Accepted Manuscript

Survival advantage for patients accepting the offer of a circulatory death liver transplant

Rhiannon Taylor, Elisa Allen, James A. Richards, Aaron M. Goh, James Neuberger, David Collett, Gavin J. Pettigrew, On behalf of members of the Liver Advisory Group to NHS Blood Transplant,
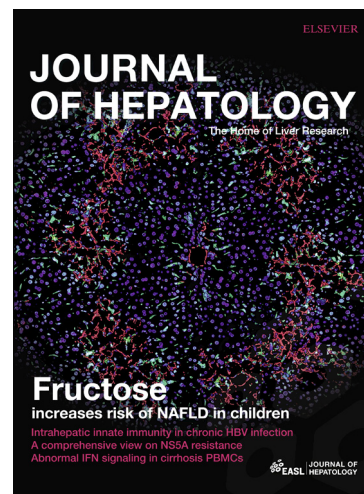
Please cite this article as: Taylor, R., Allen, E., Richards, J.A., Goh, A.M., Neuberger, J., Collett, D., Pettigrew, G.J., On behalf of members of the Liver Advisory Group to NHS Blood Transplant, Survival advantage for patients accepting the offer of a circulatory death liver transplant, *Journal of Hepatology* (2019), doi: https://doi.org/10.1016/j.jhep.2018.12.033

Survival advantage for patients accepting the offer of a circulatory death liver transplant

Rhiannon Taylor[1], Elisa Allen[1], James A. Richards[2], Aaron M. Goh[2], James Neuberger[3], David Collett[1], Gavin J. Pettigrew[2*]

On behalf of members of the Liver Advisory Group to NHS Blood and Transplant

[1] Statistics and Clinical Studies, NHS Blood and Transplant, Fox Den Road, Stoke Gifford, Bristol, BS34 8RR
[2] University Department of Surgery, Addenbrooke's Hospital, Hill Road, Cambridge, CB2 0QQ
[3] University Hospital Birmingham NHS Foundation Trust, Mindelsohn Way,

Birmingham, B15 2TH

* Corresponding author: Mr Gavin Pettigrew, Department of Surgery, Box 202, Level E9, Addenbrooke's Hospital, Cambridge Biomedical Campus, Hills Road, Cambridge, CB2 0QQ, UK. Email: gjp25@cam.ac.uk. Tel: 01223 336976. Fax 01223 762523.

KEYWORDS

Liver Transplantation

Liver Failure

Waiting list survival

Donation after circulatory death

Donation after brainstem death

Word Count: 3869
Number of Figures: 4

CONFLICT OF INTEREST

FINANCIAL SUPPORT

in collaboration with Newcastle University and in partnership with NHS Blood and Transplant (NHSBT).

CONTRIBUTORS

All authors conceived and designed the study on behalf of the Liver Advisory Group to NHS Blood and Transplant. RT, EA, DC acquired and performed the analysis. All authors provided intellectual input, analysed and interpreted the data, critically revised the manuscript, and approved the final manuscript. GJP is guarantor that all authors satisfy the ICMJE recommendations on authorship.

Abstract

BACKGROUND & AIMS

Donation after circulatory death (DCD) in the UK has tripled in the last decade. However, outcomes following DCD liver transplantation are poorer than for brain-stem death (DBD) liver transplants.

This study examines whether a recipient to should accept a "poorer quality" DCD organ, or wait longer for a "better" DBD organ.

METHODS

Survival following deceased donor liver transplantation performed between 2008 and 2015 was compared by Cox regression modelling to assess the impact on patient survival of accepting a DCD liver compared to deferring for a potential DBD transplant.

RESULTS

953 (23%) of the 3949 liver transplantations performed utilised DCD donors. Five-year transplant survival was poorer following DCD than DBD transplantation (69·1% (DCD) vs 78·3% (DBD); $p <0·0001$: adjusted hazard ratio [HR] = 1·65, 1·40 – 1·94).

Of the 5798 patients registered on the transplant list, 1325 (23%) died or were removed from the list without receiving a transplant. Patients who received DCD livers had a lower risk-adjusted hazard of death than those who remained on the waiting list for a potential DBD organ (adjusted HR 0·55, 0·47 – 0·65). The greatest survival benefit was in those with the most advanced liver disease (adjusted HR 0·19 (0·07, 0·50).

CONCLUSIONS

Although DCD liver transplantation has poorer transplant outcomes, the individual's survival is enhanced by accepting a DCD offer particularly for patients with more severe liver disease. DCD liver transplantation improves overall survival for UK listed patients and should be encouraged.

LAY SUMMARY

This study looks at patients who require a liver transplant to save their lives; this liver can be donated by a person who has died either after their heart has stopped (donation after cardiac death, DCD) or after the brain has been injured and can no longer support life (donation after brainstem death, DBD).

We know that livers donated after brainstem death function better than those after cardiac death, but there are not enough of these livers for everyone, so we wished to help patients to decide whether it was better for them to accept an early offer of a DCD liver than waiting longer to receive a "better" liver from a DBD donor.

We found that patients were more likely to survive if they accepted the offer of a liver transplant as soon as possible (DCD or DBD), especially if their liver disease was very severe.

HIGHLIGHTS

- This study details the UK experience of DCD liver transplantation:
    - Confirming outcomes for DCD are inferior to DBD liver transplantation.
    - Identifying a survival advantage in accepting a DCD offer rather than waiting for a "better" DBD liver.
    - This is most pronounced in patients with more advanced disease.
- Impact on clinical practice
    - Facilitating discussions with individuals about accepting or declining a DCD liver offer.
    - Providing strong support for the use of DCD livers in all patients.

INTRODUCTION

Rates of liver failure are increasing dramatically in the UK [1] and over a million people worldwide die of cirrhosis every year [2]. Liver transplantation is the only effective treatment for end-stage liver disease and provides an average of 17-22 years of additional life [1][3][4]. Access to liver transplantation is limited by donor organ availability, and over the last decade, as the incidence of liver disease has increased [1], the number of patients on the liver transplant waiting list in the UK has roughly doubled. Consequently, by two years, about 13% of listed patients will no longer be eligible for liver transplantation because of death or deterioration in their condition [5][6]. These waiting-list pressures have prompted focus on the use of organs from donation after circulatory death (DCD) donors, with numbers of DCD donors increasing markedly over the last decade, such that they now almost match annual numbers of donation after brain death (DBD) donors in the UK [5]. Worldwide, only the Netherlands achieves similar numbers of DCD donors per million population [7].

While this increase in DCD donor activity has transformed UK transplant practice, DCD organs are generally regarded as sub-optimal, because of the additional warm ischaemic 'hit' they are subject to during retrieval. Published series report higher incidences of primary non-function (PNF) and ischaemic cholangiopathy following DCD liver transplantation, resulting in inferior short and long-term outcomes [8-15]. These poorer outcomes for DCD transplantation have undoubtedly influenced the decision to select a particular liver for transplantation, and it is notable that in the UK, a much higher proportion of kidneys than livers are transplanted from potential DCD donors [5]. This is emblematic of a wider challenge posed to the transplant community: whether the increasing demand for transplantation merits increased utilisation of less optimal organs that are associated with poorer outcomes. Available evidence suggests that, despite the potential for such organs to increase liver transplant numbers substantially, decline in the quality of available organs often results in decreased utilisation rates [16]. This may reflect that the responsible clinician often finds it difficult to justify, for a particular individual, the use of a 'marginal' liver organ that is associated with higher morbidity and mortality than would be anticipated with a more optimal liver graft. Such a consideration overlooks, however, the potential for excess deaths while waiting for that more optimal organ.

Thus, key to increased utilisation of marginal or DCD liver allografts is whether their use offers a survival advantage *from the point of listing* for the recipient population.

5

Addressing the important question of whether a recipient should accept a "poorer quality" DCD organ or wait longer for a "better" DBD organ is, however, difficult, and a prospective trial would raise challenging practical and ethical concerns. Here, we perform a cohort analysis of the NHS Blood and Transplant (NHSBT) UK Transplant Registry (UKTR); a prospectively maintained database that records outcomes from listing for liver transplantation for all UK patients, and that includes data on over 1400 DCD liver transplants that have now been performed in the UK. We show that outcomes following DCD liver transplants are poorer than following DBD liver transplantation, but that the individual's survival prospects are enhanced by accepting, rather than rejecting, a DCD offer.

