

A national registry analysis of kidney allografts preserved with Marshall's Solution in the United Kingdom

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Abbreviations:

95%CI: 95% Confidence Interval

CIT: Cold Ischaemic Time

CRF: Calculated Reaction Frequency

DBD: Donation after Brain Death

DCD: Donation after Circulatory Death

DGF: Delayed Graft Function

HR: Hazard Ratio

HLA: Human Leucocyte Antigen

OR: Odds Ratio

PNF: Primary Non-Function

UW: University of Wisconsin Solution

Abstract

Background

The preservation fluids most commonly used for renal allograft preservation in the UK are University of Wisconsin Solution (UW, £120/litre) and Marshall's Solution (Hyper-osmolar Citrate, £10/litre). The aim of this study was to compare the outcomes of deceased donor renal allografts preserved with these fluids using data from the UK national transplant registry.

Methods

Data regarding transplants performed between January 1st 2005 and December 31st 2008 was analysed (n=5,027 kidneys). Kidneys from Donation after Brain Death (DBD) and Donation after Circulatory Death (DCD) were included. Following univariate analysis, multivariate logistic and linear regression models were fitted for adult recipients of first grafts (n=3,703 kidneys).

Results

Marshall's Solution was associated with longer cold ischaemic time, older donors, kidney-only donors, donors with hypertension and DBD (all $p < 0.01$). After adjusting for confounding, the choice of preservation fluid was not associated with the risk of PNF (OR=0.82, 95%CI 0.46-1.46, $p=0.50$), DGF (OR=1.22, 95%CI 0.96-1.56, $p=0.11$), acute rejection (OR=0.95, 95%CI 0.76-1.19, $p=0.63$), renal function at one year (Coefficient =0.97, 95%CI 0.91-1.04, $p=0.41$) or graft survival (DBD HR=0.71, 95%CI 0.46-1.10, $p=0.12$, DCD HR=0.99, 95%CI 0.58-1.73, $p=1.00$).

Conclusions

Marshall's solution has been used for the preservation of large numbers of kidneys in the UK. It is associated with transplant outcomes that are equivalent to those with UW Solution. Thus on the basis of this analysis and cost a strong case can be made for the continued use of Marshall's Solution as a preferred fluid for renal allograft preservation.

Introduction

Over 1,900 kidneys from deceased donors are now transplanted in the United Kingdom every year ¹ and the majority are preserved by static cold storage. ² Hypothermic machine perfusion has been slow to grow in popularity in the UK, perhaps because results of renal transplantation have remained acceptable and analyses of cost-effectiveness have been unconvincing. ^{2,3} A recent systematic review failed to show that hypothermic machine preservation was associated with improved graft survival. ⁴ In the UK, the most commonly used preservation fluids for static cold storage are Marshall's Solution (Hyper-osmolar Citrate, *Soltran*®, *Baxter*) and University of Wisconsin Solution (UW, *Viaspan*®, *Bristol-Meyers Squibb*, also supplied as *SPS-1*®, *Organ Recovery Systems* and *Belzer UW Cold Storage Solution*®, *Bridge to Life*).

University of Wisconsin Solution was developed by Belzer and Southard in the 1980s, primarily for pancreas preservation. ⁵ It has since been used successfully for the preservation of kidneys, liver, pancreas and small bowel allografts. Marshall's Solution was developed by Marshall, Escott and Ross at the University of Melbourne, Australia, and has been used since the late 1970s. It is used predominantly in Australia and the UK, but with few detailed, published comparisons with other preservation fluids. ⁶⁻⁹ Marshall's Solution is by far the cheaper of the two fluids, costing approximately £10 per litre (US\$17), whereas UW costs approximately £130 per litre (US\$220). Both fluids incorporate a mixture of electrolytes, buffers, impermeant molecules and free radical scavengers, Table 1. ⁶ However, there are key differences such as the inclusion of the large molecule Hydroxyethyl Starch (HES) and the nutrient adenosine in UW.

University of Wisconsin Solution and Marshall's Solution have never been compared in a randomised controlled trial (RCT), and in fact, there is limited evidence comparing Marshall's Solution to any other currently used preservation solution. ⁶

The changing donor population now required to meet the increasing demands of kidney transplant waiting lists suggests that it is timely to re-examine the effectiveness of Marshall's Solution as a preservation fluid. The aim of this study was to compare the outcomes of renal allografts preserved with Marshall's Solution and those preserved with UW.

