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Short- and Long-Term Outcomes with the Use of Kidneys and Livers Donated after Cardiac Death

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The shortage of deceased donor kidneys and livers for transplantation has prompted the use of organs from donors deceased after cardiac death (DCD). We used the UNOS database to examine patient and graft survival following transplantation of DCD organs compared to those following grafts from donors deceased after brain death (DBD; for livers, grafts from donors $<$ 60 years old were labeled '$<$ 60 yrs'). Of 44035 deceased donor kidney transplant recipients, 1177 (3%) received a DCD kidney. There was no difference in patient or graft survival at 5 years (DCD vs. DBD: 81.3% vs. 80.8% and 66.9% vs. 66.5%; $p = 0.70$ and $p = 0.52$ respectively). Of 24688-deceased donor liver transplant recipients, 345 (1.4%) were from DCD donors and 20289 (82%) were from '$<$ 60 yrs' DBD donors. Three-year patient and graft survival were inferior in the DCD group (DCD vs. '$<$ 60 yrs' DBD: 77% vs. 80% and 65% vs. 75%; $p = 0.016$ and $p < 0.0001$ respectively) but were comparable to current alternatives, '$\geq$ 60 yrs' DBD livers (donor age $\geq$ 60) and split livers. DCD livers are a reasonable option when death is imminent. Our study demonstrates good outcomes using DCD kidneys and livers and encourages their use.

Key words: Donation after cardiac death, kidney transplant, liver transplant, non-heart-beating donors

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Introduction

Transplantation is the only treatment option for those with end-stage liver disease who are certain to die otherwise. While for those with end-stage renal disease dialysis can be used to provide renal replacement therapy to sustain life, there is strong evidence that kidney transplant confers a far greater survival advantage over dialysis (1). Over the last two decades there have been significant improvements in surgical techniques and immunosuppressive agents. This has led to better patient and graft survival rates in all types of organ transplantation. The success of clinical transplantation has been limited by the ever-growing demand as reflected by longer waiting list and waiting time. This has resulted in an increasing number of transplant candidate deaths while awaiting transplant (2).

To overcome this challenge, alternative sources of organs for transplantation must be identified. Possible sources of kidneys and livers for transplantation are live donors, organs from older donors and from donors that donated after cardiac death. Currently the majority of the organs are procured from donors that donated after brain death (DBD). There are some potential donors who have sustained irreversible neurological injury but do not meet the formal criteria of brain death. These patients also carry a grim prognosis, and often are taken off organ-perfusion support for clinical reasons unrelated to organ donation. Unlike the conventional DBD donors, these patients can maintain some cardiopulmonary function but not enough to sustain life after cessation of organ-perfusion support. The organs from such donors are retrieved only after complete cardiopulmonary arrest. Hence these donors are referred to as donors that donated after cardiac death (DCD). The organs from these donors have been considered suboptimal due to the additional ischemic insult during a failing circulation after withdrawal of organ-perfusion support until death occurs. They have been used mainly for liver and kidney transplantation. Historically there have been two types of such DCD donors, controlled and uncontrolled. The former refers to the situation where the discontinuation of organ-perfusion support measures occurs in a planned fashion, the ischemia time is known, and the organs are recovered promptly after cardiac death. In the latter the patients are dead on arrival or have unplanned cardiac arrest. Only the controlled DCD organs are considered in this analysis.

The organs from these donors are widely used in Europe and Japan but are less often used in the United States. This is mainly due to ethical constraints and lack of sufficient information on graft outcomes. There have been some small single center reports (3–7) and a few retrospective studies using the national database (8–10) evaluating the outcomes of DCD liver and kidneys. Recent studies have shown acceptable patient and graft survival rates with the use of DCD organs when compared to outcomes with the use of DBD organs. DCD organs have been used for transplantation at a limited number of centers (11). These centers are

typically high volume centers and have greater experience in transplantation. It is conceivable that the centers performing DCD organ transplants may have far better outcomes with the use of DBD organs when compared to the outcomes at centers not performing one. Therefore it is important to account for correlation of outcomes within a center. With growing experience in the procurement and preservation of DCD organs the outcomes with their use may have improved. For this report the short- and long-term outcomes of organs from DCD donors were compared to outcomes of recipients of organs from conventional, DBD donors. In an effort to overcome the above concerns the analyses was restricted to more recent transplants, and adjustments were made for within center effect. In contrast to the DBD organs, the DCD organs have incurred additional injury at the time of procurement. It is therefore conceivable that prolonged cold ischemia time may be more detrimental to DCD organs. In our study we have also assessed the impact of cold time and sharing on graft survival by donor type to address the allocation policies for the DCD organs. The outcomes with the use of DCD livers were also compared to current alternative sources of liver for transplantation, livers from older donors and split livers.