6

MATERIALS & METHODS

Study design and setting

Livers from controlled DCD donors (Maastricht category 3), defined as donors awaiting circulatory arrest after withdrawal of life-supporting treatment (WLST) [17], were included. Since April 2010, organ retrieval was performed by dedicated National Organ Retrieval Service (NORS) teams, according to a nationally agreed protocol [18]. In brief, WLST occurred in the intensive care unit or anaesthetic room, and vital signs from the time of withdrawal until cardiac arrest, defined as the 'agonal phase', were continuously monitored. Pre-mortem interventions, (such as heparin administration) aimed specifically at facilitating organ donation, are not permissible in the UK. After cardiorespiratory arrest, a 'stand-off' time of five minutes was observed before death was confirmed by an independent medical practitioner and procurement could begin [19]. Although UK organ retrieval teams wait a minimum of three hours from WLST before abandoning retrieval [20], liver donation is typically only pursued for the first hour.

DCD retrieval proceeded using a rapid retrieval technique, via a midline laparotomy, with dual aortic and portal venous perfusion with University of Wisconsin solution (ViaSpanTM, Bristol-Myers Squibb Pharma, Garden City, NY, USA) containing 25,000 units of heparin per litre in the first two bags. Topical cooling was achieved with crushed frozen saline. UK NORS teams routinely wait three hours from WLST before abandoning retrieval if cardiorespiratory arrest has not occurred [20], but the duration of agonal phase for DCD livers implanted was considerably shorter (median (IQR) 15 minutes (11, 20)). During the study period, 50 DCD livers were machine perfused, either by Normothermic Regional Perfusion (NRP) (n=20) or *ex situ* immediately following retrieval (n=30); no liver was subject to hypothermic machine perfusion. Information recorded at retrieval included the retrieval surgeon's assessment of the liver appearance: either 'healthy' or 'suboptimal'.

DCD livers were allocated in the UK according to broadly similar principles to DBD livers [21], but with some slight modifications, in that the DCD liver was first offered to the designated local centre, and then to two or three regionally linked centres, before offering to all remaining centres via a 'fast-track' scheme. Selection of a specific recipient was at the discretion of the accepting centre, but factors influencing that

7

decision included blood group compatibility, donor and recipient size match, primary liver aetiology, and perceived clinical urgency.

Influence of DCD liver transplantation on post-transplant survival

Data on 3949 first adult elective NHS group 1 (NHS-entitled) liver-only transplants performed in the UK using livers from deceased donors between January 1, 2008 and December 31, 2015 were analysed. The reported size of the study cohort excludes 415 transplants with missing values in one or more of the recipient, transplant or donor factors or with missing survival information.

The primary outcome was 5-year transplant survival after transplantation, which was defined as the time from transplant to the earlier of patient death or re-transplant. If a patient was alive at the end of the follow-up period or lost to follow-up, then their survival was censored at the last known survival date while patients who survived for longer than 5-years (1825 days) were censored at 5 years. Unadjusted and adjusted survival were estimated and stratified by donor type. Primary non-function (PNF) was defined as poor graft function necessitating re-transplantation or culminating in death within 14 days, excluding rejection and vascular thrombosis. Graft failure was defined as death related to graft failure, or re-transplantation. Cold ischaemic time was defined as the time between commencement of cold perfusion in the donor and warm re-perfusion in the recipient.

Impact of accepting a DCD liver compared with waiting for a potential DBD liver

Data on 5825 UK adult elective NHS-entitled patients who were registered on the elective waiting list for first liver-only transplantation between January 1, 2008 and December 31, 2015 were analysed. Survival status to May 10, 2017 was extracted from the UKTR and the Office for National Statistics (ONS). At this date, 81 patients were still active on the transplant list; their outcome was unknown at time of analysis.

To determine how the extant policy allowing DCD liver utilisation affected survival from waiting list entry compared to excluding DCD-donors and hypothetically waiting for DBD livers, the analytical technique of sequential stratification was used [22]. This technique uses observational data to emulate data from a hypothetical randomised trial allowing outcome comparisons between patients who receive a particular treatment at a given time and those waiting for a different treatment, akin to the analysis performed by Bonser et al [23]. The time origin was taken to be the waiting list registration date and each DCD donor transplant was regarded as an index case. A

stratum was then formed from each index case and a control group of all patients on the transplant list for the same length of time (in days) or longer and eligible to receive that same liver (i.e. blood group and size compatible). A control patient who received a DBD transplant was followed up until death or last known follow-up post-transplant and were not censored at time of DBD transplant. However, a control patient who received a DCD transplant were censored at the DCD transplant (as they would no longer have had the opportunity of a DBD liver) and were then another index patient with a separate group of control patients. Although such censoring of control patients constitutes informative censoring, an inverse probability of censoring weighted (IPCW) approach was not adopted, because this would greatly add to the complexity of the analysis. In addition, experience using the UK Transplant Registry database suggests that adjustments for non-informative censoring have relatively small impact on subsequent inference.

The survival time of the index case was censored if they were alive at 10 May 2017. The survival times of those in the control group were censored either at the time of removal (from tumour progression or worsening of clinical condition) from the list (if date of death unknown), at the time of transplant from a DCD donor, or at 10 May 2017 if still alive.

Statistical Analysis

Donor, recipient, and transplant characteristics were compared, stratified by donor type, using Fisher's exact test, chi-squared, or the Mann-Whitney test, as appropriate. Unadjusted transplant survival estimates, stratified by donor type, were calculated for different times post-transplant using Kaplan-Meier estimation methods and assessed using the log-rank test as was survival conditional on 90 day and 1-year survival. Cox proportional hazards regression modelling was used to assess whether donor type influenced transplant survival after adjusting for the final set of relevant risk factors. A stepwise procedure was utilised for variable selection.

To account for competing risks, cumulative incidence functions for graft failure (defined as above) and deaths with a functioning graft were compared between DBD and DCD donors using Gray's test/Fine Gray model for competing risks.

A stratified Cox regression model was used to estimate the hazard of mortality from accepting a DCD donor liver compared to continued waiting for a potential DBD donor transplant, after adjustment for other relevant recipient risk factors: recipient

9

age; BMI; log (creatinine); log (bilirubin); log(INR); serum sodium; blood group; gender; ethnic origin; disease group; grouped registration year; transplant centre; patient location (in-patient, out of hospital); ventilation status; renal replacement therapy; ascites; HCV and previous abdominal surgery. Stratification produced separate baseline hazards for each of the strata defined by the index cases.

Multiple imputation (MI) was used to impute values for factors with missing values when appropriate. MI was implemented in SAS 9.3, using chained equations. The imputation model considered all variables in the analysis but also the outcome variables; survival time and censoring indicator. Twenty-one imputation datasets were generated, with 50 burn-in iterations preceding each imputation set [24]. Data from the 415 patients that were excluded (see above) were not imputed, because this information was not missing completely at random, and was instead was due to particular centres not submitting the required data.

Public and Patient Involvement

The draft manuscript has been reviewed by the NHSBT liver patient group) and upon confirmation of acceptance for publication, the findings will be disseminated to the major UK liver patient groups.

Patient Consent

Consent for use of anonymised data for outcome analysis is obtained from patients at registration onto the national transplant waiting list.

RESULTS

Comparison of outcomes for DCD and DBD liver transplantation

Of the 3949 transplants performed during the study period, 903 (23%) utilised livers from DCD-donors (Table 1). DCD liver transplant activity increased annually throughout the study period (Figure s1), although, as previously reported [8], utilisation rates differed between different UK liver transplant centres (Table 2). Compared to DBD donors, DCD donors were younger, had a lower BMI and were more likely to have died from trauma than from a cerebrovascular accident (Table 1). DCD liver recipients were more likely to have lower UKELD [25] and MELD [26] scores and less likely to have had previous abdominal surgery or be in-patients at the time of transplantation (Table 2); this suggested a tendency to select lower risk individuals as DCD liver recipients. DCD liver recipients were more likely to have cancer as their primary liver aetiology.

Transplant survival was found to be poorer following DCD liver transplantation, with the difference apparent by 90 days and maintained over five years (Figure 1a; 5 year survival 69·1% DCD vs. 78·3% DBD; p <0·0001). Patient survival was also poorer (Figure 1b). This difference in long-term outcomes is not simply due to differences in early post-transplant graft failure or mortality, because the divergence in transplant survival outcomes was sustained at five years, conditional on transplant survival beyond either the initial 90 days (Figure 1c) or the first year (Figure 1d) after transplantation.

