD and DBD liver transplant recipients. DCD ($n = 1113$) DBD ($n = 42,254$).

Recipient characteristics	DCD (n = 1113) mean ± SD	DBD (n = 42,254) mean ± SD	*p* value
Age at transplant (years)	53.5 ± 9.5	51.6 ± 10.1	<0.001
Calculated MELD score	18.7 ± 8.2	20.2 ± 9.1	<0.001
Body mass index	28.0 ± 5.8	27.9 ± 5.9	0.83
	n (%)	n (%)	
Gender (male)	781 (70.2%)	27,853 (65.9%)	0.003
Race/ethnicity			0.001
white	873 (78.4%)	31,710 (75.1%)	
black	93 (8.4%)	3484 (8.3%)	
hispanic	121 (10.9%)	4948 (11.7%)	
other	25 (2.3%)	2055 (4.9%)	
Liver disease etiology			0.03
acute hepatic necrosis/fulminant	94 (8.5%)	3925 (9.3%)	
non-cholestatic cirrhosis	787 (70.7%)	29,419 (60.6%)	
cholestatic cirrhosis	101 (9.1%)	4274 (10.1%)	
metabolic disease	26 (2.3%)	1120 (2.7%)	
malignant neoplasms	98 (8.8%)	2888 (6.8%)	
missing	1 (0.1%)	69 (0.2%)	
Hepatitis C virus serology			<0.001
positive	417 (47.0%)	16,150 (45.9%)	
unknown	155 (14.9%)	4056 (10.3%)	
Hepatocellular carcinoma	247 (20.2%)	6887 (13.0%)	<0.001
Mechanical, ventilated or organ perfusion support at transplant	55 (4.9%)	3021 (7.2%)	0.004
Renal insufficiency at transplant	289 (26.7%)	9378 (29.1%)	0.08
Medical condition			<0.001
at home	862 (77.5%)	29,063 (68.8%)	
in hospital (not ICU)	144 (12.9%)	6678 (15.8%)	
in ICU	107 (9.6%)	6492 (15.4%)	
Donor characteristics	**mean ± SD**	**mean ± SD**	***p* value**
Age (years)	36.4 ± 15.4	40.2 ± 17.6	<0.001
Body mass index	25.9 ± 5.5	25.9 ± 5.7	0.98
Cold ischemia time (hours)	7.7 ± 3.6	8.0 ± 3.7	0.12
Warm ischemia time (minutes)	15.6 ± 9.4		
	n (%)	n (%)	
Gender (male)	724 (65.1%)	25,006 (59.2%)	<0.001
Race/ethnicity			<0.001
white	952 (85.5%)	30,642 (72.5%)	
black	88 (7.9%)	5641 (13.4%)	
hispanic	54 (4.9%)	4737 (11.2%)	
other	15 (1.4%)	1134 (2.7%)	
Cause of death			<0.001
anoxia	321 (28.8%)	4385 (10.4%)	
stroke	241 (21.7%)	18,874 (44.7%)	
trauma	479 (43.0%)	17,871 (42.3%)	
other	61 (5.5%)	732 (1.7%)	
Pressors prior to donation	297 (26.7%)	34,852 (82.5%)	<0.001
Regional/national sharing	363 (32.6%)	11,443 (27.1%)	<0.001