Materials and Methods

Patients

The Organ Procurement and Transplant Network (OPTN)/United Network for Organ Sharing (UNOS) database as of September 14, 2005, was used for the analyses. This database contains information on all the kidney and liver transplants that have been performed in the United States and reported to the OPTN since October 1, 1987. Since the year 1993, the OPTN has also been collecting data on whether organs were retrieved from DBD or DCD donors. In 1997 Institute of Medicine declared that the recovery of DCD organs was medically effective and ethically acceptable. Their use has increased thereafter. This analysis was restricted to all adult patients who underwent a primary deceased donor kidney or liver only transplant between January 1, 1998, and June 30, 2004. These recipients were grouped according to the donor type: 1) donors that donated after cardiac death (DCD); 2) donors that donated after brain death (DBD). For the livers, the DBD group was further categorized as '$<$ 60 yrs' livers (procured from donors less than 60 years of age), '$\geq$ 60 yrs' livers (procured from donors 60 years of age or older) and split livers. Recipients of organs from donors with missing information on mechanism of death (cardiac/brain death) and from donors with uncontrolled cardiac death were excluded.

Outcomes

The primary endpoints for both the kidney and liver analyses were patient and graft survival. Secondary endpoints emphasized the impact of cold ischemia and sharing on graft survival and postoperative outcomes. For the kidney transplants the following postoperative outcomes were evaluated: incidence of delayed graft function (DGF), length of initial hospitalization and rate of rejection within first 6 months of transplantation, and for the liver transplants: occurrence of primary nonfunction (graft failure within 7 days of transplantation), length of initial hospitalization and retransplant rates.

Data

Baseline recipient and donor characteristics as well as other variables that are known to affect the graft outcome by prior center specific UNOS analyses were compared. For the kidney transplants the following characteristics were analyzed: donor age, sex and race, cause of death and organ quality (expanded criteria donors vs. standard criteria donor); recipient age, sex and race, diabetes as a cause of renal failure, waiting time and peak panel reactive antibody (PRA); HLA mismatch, preservation technique (machine perfusion vs. cold storage) and cold ischemia time. For the liver transplants the following characteristics were evaluated: donor age, sex and race; recipient age, sex, race, pretransplant serum bilirubin, creatinine; need for recipient ICU admission pretransplant, hepatitis C infection (HCV) and cold ischemia time. The model for end stage liver disease (MELD) score was formally accepted as a tool for liver allocation only in 2002 and therefore was not available for comparison. Instead the actual serum bilirubin and creatinine were compared in the two groups. The coagulation time was reported either as prothrombin time or INR and therefore could not be consistently compared in the two groups. There was a wide range in the duration of warm ischemia time across different centers, possibly due to lack of a uniform definition and therefore was not accounted for in our analyses.

Statistics

Normally distributed continuous variables were compared using the *t*-test. Chi-square tests were used to compare categorical variables. All tests of statistical significance were two tailed, and $\alpha \leq 0.05$ was deemed to be statistically significant. Kaplan-Meier (KM) survival estimates were used to evaluate the patient and graft survival in the two groups. Comparisons were made using the log rank test. Graft survival comparisons were made without censoring for patient death. Cox proportional hazard models were constructed to correct for baseline differences in donor and recipient characteristics that are known by prior center specific UNOS analyses to affect patient and graft survival. We accounted for the center effect by 'clustering' the analysis by center, using a 'robust' variance estimate (12). For the Cox models we restricted our analyses to only those centers that have performed at least one DCD transplant during the study period. The kidney model included the following variables: donor type (DCD vs. DBD), donor age, sex, race and cause of death; recipient age, sex, race, cause of underlying renal failure, peak PRA and duration of dialysis; cold ischemia time, preservation techniques (pump perfusion vs. cold storage) and HLA mismatch; share type (local, regional, national allocation), transplant year and center. The number of variables adjusted in the liver Cox model was limited due to the small number of events in the DCD group. The impact of each of the covariate was analyzed first in univariate Cox models and only those that had statistically significant impact on the outcome were included in the final adjusted model. The final model adjusted for donor type (DCD, '$<$ 60 yrs' DBD, '$\geq$ 60 yrs' DBD and split), donor age, recipient age, recipient pretransplant serum creatinine and bilirubin and need for ICU stay prior to transplant, recipient HCV status, cold ischemia time, share type and transplant center.