Materials and methods

Study Population

The UK Transplant Registry is held and maintained by National Health Service Blood and Transplant (NHSBT). It is a legal requirement for all transplant centres in the UK to report all kidney transplants to this registry. The proposal for this study was reviewed by the Kidney Advisory Group of NHSBT and approved before any anonymised data were provided. Data regarding deceased donor kidney transplants performed between January 1st 2005 and December 31st 2008 was requested to allow for at least three years follow up for all recipients. 5,027 kidney transplants were performed during the study period, of which 3,838 (76%) were kidneys from Donation after Brain Death (DBD) and 1,189 (24%) from Donation after Circulatory Death (DCD). The number of kidney transplants performed each year showed a steady increase during the inclusion period, from 1,187 in 2005, to 1,369 in 2008. Kidneys with errors in CIT recording (n=30), that were not first grafts (n=744), were transplanted into paediatric recipients (n=267) or were machine perfused (n=283) were excluded from multivariate analysis (n=3,703 kidneys included). If the preservation method was unknown (machine perfusion versus static cold storage) kidneys were treated as having had static cold storage (n=453), this being the predominant method of preservation in the UK at the time.

The transplant registry did not contain all relevant information regarding preservation protocols, and so preservation protocols were requested from each retrieval and renal transplant team in the UK. Information regarding differences in perfusion protocol for kidney-only and multi-organ donors was requested, as well as any differences between DBD and DCD retrievals. Responses were returned from all renal transplant centres. The authors then deduced the preservation protocol for each kidney from the date of transplantation, retrieval team and the local retrieval protocols provided.

Outcomes

The primary outcomes were Primary Non-Function (PNF, never functioning graft) and Delayed Graft Function (DGF, the requirement for dialysis within the first week after transplantation) as reported to NHSBT by each transplant centre. Survival outcomes assessed were: graft survival (death censored) and patient survival. Renal function was assessed by serum creatinine at one year after transplantation. Acute rejection episodes were reported to NHSBT by each transplant centre.

Statistical analysis

Data were analysed using the statistical programme Stata[®] version 13 (Statacorp LP, Texas, USA). In univariate analysis, binary variables were assessed with Chi-Squared Test, continuous variables with Student's T-Test and survival outcomes with log rank test. Donor terminal creatinine was transformed to log(creatinine) for multivariate analysis. Multivariate logistic and linear regression models were fitted in a backwards, stepwise fashion to analyse relationships between donor, recipient and transplant factors and transplant outcomes. Cox's proportional hazards regression models were fitted to analyse the combined effect of variables on survival outcomes. Hazard Ratios (HR) for recipient age and donor age are presented as the HR between two individuals one year apart in age. The multivariate analysis included only patients with complete data on variables that were selected on the basis of univariate analysis, or prior analyses which have indicated associations. A P-value of <0.1 was used as a threshold for maintaining a variable in the predictive

models. Regression analyses were repeated re-inserting preservation fluid information with preserved values in a sensitivity analysis. Missing data were not imputed and individuals for whom relevant data were not available were excluded from the analysis. Results of multivariate analysis are presented as Odds Ratio (OR), Hazard Ratio (HR), or as Coefficient of linear relationship comparing UW to Marshall's Solution, with 95% Confidence Intervals (95%CI).

Results

Data were available for 5,021 recipients regarding graft survival (99.88%), 5,001 regarding CIT (99.48%), 4,887 regarding acute rejection episodes (97.22%) and 4,671 regarding initial graft function (92.91%). Donor and recipient demographics showed 100% completeness. However, we suspect that for up to 15% there is missing information regarding the anti-proliferative immunosuppressive drug prescribed, as the prescription rates for azathioprine and mycophenolate combined is lower than expected.

Donor and recipient factors

A summary of donor, recipient and transplant factors in this population are described in table 2. Mean age of donors was 45 years (range: 1-82 years), mean recipient age was also 45 years (range: 1-85 years). Donor and recipient ethnicity were homogenous, with white ethnicity making up over 96% of donors and 80% of recipients. Many donors had multiple organs retrieved: the liver was donated as well as kidneys in 77% of kidney donors and the pancreas also in 29%. The most common causes of death were intracranial haemorrhage (60%) and trauma (15%). Hypertension was a pre-existing co-morbidity in 22% of donors. The majority of transplants were first grafts (85%) and second grafts (12%). There were very few third or fourth grafts (2% and <1% respectively). Prednisolone was prescribed for the majority of patients at the time of transplantation (82%) but the withdrawal of steroids was not assessed in this study. Complete data regarding antibody induction were not collected by the registry during the study period, with only the use of anti-thymocyte globulin (2%) and muromonab (<1%) recorded.