The Cox regression model analysis considered all pre-transplantation factors shown in Table 1 and 2. Five risk factors were identified as statistically significant predictors of 5-year survival: donor age, recipient age, primary liver aetiology, inpatient status, and organ appearance (Table s1). The adjusted hazard ratio (HR) for 5-year survival for DCD relative to DBD transplantation was 1·65 (95% CI 1·41, 1·95; p<0·0001). There was no statistically significant interaction between donor type and either UKELD (HR: 1·61 (1·36, 1·91 for a particular UKELD value) (p=0·15) or primary liver aetiology (p=0·75). Thus, although outcomes for DCD liver transplantation are generally poorer than for DBD liver transplantation, there does not appear to be a specific recipient group for whom DCD liver transplantation is more disadvantageous.

Competing risk analysis (Figure 2a) demonstrated that the poorer survival for the DCD liver cohort is likely due to the higher failure rates associated with DCD liver

transplantation. This reflects an increased incidence of PNF (3·54% (DCD) vs. 1·25% (DBD) $p<0\cdot0001$). However, the rate of graft failure was also higher at later time points, indicating greater on-going attritional graft loss (Figure 2b). Consequently, a greater proportion of the DCD liver recipients died from graft failure: in contrast, the proportions of patients dying with a working graft were similar (Figure 2c).

Is it better to accept a DCD liver or wait for a potential DBD liver?

The above results raise the question of whether it would be better for an individual to accept a DCD liver or to defer for a better 'quality' DBD liver. Figure 3 depicts outcomes for the registrants on the liver transplant list during the trial period. Twenty-three per-cent (1031/4392) of the patients transplanted received livers from DCD donors, generating 1031 strata for the sequentially stratified model. Crucially, this model revealed that recipients of DCD donor livers had a substantially lower *unadjusted* hazard of death post-registration relative to remaining on the list for a potential DBD-donor transplant (Table 3).

A number of recipient factors were identified as statistically significant and these were incorporated into the stratified Cox model (data not presented). Donor type was subsequently added to the model. This approach confirmed that compared to waiting for a potential DBD liver, the *risk-adjusted* HR for post-registration mortality is consistent with the unadjusted analysis (Table 3). The survival advantage that the sequential stratification models for accepting a DCD liver is illustrated in Figure 4.

The potential survival benefit of using a DCD liver is influenced by a number of principal factors: the rate of de-listing or death while on the waiting list, and the survival differences following transplantation for DCD and DBD organs. It was notable that over the study period there was a marked difference in waiting list outcomes (Figures 5a and 5b), with waiting-list mortality (censored for transplantation) significantly greater in the earlier (2008-2011) than in the later (2012-2015) era. This difference does not appear to reflect differences in access to transplantation, because the median time to transplant was similar in both eras (140 (95% CI 131, 149) and 134 (125, 143) days for 2008-2011 and 2012-2015, respectively), and may instead be due to either slight differences in the characteristics of the patients listed in the two eras (such as UKELD and the requirement for renal support (Table 2)), or to improved management of patients while on the waiting list. In contrast, survival following transplantation in the two eras

was similar (Figure 5c). Notably, despite the improved waiting-list survival in the later study era, the analysis revealed that the survival benefit associated with DCD liver transplantation was, if anything, greater for the 2012-2015 era (Table 3).

When is the use of a DCD liver most advantageous?

The decision to transplant a liver is made following consideration of the perceived risk-benefit for a particular patient. The results above raise the question whether there are particular recipient circumstances in which the use of a DCD liver would be particularly advantageous. In this respect, the use of 'sub-optimal' liver organs in recipients with particularly advanced liver disease remains controversial. The analysis was therefore adapted to assess the relative benefit of using DCD livers in recipients with different severity of liver disease, by incorporating the patients UKELD score at registration (either as a continuous or categorical variable). UKELD score was designed to predict mortality on the UK liver transplant waiting list [25], and similar to the US MELD system [26], a higher score indicates more severe liver disease. As shown in Table 4, the survival benefit associated with accepting DCD livers increases with the recipient's UKELD score, such that for every unit increase of UKELD, the hazard of death after accepting a DCD liver relative to waiting for a potential DBD liver decreases by 0·92 (CI: 0·89, 0·96). This is most strikingly evident when considering UKELD as a categorical variable, with the hazard ratio for death associated with DCD liver use in patients with particularly severe liver disease (UKELD > 62) approximately 1/3 of that calculated for patients with mild disease (UKELD – 51-53, Table 4). This analysis therefore provides strong support for a policy whereby DCD organs are transplanted preferentially into the sickest patients on the waiting list. Similar results were observed when the modelling was performed using US MELD score as the marker of disease severity (Table s2).

DISCUSSION

In support of the existing literature [8-14], registry analysis of the UK liver transplant outcomes confirms that survival following DCD liver transplantation is poorer than following DBD liver transplantation. However, the important findings from this study are that accepting a DCD liver conferred a survival advantage over waiting for a more optimal DBD liver, and that the survival advantage was greatest for patients with more advanced liver disease. Thus, our data suggest that the current policy of selecting sicker recipients for "optimal" (DBD) grafts, because of the perception that the use of "sub-optimal" (DCD) organs in sicker recipients is associated with particularly poor outcomes, may deny these patients an important chance for survival.

Our findings therefore mirror a recent analysis by Mclean et al., that reported that UK liver recipients with a MELD score >15 have a significant increase in their quality of life from accepting, rather than rejecting, a DCD liver offer [27]. However, the Mclean analysis was performed by using Markov modelling, and the critical difference is that the sequential stratification method adopted in the present study matches a patient who receives a DCD liver with all those who were eligible to receive that liver and who had been registered for the same number of days. This means that the comparison between receiving a DCD liver and waiting for another offer is adjusted for time on the registration list; the sequential stratification approach thus essentially performs a hypothetical randomised trial.

Current UK utilisation patterns of deceased-donor organs suggest that concerns relating to outcomes continue to limit utilisation of liver grafts from potential DCD-donors. The outcomes for those DCD livers that were unused during the study period, had they been transplanted, is clearly speculative. However, it seems probable, given the marked survival advantage for accepting a DCD liver relative to waiting for a potential DBD liver, that their use would have further improved survival for the listed population, particularly for recipients with more advanced liver disease. We anticipate that our analysis will provide the contextual basis for discussing with individual patients their relative risks of accepting a DCD liver, and that an appreciation of their likely survival benefits from doing so, will change current practices relating to DCD liver utilisation and lead to fewer organ discards. Given the

14

potentially large DCD donor pool, this has the scope to increase liver transplant numbers substantially.

We believe our analysis has important implications for ongoing developments in UK liver transplant practice. Most pertinently, the recently introduced UK liver allocation scheme [28] allocates livers nationally, to the named recipient with the greatest calculated 'transplant benefit score'. This score ranks recipients according to the number of additional years of life they gain from a transplant, and will therefore generally prioritise the sickest patients on the waiting list. Only DBD livers are currently allocated through the new allocation scheme, and therefore the very group of patients who, by a similar transplant benefit evaluation, would likely derive most benefit from the potential DCD liver pool, may be denied that opportunity because of the presumption they will soon be allocated a DBD liver. Our analysis therefore highlights the importance of extending the scheme to additionally incorporate national DCD liver offering.

The second aspect of change in UK liver practice concerns the increasing use of *in situ* or *ex vivo* warm perfusion of liver organs for transplantation. Although still under trial evaluation, these approaches offer the potential for improving outcomes by 'resuscitating' DCD liver organs and for providing an additional means of selecting only those livers likely to be associated with favourable transplant outcomes [29-36]. Our analysis suggests that the real benefit of these approaches would be in increasing DCD liver utilisation rates; and further cautions that if warm perfusion technologies were associated with a paradoxical decrease in DCD liver transplant rates, then this would likely reduce survival of the wait-listed UK liver transplant population. Reassuringly, the recent Nasrala study of *ex vivo* normothermic perfusion reports a reduction in DCD liver discard rates [37].