The impact of cold ischemia time and sharing on DCD organs were evaluated by testing for an interaction of each with the donor type in the adjusted Cox proportional hazard model for graft survival. A three-way interaction between donor type, cold time and sharing was also tested in the adjusted kidney Cox model, but not for livers as there were too few events in DCD group. Additionally unadjusted KM analyses were used to compare the one-year graft survival at the extremes of cold ischemia time ($<$ 25th percentile and $>$ 75% percentile) and share types in the two groups.

SAS v 9.1 (SAS Institute, Cary, NC) or S-Plus 6.2 (Insightful Corp., Seattle, WA) was used to perform the statistical analyses and generation of graphics.

Results

Kidney

A total of 44035 adult patients were identified from the UNOS database that had undergone a primary deceased donor kidney transplant between January 1, 1998, and June 30, 2004. The cohort included 42858 (97%) recipients that had received their kidney from DBD donors. The remaining 1177 (3%) were from DCD donors. Table 1 shows the comparison of the renal transplant donor, recipient and renal allograft characteristics between the two groups. There was a greater proportion of white male donors in the DCD group. There were fewer expanded criteria donors in the DCD group and, not surprisingly, fewer donors with cerebrovascular accident as a cause of death. On the other hand the recipients in the DCD group were less likely to be sensitized. There were greater proportions of zero HLA mismatch kidney transplants in the DBD group than the DCD group. Almost half of the DCD kidneys were pumped. Cold ischemia time was similar in the two groups. Figure 1 displays the KM estimates of the patient survival and graft survival in the two groups. There is no difference in the patient and graft survival up to 5 years of follow up (DCD vs. DBD: patient survival: 81.3% vs. 80.8%, $p = 0.70$; graft survival: 66.9% vs. 66.5%, $p = 0.52$). Table 2 shows the results of the Cox proportional hazard model for the graft survival. Even after adjusting for all the covariates in the Cox proportional hazard model there was no impact of donor type on either the patient and graft survival.

In contrast to the DBD organs the DCD organs are exposed to varying duration of warm ischemia time while awaiting cardiopulmonary arrest. It is conceivable that cold ischemia time would have a greater adverse impact on the graft survival of DCD kidneys than the DBD kidneys. We found that there was no significant interaction between donor type and cold ischemia time ($p = 0.43$), nor between donor type and share type ($p = 0.07$) in the adjusted Cox model; nor was there a significant three-way interaction between donor type, cold ischemia time and share type ($p = 0.25$). In Kaplan-Meier analysis uncorrected for covariates there was no difference in 1-year graft survival in the two groups at the lower cold ischemia time (<14 h: DCD 89% vs. DBD 91%, $p = 0.85$). At higher cold time (>24 h) the 1-year graft survival among the DCD kidney recipients was slightly inferior (85% vs. 88%; $p = 0.13$) but the difference did not reach statistical significance. One-year graft survival of the DCD kidneys was similar to DBD kidneys when shared locally and slightly inferior when shared regionally or nationally (DCD vs. DBD, local: 89.3% vs. 89%, $p = 0.682$; regional: 81% vs. 87%, $p = 0.437$; national: 82.7% vs. 89.5%, $p = 0.0089$).

There is reluctance to use DCD kidneys due to high incidence of DGF and concerns for length of stay and increased frequency of rejection. The length of hospitalization was not different in the two groups once corrected for occurrence of DGF (no DGF: DCD 8.1 vs. DBD 7.8 days; with DGF: DCD 13.3 vs. DBD 13.0 days). However, the