Retrieval and preservation protocols

Retrieval and transplant activity was spread between all renal transplant centres in the UK during the inclusion period. All teams reported that they used either Marshall's Solution and/or UW for static cold storage of kidneys during the inclusion period.

Slightly more kidneys had initial aortic flush in the donor with Marshall's Solution than with UW (52% versus 42%). A small number (n=299, 6%) had a mixture of UW and Marshall's Solution in aortic flush due to a perfusion protocol used when King's College Hospital, London, was the multi-organ retrieval team and a pancreas was also being retrieved. This protocol used one litre of UW solution initially, then the superior mesenteric artery was clamped and further aortic perfusion was done with Marshall's Solution.

For flush on the back-table and storage of kidneys, Marshall's Solution was used far more than UW (79% versus 21%). Given the mixing of aortic flush fluids, and, mixing where the aortic flush differed

from the storage fluid, a total of 1,263 kidneys (28%) had mixing of preservation fluids at some stage during the preservation period.

The mean Cold Ischaemic Time (CIT) was 17.59 hours (standard deviation +/- 5.41 hours). Only a small number of kidney allografts were machine perfused prior to transplantation (approximately 6%).

Overall outcomes

Overall event rates for adverse and survival outcomes were within expected ranges for both preservation fluids, Table 2. Primary Non-Function rate was 3% and rate of DGF was 28%. One year graft survival (death censored), patient survival and transplant survival (transplant loss includes death with a functioning graft) were 96%, 97% and 94% respectively.

The use of Marshall's Solution compared to UW as kidney storage fluid was associated with longer CIT (17.63 +/- 5.46 hours versus 16.91 +/- 5.31 hours, $p<0.01$), older donors (45.72 +/- 15.90 years versus 43.31 +/- 15.65 years, $p<0.01$), non-liver donors ($p<0.01$), non-pancreas donors ($p<0.01$), donor hypertension (23% versus 16%, $p<0.01$) and donation after brain-death ($p<0.01$).

Multivariate analysis

The risk of PNF was not associated with the choice of preservation fluid used for aortic flush (OR=0.81, 95%CI 0.51-1.29, $p=0.37$), kidney storage (OR=0.82, 95%CI 0.46-1.46, $p=0.50$) or the mixing of preservation fluids (OR=0.66, 95%CI 0.38-1.16, $p=0.15$). Full data of the included variables at the start and end of all stepwise regressions can be found in Supplemental Tables 4-9.

The risk of DGF was also not associated with the choice of preservation fluid used for aortic flush (OR=0.96, 95%CI 0.79-1.17, $p=0.70$), kidney storage (OR=1.22, 95%CI 0.96-1.56, $p=0.11$) or mixing of preservation fluids (OR=0.82, 95%CI 0.67-1.02, $p=0.07$).

Graft survival was assessed separately for DBD and DCD kidneys given the different predictive value of DGF apparent in the univariate analysis. For DBD kidneys graft survival was not influenced by the choice of preservation fluid for aortic flush (HR=0.89, 95%CI 0.68-1.18, $p=0.42$), kidney storage (HR=0.71, 95%CI 0.46-1.10, $p=0.12$) or mixing of preservation fluids (HR=1.05, 95%CI 0.79-1.38, $p=0.74$). For DCD kidneys graft survival was also not associated with the choice of preservation fluid for aortic flush (HR=1.38, 95%CI 0.78-2.45, $p=0.27$), kidney storage (HR=0.99, 95%CI 0.58-1.73, $p=1.00$) or mixing of preservation fluids (HR=1.72, 95%CI 0.92-3.24, $p=0.09$).

Patient survival was not associated with the choice of preservation fluid used for aortic flush (HR=0.95, 95%CI 0.74-1.22, $p=0.67$), kidney storage (HR=1.01, 95%CI 0.74-1.38, $p=0.97$) or mixing of preservation fluids (HR=1.12, 95%CI 0.87-1.45, $p=0.39$). Serum creatinine at 12 months after transplantation was not associated with the choice of preservation fluid used for aortic flush (Coefficient=1.00, 95%CI 0.94-1.05, $p=0.74$), kidney storage (Coefficient=0.97, 95%CI 0.91-1.04, $p=0.41$) or mixing of preservation fluids (Coefficient=1.00, 95%CI 0.95-1.06, $p=0.92$). Acute rejection was not associated with the choice of preservation fluid used for aortic flush (OR=1.00, 95%CI 0.83-1.22, $p=0.96$), kidney storage (OR=0.95, 95%CI 0.76-1.19, $p=0.63$) or mixing of preservation fluids (OR=1.02, 95%CI 0.83-1.25, $p=0.85$).