There are several limitations to our study. We did not consider the potential for living donor livers or the presumed quality of the DBD liver in our analysis, and it is possible, for example, that survival from listing may be better improved by increased use of more 'marginal' DBD organs, rather than DCD organs. Against this, only 214 adult living donor liver transplants were performed in the seven years of the study, which is unlikely to have impacted on overall UK survival rates for wait-listed patients. Similarly, the definition of an expanded criteria donor for liver transplantation remains vague, and often adopts donor criteria that were established as predictors for kidney allograft survival [38].In contrast, DCD liver transplants are undoubtedly viewed as a

15

distinct entity from DBD liver transplantation, and hence, the analysis of survival benefit for accepting a DCD liver focuses on a real clinical dilemma. The main limitation of our study is that, as a registry analysis, it may miss confounding factors that are not recorded by the registry. Hence, the use of DCD organs in high-risk recipients may have occurred in highly select occasions, with the recipient generally considered healthier than evident from the UKELD score. Such individual variation would not be captured by the analysis. We think this unlikely, because relatively large numbers of DCD transplants (n=192) were performed into the sicker (UKELD ≥ 58) recipients. Similarly, the perceived survival benefit associated with DCD liver transplantation pertains to the particular pressures of UK liver transplant practice during the study period. This advantage is dependent upon three main factors: the mortality on the waiting list, and the survival outcomes following DCD and DBD transplantation. Hence alterations in any of these factors would alter the relative survival advantage of using a DCD liver, potentially limiting the applicability of our findings to other countries; the survival advantage would, for example, be more modest or non-existent if waiting list mortality was minimal in a particular country due to high DBD donation rates. Notwithstanding, UK liver waiting list mortality is roughly equivalent to other EU countries, and if anything less than in the US [39]. Reported outcomes for DCD liver transplantation in other countries are also broadly similar to the UK experience. Hence, it is likely that the DCD-donor pool will offer similar survival advantages to the waiting list population in these countries.

Conclusions

These limitations notwithstanding, our findings suggest that there needs to be a better evaluation of the risks associated with waiting for liver transplantation, and that an increased awareness of the survival benefit associated with DCD liver transplantation, particularly for those recipients with the more severe disease, would likely lead to wholesale changes in liver transplant practice. Such a change in practice should not be reliant upon introduction of machine perfusion technologies.

ACKNOWLEDGEMENTS

ETHICAL APPROVAL

All patients provide consent, at time of listing onto the NHSBT Transplant Registry, for use of their data for analyses of outcomes.

DATA SHARING

Data are available from the NHSBT.

TRANSPARENCY

The lead author affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned have been explained.

REFERENCES

1. Leon DA, McCambridge J. Liver cirrhosis mortality rates in Britain from 1950 to 2002: an analysis of routine data. *Lancet* 2006;367(9504):52-6. doi: 10.1016/s0140-6736(06)67924-5 [published Online First: 2006/01/10]

2. Byass P. The global burden of liver disease: a challenge for methods and for public health. *BMC Med* 2014;12:159. doi: 10.1186/s12916-014-0159-5

3. Barber K, Blackwell J, Collett D, et al. Life expectancy of adult liver allograft recipients in the UK. *Gut* 2007;56(2):279-82. doi: gut.2006.093195 [pii]

10.1136/gut.2006.093195 [published Online First: 2006/09/30]

4. Abt PL, Desai NM, Crawford MD, et al. Survival following liver transplantation from non-heart-beating donors. *Ann Surg* 2004;239(1):87-92. doi: 10.1097/01.sla.0000103063.82181.2c [published Online First: 2003/12/20]

5. NHS Blood and Transplant. Organ donation and Transplantation Activity Report 2014/15. 2015 [Available from: http://nhsbtmediaservices.blob.core.windows.net/organ-donation-assets/pdfs/activity_report_2014_15.pdf.

6. NHS Blood and Transplant: Annual Report on Liver Transplantation 2016 [Available from: https://nhsbtdbe.blob.core.windows.net/umbraco-assets-corp/1314/organ_specific_report_liver_2016.pdf.

7. Summers DM, Watson CJ, Pettigrew GJ, et al. Kidney donation after circulatory death (DCD): state of the art. *Kidney Int* 2015 doi: 10.1038/ki.2015.88 [published Online First: 2015/03/19]

8. Callaghan CJ, Charman SC, Muiesan P, et al. Outcomes of transplantation of livers from donation after circulatory death donors in the UK: a cohort study. *BMJ Open* 2013;3(9):e003287. doi: 10.1136/bmjopen-2013-003287

9. Mallik M, Callaghan CJ, Hope M, et al. Comparison of liver transplantation outcomes from adult split liver and circulatory death donors. *Br J Surg* 2012;99(6):839-47. doi: 10.1002/bjs.8755 [published Online First: 2012/04/19]

10. Laing RW, Scalera I, Isaac J, et al. Liver Transplantation Using Grafts From Donors After Circulatory Death: A Propensity Score-Matched Study From a Single Center. *Am J Transplant* 2016;16(6):1795-804. doi: 10.1111/ajt.13699 [published Online First: 2016/01/05]

11. Axelrod DA, Dzebisashvili N, Lentine KL, et al. Variation in biliary complication rates following liver transplantation: implications for cost and outcome. *Am J Transplant* 2015;15(1):170-9. doi: 10.1111/ajt.12970 [published Online First: 2014/12/24]

12. DeOliveira ML, Jassem W, Valente R, et al. Biliary complications after liver transplantation using grafts from donors after cardiac death: results from a matched control study in a single large volume center. *Ann Surg* 2011;254(5):716-22; discussion 22-3. doi: 10.1097/SLA.0b013e318235c572 [published Online First: 2011/11/02]

13. Foley DP, Fernandez LA, Leverson G, et al. Biliary complications after liver transplantation from donation after cardiac death donors: an analysis of risk factors and long-term outcomes from a single center. *Ann Surg* 2011;253(4):817-25. doi: 10.1097/SLA.0b013e3182104784 [published Online First: 2011/04/09]

14. Jay CL, Lyuksemburg V, Ladner DP, et al. Ischemic cholangiopathy after controlled donation after cardiac death liver transplantation: a meta-analysis. *Ann Surg* 2011;253(2):259-64. doi: 10.1097/SLA.0b013e318204e658 [published Online First: 2011/01/20]

15. O'Neill S, Roebuck A, Khoo E, et al. A meta-analysis and meta-regression of outcomes including biliary complications in donation after cardiac death liver transplantation. *Transplant International* 2014;27(11):1159-74. doi: 10.1111/tri.12403

16. Orman ES, Barritt ASt, Wheeler SB, et al. Declining liver utilization for transplantation in the United States and the impact of donation after cardiac death. *Liver Transpl* 2013;19(1):59-68. doi: 10.1002/lt.23547 [published Online First: 2012/09/12]

17. Kootstra G, Daemen JH, Oomen AP. Categories of non-heart-beating donors. *Transplant Proc* 1995;27(5):2893-4.

18. NHS Blood and Transplant: National Standards for Organ Retrieval from Deceased Donors 2016 [Available from: https://nhsbtdbe.blob.core.windows.net/umbraco-assets-corp/1405/nors_retrieval_standards.pdf.

19. Academy of Medical Royal Colleges: A code of practice for the diagnosis and confirmation of death 2008 [Available from: http://aomrc.org.uk/wp-content/uploads/2016/04/Code_Practice_Confirmation_Diagnosis_Death_1008-4.pdf.

20. Reid AW, Harper S, Jackson CH, et al. Expansion of the kidney donor pool by using cardiac death donors with prolonged time to cardiorespiratory arrest. *Am J Transplant* 2011;11(5):995-1005. doi: 10.1111/j.1600-6143.2011.03474.x [published Online First: 2011/04/01]

21. Neuberger J, Gimson A, Davies M, et al. Selection of patients for liver transplantation and allocation of donated livers in the UK. *Gut* 2008;57(2):252-7. doi: 10.1136/gut.2007.131730 [published Online First: 2007/09/27]

22. Schaubel DE, Wolfe RA, Port FK. A sequential stratification method for estimating the effect of a time-dependent experimental treatment in observational studies. *Biometrics* 2006;62:910-17.