Table 1: Characteristics of kidney transplant donors, recipients and allografts

	DCD (N = 1177)	**DBD** (N = 42858)	p-value
Donors			
Age (year)	37.0 (16.1)	37.2 (17)	0.737
Male (%)	65%	58%	< 0.001*
Race			
White (%)	87%	74%	< 0.001*
Black (%)	7.1%	11%	< 0.001*
CVA (%)	24%	42%	< 0.001*
Expanded criteria donors (%)	11%	17%	< 0.001*
Recipients			
Age (year)	50.4 (12.5)	49.6 (12.8)	0.04
Male (%)	60.0%	60.5%	0.92
Race			
White (%)	52%	52%	0.99
Black (%)	33%	30%	0.06
DM (%)	24%	24%	0.90
Waiting time (days)	1146.4 (873.4)	1169.2 (968.1)	0.4
Sensitization			0.005*
PRA < 9 (%)	82.2%	78.3%	
PRA 10–79 (%)	13.08%	16.2%	
PRA > 80 (%)	4.76%	5.5%	
Allografts			
Zero HLA MM	7%	14.67%	< 0.001*
Pump perfusion	46%	11%	< 0.001*
Cold ischemia time (hrs)	19.2 (7.6)	19.3 (7.9)	0.74

() denotes ± standard deviation, * denotes $p < 0.05$.
CVA = cerebrovascular accidents; DM = diabetes mellitus; PRA = peak reactive antibody; MM = mismatch.

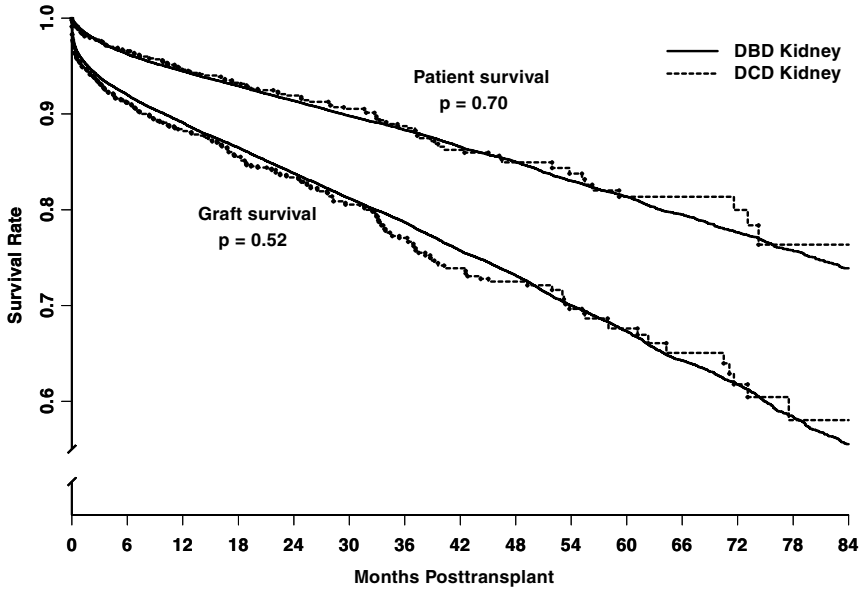

Figure 1: Comparison of patient and graft survival between the recipients of DCD kidneys and DBD kidneys.

Table 2: Results of Cox proportional hazard model for renal graft survival

Variable	Hazard ratio (95% CI)	p-value
Donors		
Type (DCD vs. DBD)	1.13 (0.97 – 1.32)	0.10
Age (quadratic)	†	< 0.0001*
Female	1.05 (1.01 – 1.10)	0.019*
Race (black vs. white)	1.17 (1.08–1.27)	< 0.0001*
Cause of death (CVA vs. head trauma)	1.21 (1.14–1.29)	< 0.0001*
Expanded criteria donor	1.05 (0.97–1.14)	0.23
Recipients		
Age (quadratic)	†	< 0.0001*
Female	0.93 (0.89–0.98)	0.006*
Race (black vs. white)	1.15 (1.09–1.22)	< 0.0001*
Diabetes as a cause of renal failure (vs. GN)	1.35 (1.26–1.45)	< 0.0001*
Peak PRA (per 10% difference)	1.04 (1.03-1.05)	< 0.0001*
Duration of dialysis in months (quadratic)	†	< 0.0001*
Renal allografts		
Cold ischemia time (per h)	1.01 (1.00–1.01)	< 0.0001*
Pumped perfusion (vs. cold storage)	0.88 (0.77–1.01)	0.067
Zero HLA mismatch (vs. 4 mismatch)	0.77 (0.70–0.84)	< 0.0001*
Share type		
Regional versus local	1.12 (1.02–1.24)	0.023
National versus local	1.10 (1.01–1.19)	0.026
Transplant year (per year)	1.00 (0.98–1.01)	0.68

†A unique hazard ratio cannot be defined for a quadratic relationship.