Discussion

This study has analysed the outcomes of kidneys preserved by static cold storage in the UK over a four year period. The analysis was based upon a robust data set from a national registry with excellent follow up. Marshall's Solution has never been compared to any other currently used preservation fluids in a randomised controlled trial, so this study presents unique results.⁶ It is difficult to identify the results of kidneys preserved solely with Marshall's Solution in previously published reports, so there is little good quality data regarding its efficacy. Nicholson et al have previously published a report comparing outcomes of live donor and deceased donor kidneys preserved with Marshall's Solution in the UK; 301 deceased donor kidneys were included. The DGF rate was 21% for DBD and 84% for uncontrolled DCD, and one year graft survival was 84% and 86% respectively.⁷ In a multicentre, multinational analysis, Opelz and Dohler found Marshall's Solution had been used to preserve approximately 5% of kidneys between 1990-2005.¹⁰ In their analysis the increasing risk of graft loss at longer CIT was worse with Marshall's Solution than with UW, however relative risk of failure was the same below 24 hours CIT.¹⁰ Experimental studies have indicated that the more viscous UW Solution cools kidneys more slowly than Marshall's Solution, but causes less tissue oedema and cellular injury seen on histological analysis.¹¹

In this study the use of Marshall's Solution was associated with variables that may be related to worse renal transplant outcomes, including longer CIT, older donors/recipients and donor hypertension. This may be explained by the apparent preference of some centres for UW when a liver and/or pancreas is retrieved. A multivariate analysis accounting for these potential confounders allowed us to assess the influence of the preservation fluid alone. Marshall's Solution compared to UW Solution, as either aortic flush or kidney storage fluid, was not associated with an increased risk of PNF, DGF, acute rejection or higher serum creatinine at 12 months. Marshall's Solution was also associated with equivalent patient and graft survival.

Some centres mixed preservation fluids, either by mixing the aortic flush in pancreas donors (a relatively small number) or by flushing and storing kidneys with Marshall's Solution after an aortic flush in the donor with UW. The biochemical effect of mixing these two fluids is unknown; however there was a trend towards worse DCD graft survival with mixing of fluids. Why, if true, this should be associated with worse graft survival in DCD but not DBD is unclear. Potentially the association may not be causal, and may be related to an unknown confounder in DCD retrievals. Graft survival in our analysis was found to be equivalent between DCD and DBD kidneys, in keeping with other recent analyses of renal transplant outcomes². The equal graft survival was apparent despite the much greater risk of DGF in DCD kidneys. This may be explained by the fact that in this study, DGF was associated with worse graft survival in DBD kidneys, but not in DCD kidneys. Delayed graft function has been established as a risk factor for poor graft survival in several previous studies,¹²⁻¹⁶ and related to poor renal function in others, if not directly to survival.¹⁷ However, these studies were based largely (if not entirely) on the transplantation of kidneys from DBD. The aetiology of DGF may be different in these two donor types, and therefore be of a different predictive value in each. There are now several studies of DCD cohorts which have not found DGF to be a risk factor for graft loss.^{2,}

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The only preservation factor associated with significantly higher risk of DGF and PNF was CIT. In this analysis CIT was not associated directly with worse graft survival. This may be due to the inclusion of

both CIT and DGF in the model for DBD kidney survival; the covariance meaning that CIT was dropped from the model. It may also be due to the relatively short length of CIT in this study (mean 17 hours), although this is consistent with another recent analysis of UK data.²² Summers et al have recently shown that DCD kidneys are more sensitive to increasing CIT than DBD kidneys.²² Previous analyses of DBD kidney transplant outcomes in the UK showed no increase in risk of transplant failure up to 21 hours CIT.²³ A threshold of 18 hours was used for this study as this length of CIT has been shown in a multicentre analysis to be a key threshold above which graft loss increases.¹⁰ A maximum of 18 hours CIT has recently been introduced as an audit standard for the transplantation of DBD kidneys in the UK.²⁴

The key limitation of this study is the use of registry data in retrospect. The use of such data is subject to confounding variables that cannot be taken into account; however, many variables that may be related to transplant outcomes were adjusted for in this analysis. Causation can be difficult to prove in retrospective studies, and interpretation of the results requires a careful appraisal of the underlying science and the apparent associations shown in the data. The accuracy of the database also depends on the quality of the information fed back to the central co-ordinator from each transplant centre. The second key limitation is that the preservation solutions used were deduced by the authors from date of transplant and protocols at each retrieval centre and therefore there must be some uncertainty about the results. The preservation protocols that have been reported are descriptions of procedure in general and there may also have been slight variations between surgeons from each centre.