23. Bonser RS, Taylor R, Collett D, et al. Effect of donor smoking on survival after lung transplantation: a cohort study of a prospective registry. *Lancet* 2012;380(9843):747-55. doi: 10.1016/S0140-6736(12)60160-3

24. White IR, Royston P, Wood AM. Multiple imputation using chained equations: Issues and guidance for practice. *Stat Med* 2011;30(4):377-99. doi: 10.1002/sim.4067

25. Barber K, Madden S, Allen J, et al. Elective liver transplant list mortality: development of a United Kingdom end-stage liver disease score. *Transplantation* 2011;92(4):469-76. doi: 10.1097/TP.0b013e318225db4d [published Online First: 2011/07/22]

26. Malinchoc M, Kamath PS, Gordon FD, et al. A model to predict poor survival in patients undergoing transjugular intrahepatic portosystemic shunts. *Hepatology* 2000;31(4):864-71. doi: 10.1053/he.2000.5852 [published Online First: 2000/03/25]

27. McLean KA, Camilleri-Brennan J, Knight SR, et al. Decision modeling in donation after circulatory death liver transplantation. *Liver Transpl* 2017;23(5):594-603. doi: 10.1002/lt.24715

28. Deceased Donor Liver Distribution and Allocation: NHSBT; 2018 [Available from: https://nhsbtdbe.blob.core.windows.net/umbraco-assets-corp/9862/pol196-liver-allocation-policy.pdf.

29. Barbas AS, Knechtle SJ. Expanding the Donor Pool With Normothermic Ex Vivo Liver Perfusion: The Future Is Now. *Am J Transplant* 2016;16(11):3075-76. doi: 10.1111/ajt.13959 [published Online First: 2016/10/28]

30. Butler AJ, Randle LV, Watson CJ. Normothermic regional perfusion for donation after circulatory death without prior heparinization. *Transplantation* 2014;97(12):1272-8. doi: 10.1097/TP.0000000000000082

31. Oniscu GC, Randle LV, Muiesan P, et al. In situ normothermic regional perfusion for controlled donation after circulatory death--the United Kingdom experience. *Am J Transplant* 2014;14(12):2846-54. doi: 10.1111/ajt.12927

32. Watson CJ, Kosmoliaptsis V, Randle LV, et al. Normothermic perfusion in the assessment and preservation of declined livers prior to transplantation: hyperoxia and vasoplegia - important lessons from the first 12 cases. *Transplantation* 2017 doi: 10.1097/TP.0000000000001661

33. Watson CJE, Kosmoliaptsis V, Pley C, et al. Observations on the ex situ perfusion of livers for transplantation. *American Journal of Transplantation* 2018 doi: 10.1111/ajt.14687

34. Oniscu G, Sutherland A. Challenges and advances in optimizing liver allografts from donation after circulatory death donors. *Journal of Natural Science, Biology and Medicine* 2016;7(1):10. doi: 10.4103/0976-9668.175017

35. Minambres E, Suberviola B, Dominguez-Gil B, et al. Improving the Outcomes of Organs Obtained From Controlled Donation After Circulatory Death Donors Using Abdominal Normothermic Regional Perfusion. *Am J Transplant* 2017;17(8):2165-72. doi: 10.1111/ajt.14214

36. De Carlis R, Di Sandro S, Lauterio A, et al. Successful donation after cardiac death liver transplants with prolonged warm ischemia time using normothermic regional perfusion. *Liver Transpl* 2017;23(2):166-73. doi: 10.1002/lt.24666

37. Nasralla D, Coussios CC, Mergental H, et al. A randomized trial of normothermic preservation in liver transplantation. *Nature* 2018 doi: 10.1038/s41586-018-0047-9

38. Dimou FM, Mehta HB, Adhikari D, et al. The role of extended criteria donors in liver transplantation for nonalcoholic steatohepatitis. *Surgery* 2016;160(6):1533-43. doi: 10.1016/j.surg.2016.06.051 [published Online First: 2016/08/25]

39. Kim WR, Lake JR, Smith JM, et al. OPTN/SRTR 2015 Annual Data Report: Liver. *Am J Transplant* 2017;17 Suppl 1:174-251. doi: 10.1111/ajt.14126 [published Online First: 2017/01/05]

Table 1: Donor and transplant characteristics for first UK adult elective deceased donor liver only transplants, 1 January 2008 to 31 December 2015, by donor type.

Data are median (IQT) or number (%) as appropriate. Characteristics were compared, stratified by donor type, using chi-squared, fishers exact or Kruskal-Wallis test as appropriate.

Variable	Level	DBD (N=3046)	DCD (N=903)	p-value
Donor				
Donor age (years)	Linear	50 (39 - 61)	49 (35 - 59)	**<0·0001**
Donor BMI (kg/m²)	Linear	25·91 (23·31 – 29·05)	25·08 (22·63 – 27·69)	**<0·0001**
Donor blood group	O	1206 (39%)	422 (47%)	**<0·0001**
	A	1361 (45%)	380 (42%)	
	B	337 (11%)	91 (10%)	
	AB	142 (5%)	10 (1%)	
Donor gender	Male	1538 (50%)	542 (60%)	**<0·0001**
	Female	1508 (50%)	361 (40%)	
Donor grouped cause of death	CVA	2092 (69%)	465 (52%)	**<0·0001**
	RTA	124 (4%)	75 (8%)	
	Other trauma	129 (4%)	43 (5%)	
	Miscellanous	701 (23%)	320 (35%)	
History of diabetes	No history of diabetes	2765 (91%)	845 (94%)	**0·03**
	History of diabetes	199 (6%)	41 (4%)	
	Unknown history diabetes	82 (3%)	17 (2%)	
Transplant related				
Blood group match	Identical	3009 (99%)	879 (97%)	**0·002**
	Compatible	37 (1%)	24 (3%)	
Liver transplanted	Whole	2714 (89%)	902 (100%)	**<0·0001**
	Reduced	5 (0%)	1 (0%)	
	Split	327 (11%)	0 (0%)	
Organ appearance	Healthy	2117 (69%)	504 (56%)	**<0·0001**
	Suboptimal	598 (20%)	270 (30%)	
	Unknown	331 (11%)	129 (14%)	
Cold ischaemia time (hours)	Linear	529 (430 - 636)	429 (365 - 488)	**<0·0001**

Table 2 Recipient characteristics for first UK adult elective deceased donor liver only transplants, 1 January 2008 to 31 December 2015, by donor type

Data are median (IQT) or number (%) as appropriate. Characteristics were compared, stratified by donor type, using chi-squared, fishers exact or Kruskal-Wallis test as appropriate

Variable	Level	DBD (N=3046)	DCD (N=903)	p-value
Age (years)		55 (46 - 61)	56 (49 - 62)	**0·00040**
Blood group	O	1202 (39%)	411 (45%)	**0·00018**
	A	1332 (44%)	371 (41%)	
	B	341 (11%)	97 (11%)	
	AB	171 (6%)	24 (3%)	
Gender	Male	2019 (66%)	619 (69%)	0·20
Ethnic group	White	2675 (88%)	782 (87%)	0·26
	Asian	244 (8%)	74 (8%)	
	Black	70 (2%)	24 (3%)	
	Chinese/South East Asian	23 (1%)	14 (1%)	
	Other	34 (1%)	9 (1%)	
Disease aetiology	Cancer	673 (22%)	289 (32%)	**<0·0001**
	Hepatitis C cirrhosis (HCV)	334 (11%)	99 (11%)	
	Alcoholic liver disease (ALD)	731 (24%)	217 (24%)	
	Hepatitis B cirrhosis (HBV)	32 (1%)	11 (1%)	
	Primary sclerosing cholangitis (PSC)	348 (11%)	64 (7%)	
	Primary biliary cirrhosis (PBC)	267 (9%)	100 (11%)	
	Auto-immune & Cryptogenic disease (AID)	219 (7%)	36 (4%)	
	Metabolic liver disease	261 (9%)	58 (7%)	
	Other liver disease	181 (6%)	29 (3%)	
BMI (kg/m^2)		26·73 (23·49 - 30·68)	26·5 (23·88 - 29·67)	0·28
Creatinine (µmol/l)		78 (64 - 98)	79 (64 - 98)	0·80
Bilirubin (µmol/l)		49 (25 - 103)	39 (21 - 75)	**<0·0001**
INR		1·4 (1·2 - 1·7)	1·4 (1·2 - 1·7)	**0·00063**
Sodium (mmol/l)		137 (134 - 140)	138 (135 - 140)	**<0·0001**
Albumin (g/l)		31 (26 - 36)	32 (28 - 38)	**0·0022**
Potassium (mmol/l)		4·2 (3·9 - 4·5)	4·2 (3·9 - 4·5)	0·14
UKELD		55 (51 - 59)	53 (50 - 57)	**<0·0001**
MELD		16 (12 - 21)	15 (11 - 19)	**<0·0001**
Waiting time (days)		86 (30 - 196)	77 (31 - 165)	**0·074**