*p < 0.05; CVA = cerebrovascular accident; GN = glomerulonephritis.

incidence of DGF was twice as high in the DCD group (41% vs. 24%; p value <0.001). Despite this, the overall average length of stay differed by only one day between recipients of DBD and DCD kidneys (9.0 vs. 10.2 days, p = 0.02). The incidence of rejection at six months after transplant was similar in the two groups (9.4% in the DCD group vs. 10% in the DBD group, p = 0.49).

Liver

There were 24688 patients identified from the UNOS database that had received a primary deceased donor liver transplant between January 1, 1998, and June 30, 2004. There were 20289 (82%) patients who had received whole livers from DBD donors < 60 years old ('<60 yrs') and 3604 (15%) who had received whole DBD livers from donors 60 years old or older ('≥ 60 yrs'). 345 (1.4%) patients received livers from DCD donors, of whom 315 were less than 60 years old and 30 were 60 or older. 450 (1.8%) patients received split liver transplants, of which two were from donors 60 years old or older. Table 3 shows the comparison of donor and recipient characteristics in the four groups. There were more young male liver donors in the split group. Just as for the DCD kidney donors, there was a greater proportion of white liver donors in the DCD than in the '< 60 yrs' group, and the recipients in the DCD group were somewhat more likely to be Caucasian with lower pretransplant total bilirubin. There were fewer recipients in the DCD group requiring ICU admission pretransplant and somewhat fewer with hepatitis C infection. Cold ischemia time was similar in the four groups.

Figures 2 shows Kaplan Meier estimates of patient (a) and graft (b) survival for the four groups, limiting the DCD and split groups to those donors < 60 years old. Both the patient and graft survival were lower in the DCD than in the '< 60 yrs' group but comparable to those in the '≥ 60 yrs'

Table 3: Characteristics of liver transplants donors, recipients and allografts

	DCD (N = 345)	< 60 yrs DBD (N = 20289)	≥ 60 yrs DBD (N = 3604)	Split (N = 450)	p-value
Donors					
Age (year)	36.6 (16.4)	34.9 (14.2)	67.4(5.9)	25.0(10.2)	0.0001^
Male (%)	63%	61%	48%	74%	< 0.0001*
White (%)	85%	73%	81%	65%	< 0.0001*
Recipients					
Age (year)	52.6 (9.8)	50.7 (10.0)	53.3(9.7)	50.9(10.5)	< 0.0001*
Male (%)	69%	66%	65%	50%	< 0.0001*
White (%)	82%	76%	75%	62%	< 0.0001*
Pre-tp serum bilirubin (mg/dL)	5.0 (7.5)	6.7 (9.4)	6.0(8.6)	5.7(7.8)	< 0.0001*
Pre-tp serum creatinine (mg/dL)	1.34 (1.5)	1.28 (1.0)	1.2(1.0)	1.2(1.0)	0.033*
Patients in ICU pretransplant	11%	17%	15%	17%	0.041*
Patients with HCV	34%	39%	35%	37%	< 0.0001*
Cold ischemia time (hrs)	8.2 (3.0)	8.1 (3.7)	8.2(3.5)	8.4(4.1)	0.09

() denotes ± standard deviation; ^ by design; *denotes $p < 0.05$.
tp = transplant.

group (patient survival at three years: '< 60 yrs' 80%, DCD 77% and '≥ 60 yrs' 73% and graft survival: '< 60 yrs' 75%, DCD 65% and '≥ 60 yrs' 64%). Graft survival with split liver transplants was intermediate between '< 60 yrs' and DCD and patient survival was similar to that with '< 60 yrs' donors. The results were not meaningfully different when the older DCD and split liver transplants were included in the analysis.

Table 4 displays the results of the Cox proportional hazard model for patient and graft survival after adjusting for donor type and age, recipient's age, pretransplant serum creatinine and bilirubin, need for pretransplant ICU admission, HCV status, cold ischemia, share type and center. Not surprisingly, both patient and graft outcomes for the '≥ 60 yrs' DBD donor transplants were comparable to those for the '< 60 yrs' DBD donor transplants after adjusting for donor age. Outcomes with DCD donor liver donor transplants and split liver transplants were inferior to those with '< 60 yrs' donor livers in the adjusted Cox model (relative risk for graft failure 1.59 and 1.51 respectively and for death 1.31 and 1.33 respectively), but they were not significantly different from each other (DCD vs. split: patient survival $p = 0.92$; graft survival $p = 0.73$) The better outcomes with split liver donors than with DCD donors, noted in the unadjusted Kaplan-Meier analyses above, is attributable to other favorable donor characteristics, especially the younger donor age. Graft outcomes are more divergent than patient outcomes because of a higher rate of retransplantation in the DCD and split groups vs. '< 60 yrs' transplants (13% and 11% respectively, vs. 5.6%, $p < 0.0001$ for both comparisons). The median time to retransplantation was 54 days (0–2624 days) among the '< 60 yrs' donor group, 174 days (1–1827 days) in the DCD group and 25 days (1–899) in the split group.

As with DCD kidneys, there have been concerns whether longer cold ischemia times or nonlocal allocation have an especially deleterious effect on DCD liver graft survival. There was no significant interaction between donor type and cold ischemia time ($p = 0.60$) but a marginal interaction between donor type and share type ($p = 0.05$) in the adjusted Cox model. The impact of cold ischemia time and share type on one-year graft survival in recipients of '< 60 yrs' and DCD livers was also analyzed using unadjusted Kaplan-Meier analyses. For cold ischemia time of less than 6.2 h (25th percentile) the graft survival was lower in the DCD group, but this difference did not reach statistical significance (82.3% vs. 85%; $p = 0.21$). When the cold ischemia time was greater than 10 h (75th percentile), the graft survival was significantly lower in the recipients of DCD than '< 60 yrs' organs (73% vs. 81%; $p = 0.05$). Outcomes were less good with DCD than with '< 60 yrs' donors shared locally or regionally, but not among 31 DCD donors shared nationally (local: 77% vs. 85%, $p < 0.0001$; regional: 67% vs. 82%, $p = 0.001$; national: 80% vs. 80%, $p = 0.39$).

Primary nonfunction was more common in DCD, '≥ 60 yrs,' and split livers than among '< 60 yrs' donors (6.4%, 5.3%, 5.1% and 3.9% respectively, $p = 0.001$). The length of hospitalization among the recipients of DCD and split livers was somewhat longer than for '< 60 yrs' and '≥ 60 yrs' donor livers (21, 20, 17 and 17 days, respectively; $p = 0.0008$).

Discussion

Our study is different from other DCD studies in that it evaluates the short- and long-term outcomes of recent DCD kidney and liver transplants performed after accounting for correlation of outcomes of DBD or DCD organ transplants within a center. Our findings are restricted to 56% of kidney transplant centers and 39% of the liver transplant centers in the United States that had performed at least one DCD transplant during the study period.