In-patient status	Inpatient	469 (15%)	91 (10%)	**<0·0001**
Ventilation status	Ventilated	26 (1%)	5 (1%)	0·37
Renal support status	Renal support	149 (5%)	46 (5%)	0·81
HCV status	HCV positive	647 (21%)	233 (26%)	**0·0038**
Prior abdominal surgery	Prior abdominal surgery	401 (13%)	63 (7%)	**<0·0001**
Encephalopathy status	Encephalopathy	940 (31%)	261 (29%)	0·26
Clinically detectable ascites status	Ascites	1669 (59%)	465 (51%)	0·081
Transplant centre	Newcastle	194 (6%)	23 (3%)	**<0·0001**
	Leeds	475 (16%)	111 (12%)	
	Cambridge	359 (12%)	124 (14%)	
	Royal Free	371 (12%)	84 (9%)	
	Kings College	460 (15%)	183 (20%)	
	Birmingham	725 (24%)	297 (33%)	
	Edinburgh	462 (15%)	81 (9%)	

Table 3 Unadjusted and risk-adjusted hazard ratio of death for accepting a DCD liver relative to waiting for a potential DBD liver

| | Full time period | | 2008-2011 | | 2012-2015 | |
	N	HR (95% CI)	N	HR (95% CI)	N	HR (95% CI)
Unadjusted	5798	0·65 (0·55, 0·77)	2640	0·74 (0·60, 0·91)	3158	0·58 (0·43, 0·77)
Risk-adjusted	5798	0·55 (0·47, 0·65)	2640	0·63 (0·51, 0·78)	3158	0·44 (0·32, 0·59)

Table 4 Risk-adjusted hazard ratio of death for accepting a DCD liver relative to waiting for a potential DBD liver for UKELD

| | Full time period | | 2008-2011 | | 2012-2015 | |
	N	HR (95% CI)	N	HR (95% CI)	N	HR (95% CI)
Linear UKELD	5798	**0·92 (0·89, 0·96)**	2640	**0·91 (0·87, 0·95)**	3158	**0·92 (0·87, 0·97)**
UKELD categories						
51-53	1288	**0·61 (0·42, 0·91)**	562	**0·54 (0·32, 0·92)**	726	0·79 (0·44, 1·43)
54-57	1607	**0·48 (0·34, 0·67)**	762	**0·63 (0·43, 0·92)**	845	**0·23 (0·10, 0·51)**
≥58	1584	**0·40 (0·27, 0·56)**	756	**0·40 (0·25, 0·64)**	828	**0·34 (0·19, 0·62)**
Variant syndrome (<49)	739	1·16 (0·81, 1·66)	318	1·66 (1·03, 2·68)	421	0·81 (0·47, 1·40)
Chronic liver disease (49-62)	4580	**0·55 (0·45, 0·66)**	2081	**0·62 (0·49, 0·79)**	2499	**0·43 (0·30, 0·63)**
Top tier (≥63)	479	**0·19 (0·07, 0·50)**	241	**0·17 (0·04, 0·70)**	238	**0·16 (0·04, 0·64)**

25

FIGURE LEGENDS

Figure 1: Survival following DCD and DBD liver transplantation

Kaplan-Meier analysis of: **(A)** transplant survival, defined as time to patient death or liver re-transplantation, and **(B)** patient survival, for DCD and DBD liver transplants performed during the study period. The difference in five-year transplant survival between DCD and DBD liver transplantation was not solely a consequence of early graft failure or patient death because differences were maintained conditional upon transplant survival to 90 days **(C)** or one year **(D)**.

Figure 2: Graft and patient outcomes following DCD and DBD liver transplantation

Competing risk analysis was performed to compare outcomes following DBD (left panel) and DCD (right panel) liver transplantation with death with functioning graft and graft failure as competing risks **(A)**. Graft failure includes those patients who either underwent re-transplantation or died secondary to graft failure. Rates of graft failure are depicted in greater detail in **(B)**. Rates of death with a functioning graft were similar in the DBD and DCD cohorts **(C)**.

Figure 3: Outcomes from registration for transplantation from 2008 to 2015

[1] Includes: patients registered on the transplant list prior to 1 January 2008 (n=153); patients transplanted but not registered for a transplant with NHSBT (n=27); patients previously registered for a liver transplant (n=17); multi-organ registration but received a liver only (n=9); patients classed as paediatric at registration but adult at time of transplant (n=4); patients only ever suspended on the transplant list and never activated (n=6); and missing INR at registration (n=5),

[2] Includes patients with: missing cold ischaemia time (n=332); missing donor height or height<127cm (n=8); missing donor weight or weight ≥ 150kg (n=10); INR at transplant not reported (n=13); serum albumin at transplant not reported (n=9); potassium at transplant not reported (n=10); bilirubin at transplant not reported (n=4); serum sodium at transplant not reported (n=2); serum creatinine at transplant not reported (n=1); and post-transplant survival information not reported (n=5).

Figure 4: Graphical depiction of sequential stratification modelling

Actual survival from waiting-list registration for liver transplantation during trial period (current practice), and estimated survival if DCD livers were excluded from the donor pool, and patients instead had to wait for DBD liver offers. Time 0 relates to the time of registration / listing for liver transplantation. The curves were calculated by taking median survival time post-transplant from the estimated risk-adjusted survival curve and plotting an illustration of the survival time post-transplant, assuming an exponential distribution.

Figure 5: Registration and transplant outcomes according to listing year.

Kaplan-Meier patient survival (censored for transplantation) from point of listing for transplantation; according to year of listing **(A)**. Broadly, survival from listing differs for two eras (2008 to 2011 and 2012 to 2015 **(B)**). In contrast, survival from transplantation **(C)** was similar in the two eras and consistently poorer for DCD liver transplantation.

Figure 1
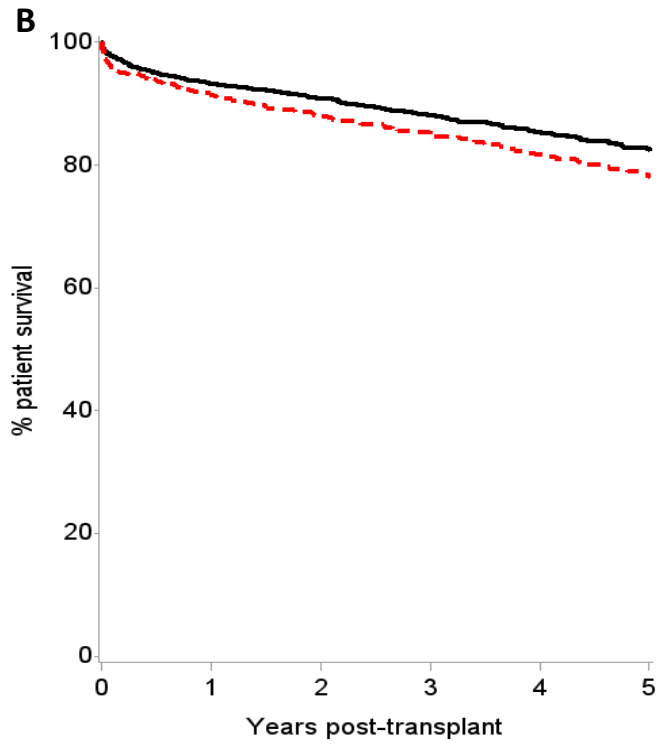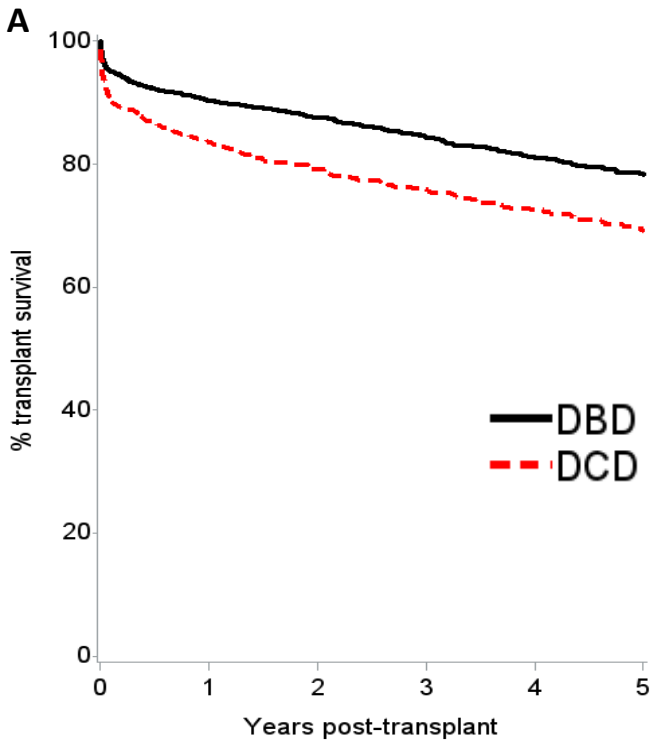
Number at risk