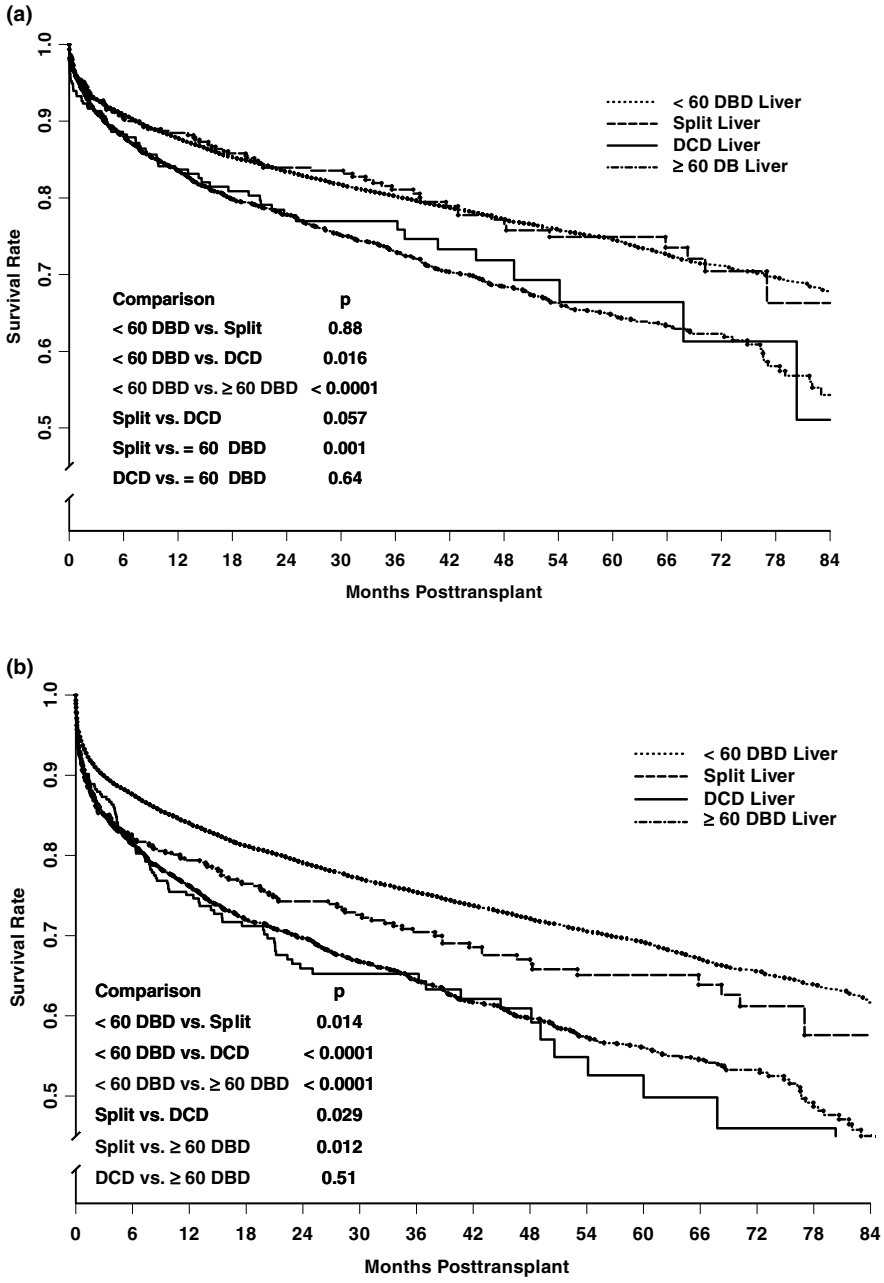

Figure 2: Comparison of patient (a) and graft (b) survival between the recipients of DCD livers, '<60 yrs' DBD livers, split DBD livers and '≥60 yrs' DBD livers.

Kidney

Our study shows that the patient and graft survival with the use of DCD kidneys is similar to that of DBD kidneys up to 5 years of follow-up in the centers performing both DCD and DBD kidney transplants. There were minor differences in the baseline donor and recipient characteristics. These differences were statistically significant mostly due to large numbers of observations in both the groups. Even after adjusting for those differences; however, the long-term patient and graft survival were comparable in the two groups. There was no significant interaction in the Cox model between donor type and either cold ischemia time or share type, but in the uncorrected Kaplan-Meier analysis of kidneys with the longest cold ischemia times the one-year graft survival from DCD donors was less good than that of kidneys from DBD donors. Similarly, the one year graft survival of DCD kidneys shared regionally and nationally was less good than those of similarly shared DBD kidneys. Thus a policy to favor local use of DCD kidneys appears reasonable.

Consistent with other studies evaluating the outcomes with use of DCD kidneys, our study also shows that there is an increased incidence of DGF with the use of DCD

Table 4: Cox proportional hazard model for the liver patient and graft survival

	Patient survival		Graft survival	
Variable	Hazard ratio (95% CI)	p-value	Hazard ratio (95% CI)	p-value
Donor type				
DCD versus '< 60 yrs'	1.31 (1.06–1.62)	0.012*	1.59 (1.35–1.86)	< 0.0001*
'≥ 60 yrs' versus '< 60 yrs'	1.03 (0.79–1.19)	0.078	1.08 (0.78–1.10)	0.38
Split versus '< 60 yrs'	1.33 (1.07–1.66)	< 0.0001*	1.51 (1.23–1.86)	<0.0001*
Split versus DCD	0.98 (0.74–1.41)	0.92	1.05 (0.71–1.27)	0.73
Donor age	†	< 0.0001*	†	< 0.0001*
Recipient age	†	< 0.0001*	†	< 0.0001*
Recipient pre-tp serum creatinine	†	< 0.0001*	†	< 0.0001*
Recipient pre-tp serum bilirubin	1.00 (1.00–1.01)	0.073	1.00 (0.99–1.01)	0.14
Need for pre transplant ICU stay	2.49 (1.17–5.52)	0.019*	3.56 (1.61–7.87)	0.0017*
HCV status	1.39 (1.29–1.50)	< 0.001*	1.27 (1.19–1.36)	< 0.0001*
Cold ischemia time	†	0.0004*	†	0.0002*
Share type				
Regional	1.04 (0.95–1.18)	0.56	1.09 (0.98–1.19)	0.087
National	1.18 (0.97–1.44)	0.098	1.16 (1.01–1.33)	0.035*