DBD	3046	2479	1944	1495	1130	800
DCD	903	658	474	347	247	160

	90 day	1 year	5 year
DBD	93·9 (93·0, 94·7)	90·3 (89·2, 91·3)	78·3 (76·4, 80·0)
DCD	88·9 (86·7, 90·8)	83·7 (81·1, 85·9)	69·1 (65·1, 72·7)
Log-rank	<0·0001	<0·0001	<0·0001

	3046	2562	2016	1562	1195	847
	903	718	520	376	267	172

	90 day	1 year	5 year
	96·5 (95·7, 97·1)	93·2 (92·3, 94·1)	82·6 (80·8, 84·2)
	94·8 (93·1, 96·1)	91·5 (89·4, 93·1)	78·1 (74·1, 81·5)
	0·023	0·062	0·0087
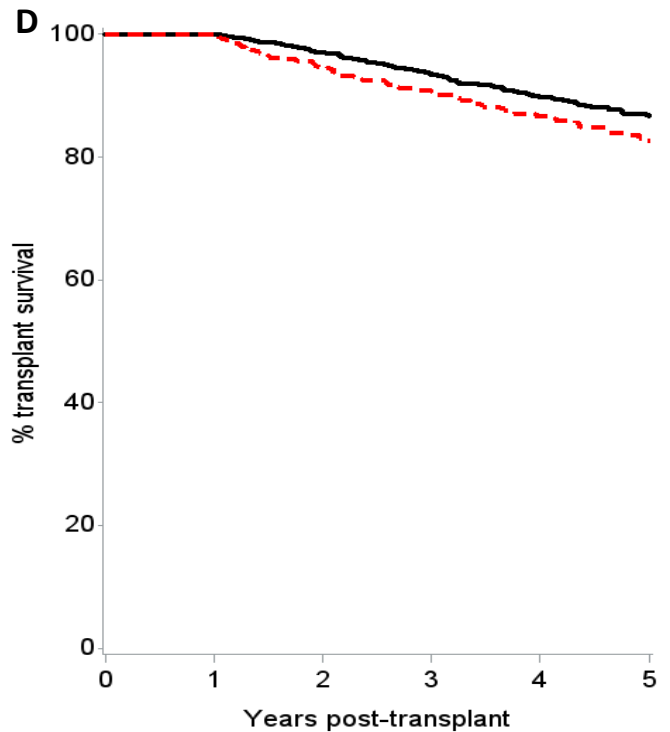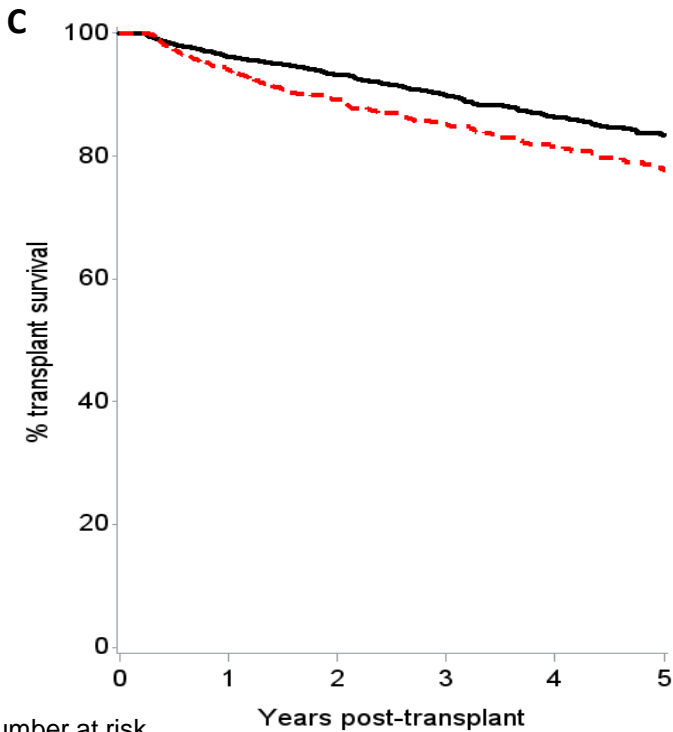
Number at risk

DBD		2479	1944	1495	1130	800
DCD		658	474	347	247	160

	1 year	3 year	5 year
DBD	96·1 (95·4, 96·8)	89·8 (88·5, 91·0)	83·4 (81·5, 85·1)
DCD	94·1 (92·2, 95·5)	85·3 (82·2, 87·8)	77·7 (73·5, 81·3)
Log-rank p-value	0·011	0·0003	0·0003

	1944	1495	1130	800
	474	347	247	160

	3 year	5 year
	93·4 (92·3, 94·4)	86·7 (84·9, 88·3)
	90·6 (87·8, 92·9)	82·6 (78·3, 86·1)
	0·0095	0·0094

Figure 2

A

DBD

Alive with functioning graft
Dead
Graft failed

90·1 87·3 83·8 80·2 77·1

7·4 9·1 11·0 13·2 14·4

2·5 3·6 5·2 6·6 8·5

Percentage of patients

Years post-transplant

DCD

83·3 78·5 74·8 71·1 66·8

13·8 17·2 20·3 22·2 23·3

2·9 4·3 4·9 6·7 9·9

Percentage of patients

Years post-transplant

B

DBD
DCD

Graft failure

Graft failure (%)

Years post-transplant

C

DBD
DCD

Death with a functioning graft

Death with functioning graft (%)

Years post-transplant

	90 day	1 year	5 year	90 day	1 year	5 year
DBD	4·8 (4·0, 5·6)	7·4 (6·5, 8·3)	14·4 (13.0, 16.0)	1·4 (1·0, 1·9)	2·5 (2·0, 3·2)	8·5 (7·2, 9·9)
DCD	9·4 (7·6, 11.4)	13·8 (11·6, 16·2)	23·3 (20·1, 26·7)	1·9 (1·1, 3·0)	2·9 (1·9, 4·2)	9·9 (7·1, 13·3)
Greys test for equality	<0·0001	<0·0001	<0·0001	0·33	0·56	0·48

Figure 3

First adult elective NHS group 1 liver only transplants (1st cohort)

First adult elective NHS group 1 liver only registrations (2nd cohort)

| 221 additional transplants[1] | 3728 transplants | ← | 5798 registrations |

| 394 transplants with information not reported at time of transplant[2] | 270 transplanted in 2016, 2017 or received a multi-organ transplant | 1325 died or removed from list | 81 active on transplant list at end of study |

| 3949 transplants | | 4392 transplants |

| 903 DCD | 3046 DBD | 1031 DCD (index cases) | 3361 DBD |

Figure 4

Figure 5

A

% time to death on the list

	1 year	3 year
2008	76·4 (70·8, 82·1)	55·0 (39·8, 70·1)
2009	80·9 (76·2, 85·6)	65·9 (57·3, 74·5)
2010	81·5 (77·2, 85·7)	65·8 (54·0, 77·6)
2011	80·8 (76·2, 85·3)	67·4 (54·0, 80·9)
2012	87·6 (84·1, 91·2)	81·1 (74·4, 87·9)
2013	86·2 (82·4, 90·0)	80·8 (72·5, 89·2)
2014	86·9 (83·5, 90·4)	80·4 (74·8, 85·9)
2015	87·4 (83·9, 90·9)	81·0 (73·4, 88·7)
Log-rank p-value	0·0006	<0·0001

months post-registration

B

% time to death on the list

	1 year	3 year
2008-2011	79·9 (77·5, 82·3)	65·1 (59·5, 70·8)
2012-2015	87·0 (85·3, 88·8)	80·5 (76·7, 84·3))
Log-rank p-value	<0·0001	<0·0001

months post-registration

Number at risk

2008-2011	2779	924	420	198	111	74	47
2012-2015	3259	1166	560	301	144	83	41

C

% transplant survival

	1 year	3 year	5 year
DBD 2008-2011	90·0 (88·3, 91·4)	84·2 (82·2, 86·0)	78·3 (76·0, 80·4)
DBD 2012-2015	90·6 (89·0, 91·9)	84·3 (82·0, 86·4)	80·3 (77·0, 83·2)
Log-rank p-value	0·55	0·8	0·95
DCD 2008-2011	81·0 (76·4, 84·7)	73·8 (68·7, 78·1)	67·7 (62·3, 72·5)
DCD 2012-2015	85·3 (82·1, 88·0)	76·5 (71·8, 80·5)	67·4 (55·1, 77·0)
Log-rank p-value	0·09	0·20	0·3