* $p < 0.05$; † A unique hazard ratio cannot be defined for a quadratic relationship.

kidneys. Despite the increased occurrence of DGF we found no difference in long-term graft or patient survival between the two groups. This finding appears initially to be at odds with the results of studies evaluating the impact of DGF on kidney graft survival in patients receiving standard DBD kidneys (13,14). DGF reflects early allograft dysfunction that can occur from variety of causes, including acute tubular necrosis from prolonged warm and cold ischemia time, early rejection and marginal quality of the donor organ. It is likely that the DGF in DCD kidneys is predominantly due to total ischemia time. While the cold ischemia time was similar in the two groups, warm ischemia time was undoubtedly longer for the DCD organs during the period following withdrawal of support. However, other studies have shown that DGF related to increased cold ischemia time does not affect long-term kidney graft outcomes (15,16). In fact, the donors in the DCD group had more favorable characteristics (greater proportions of young white male donors) than the DBD groups and there were a lower number of donors with cerebrovascular accident as their cause of death in the DCD group. Some studies have shown that there is a 'cytokine storm' at the time of brain death resulting in up-regulation of MHC molecules leading to more immune injury (17,18). In addition for those with stroke there is a release of catecholamines resulting in severe vasoconstriction leading to increased ischemia reperfusion injury. These events may have less impact in the DCD donor organs. The superior donor quality and circumstances of death together may make the DCD kidneys less vulnerable to lasting injury. Further, the rate of early rejection (within the first 6 months) was similar in the two groups. Our findings are in agreement with the results of a recent study comparing renal allograft survival between the recipients of DBD and DCD kidneys whose post transplant course was complicated with DGF. This study showed that the graft survival was better in the recipients of DCD kidney with DGF than with DBD kidney with DGF (19). Also of note, despite the increased incidence of DGF with the use of DCD kidneys the hospital stay was only one day longer than for DBD kidney recipients, probably due to availability of out-patient dialysis.

Liver

Unlike the results with the DCD kidneys we found that both the graft and patient survival were inferior with the use DCD livers as compared with '< 60 yrs' livers. As of today the only other methods to increase the availability of deceased donor livers for transplantation is by using split deceased donor livers and using livers from older donors. While the DCD livers may not be the as good as the conventional organs, they are not inferior to use of '≥ 60 yrs' DBD donor livers with respect to patient and graft survival. While uncorrected outcomes with split liver transplants were superior to those with DCD or '≥ 60 yrs' livers, this advantage was attributable entire to donor quality, especially younger age. In the adjusted Cox model, DCD livers and split livers had comparable outcomes. The frequency of primary nonfunction was higher with each of the DCD, '≥ 60 yrs', and split liver transplants compared with the '< 60 yrs' livers, but the absolute difference among liver graft types was less than 3%. Given the ever increasing demand for liver grafts, DCD livers appear to be a reasonable alternative to increasing use of older or split livers.

Although we found an only marginally significant interaction in the adjusted Cox model between donor type and share type and none between donor type and cold ischemia time, prolonged cold ischemia time, especially over 10 h, had a greater untoward effect in the uncorrected (Kaplan-Meier) analyses on the graft survival of DCD livers. The DCD livers also did less well when shared regionally. It is important to consider the additive impact of cold ischemia time and 'DCD' donor type and therefore cold ischemia time should be kept to a minimum. Again, we believe that

preference should be given to local use of DCD donor livers.

The major limitation to our study is its retrospective nature and the results of our study are highly dependent on the quality of the dataset. We cannot shed a light on procurement methods, surgical techniques, logistics of DCD organ donation and other posttransplant variables. Also the outcomes that we report reflect past practices. As such, outcomes can change if practice changes. More aggressive utilization may erode outcomes just as new advances may improve outcomes.

In conclusion the short and long term outcomes with the use of DCD kidneys are comparable to DBD kidneys and DCD kidneys should be obtained more regularly for transplantation. For the DCD livers the graft survival is somewhat inferior when compared to the livers from '$<$ 60 yrs' DBD donors. Nevertheless before declining to use such livers, it should be borne in mind that DCD liver transplants may be life saving for those who would die waiting for a '$<$ 60 yrs' DBD liver, and the graft survival is not worse than the current available alternative of '$\geq$ 60 yrs' or split DBD livers. The results of our study encourage the procurement and the use of DCD organs for transplantation.

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