Years post-transplant

Number at risk
DBD

2008-2011	1458	1288	1243	1147	1026	796
2012-2015	1588	1191	701	348	104	4

DCD

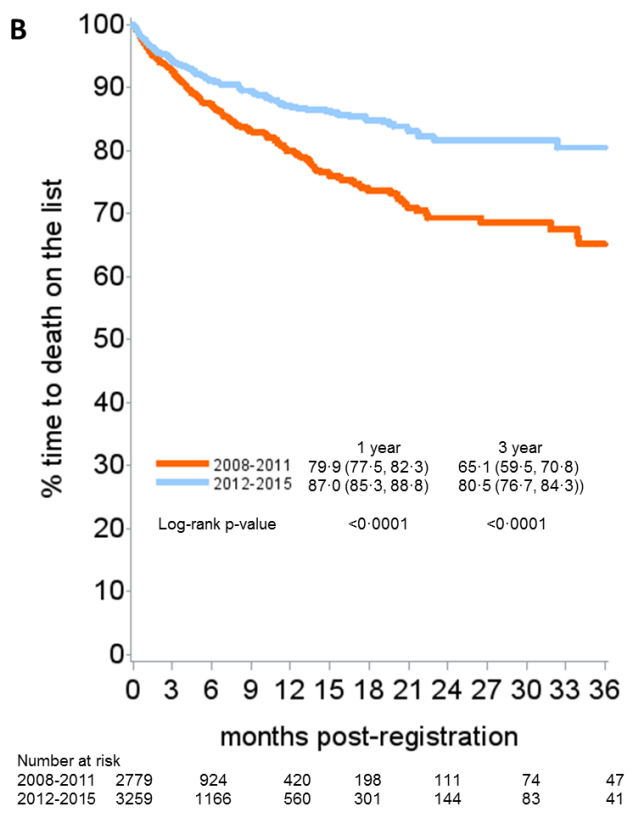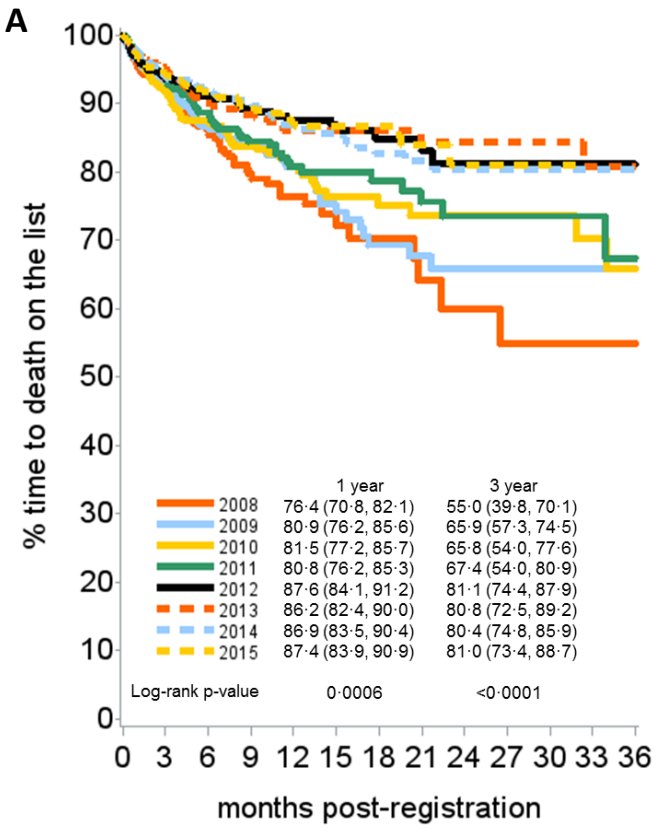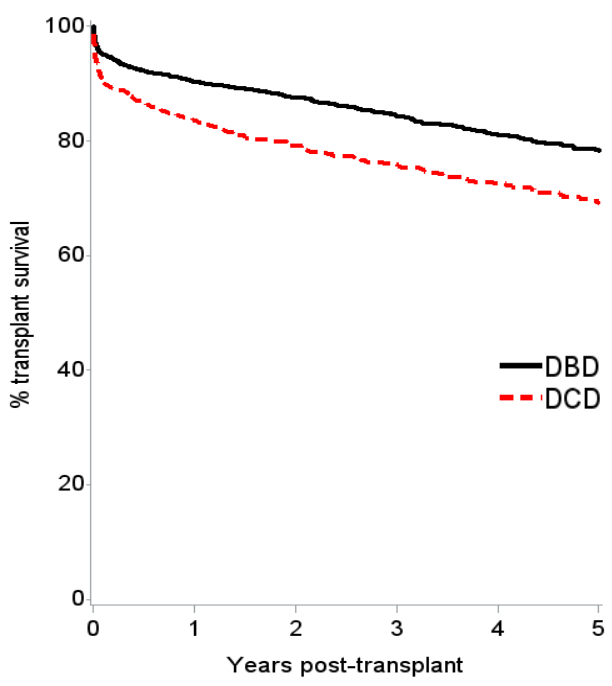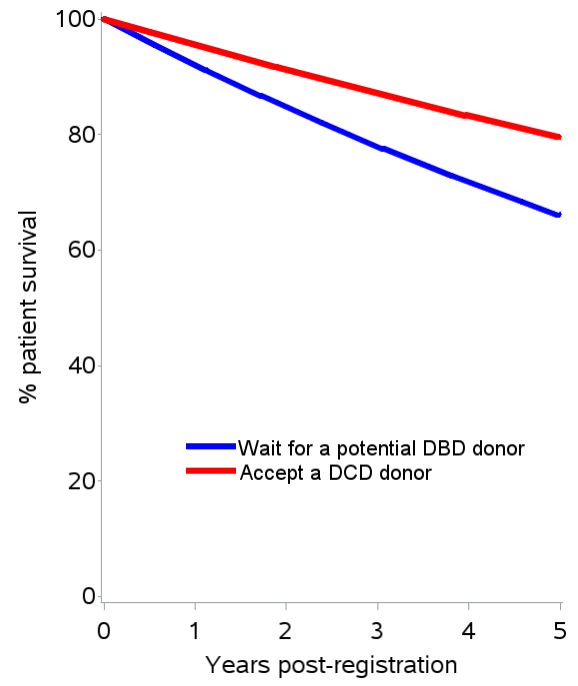|						
2008-2011	343	272	253	239	216	156
2012-2015	560	386	221	108	31	4

Although outcomes from DCD is inferior to DBD liver transplantation (A), the survival benefit of accepting an early offer of a DCD liver transplant is significant over waiting for a "better" DBD liver (B).

Survival advantage for patients accepting a circulatory death liver transplant offer

HIGHLIGHTS

- This study details the UK experience of DCD liver transplantation:
    - Confirming outcomes for DCD are inferior to DBD liver transplantation.
    - Identifying a survival advantage in accepting a DCD offer rather than waiting for a "better" DBD liver.
    - This is most pronounced in patients with more advanced disease.
- Impact on clinical practice
    - Facilitating discussions with individuals about accepting or declining a DCD liver offer.
    - Providing strong support for the use of DCD livers in all patients.