It is particularly difficult to interpret the role of the prescribed drugs as the use of one regimen is associated with the non-prescription of an alternative and therefore a covariance is introduced. For example, the apparent benefit of tacrolimus in reducing acute rejection is partly contributed to by its comparison with cyclosporine, which would typically have been the alternative drug during the inclusion period. The effect of immune suppressing drugs as a combination (for example triple therapy) was not assessed; data were not available on the use of the induction antibodies such as basiliximab and alemtuzumab, which are now commonly used in the UK. The role of immune suppression at the time of transplantation was assessed, but this will miss any associations with later changes in the regimen, such as steroid withdrawal.

We felt that adjusting by transplant or retrieval centre would introduce co-linearity with the preservation protocols and immune suppression regimens, as these would obviously vary by centre. However, this means that the issue of centre-specific effect, whether it be retrieval or transplant team, was not addressed, and is an important limitation of the study.

This work is based upon data from the UK, where the population, patient assessment and drug regimens are relatively standardised. This fact increases the applicability of these results to transplant programs in the UK. However, it affects the relevance of this work to national or supra-national renal transplant programs in other countries, where, for example, average CIT may be longer. The introduction of the National Organ Retrieval Service (NORS) since 2010 may also impact upon the standard of retrieval and preservation protocols in the UK as services become more centralised. NHSBT recommends 70ml/kg aortic flush, with additional fluid used for back-table flush and storage (approximately 500ml per kidney). A kidney only retrieval therefore may require 4-8 litres of preservation fluid. This would result in a cost-saving of £480-960 per donor by using

Marshall's solution instead of UW. In multi-organ retrievals, using Marshall's solution for kidney storage only would result in a cost-saving of £120 per donor.

Conclusion

In this large analysis of national data, the use of Marshall's Solution for the static cold storage of deceased donor kidneys across the UK is associated with acceptable transplant outcomes that are equivalent to those with UW Solution. In view of the comparative costs of Marshall's and UW Solutions there is a valid argument in favour of the continued use of Marshall's Solution as a preferred fluid for renal allograft preservation.

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Declaration of interests

All authors declare no conflicts of interest.

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Tables

Table 1. Relative composition of Marshall's Solution and UW (University of Wisconsin Solution). Citrate and Lactobionate also act as buffers. Lactobionate and Mannitol also act as a free radical scavengers. HES= Hydroxyethylene Starch, ROS= Reactive Oxygen Species.

<u>Component type</u>	<u>Component</u>	<u>Marshall's Solution</u>	<u>UW</u>
Colloids (mM)	HES	-	0.25
Impermeants (mM)	Citrate	80	-
	Lactobionate	-	100
	Mannitol	185	-
	Raffinose	-	30
Buffers (mM)	NaHCO ₃	10	-
	KH ₂ PO ₄	-	25
Electrolytes (mM)	Chloride	-	20
	Magnesium	40	5
	Potassium	84	120
	Sodium	84	30
ROS scavengers (mM)	Allopurinol	-	1
	Glutathione	-	3
Nutrients (mM)	Adenosine	-	5
Osmolality (mOsm)		400	320

Table 2. Demographics. Continuous values are given as mean +/- standard deviation (range in brackets). % is of all transplants with available data for each demographic. DBD= Donation after brain death, DCD= Donation after circulatory death, HLA=human leucocyte antigen. HLA mismatch level as described by Johnson et al 2010. ²³ Medications relate to the initial immune suppression prescribed at the time of transplantation.

Donor Factors	
Age (years)	45.27+/- 15.85 (1-82)
Terminal creatinine (μmol/l)	87.62+/-46.16 (5-702)
Gender (male/female)	2,705 (53.81%)/ 2,322 (46.19%)
Ethnicity (white/non-white)	4,869 (96.9%)/ 87 (3.10%)
Liver donated	3,880 (77.18%)
Pancreas donated	1,465 (29.14%)
Hypertension	977 (19.44%)
Donor type (DBD/DCD)	3,838 (76.35%)/ 1,189 (23.65%)
Cause of death	
Intracranial haemorrhage	3,011 (60%)
Trauma	754 (15%)
Hypoxic brain damage	472 (9%)
Recipient Factors	
Age (years)	45.53+/-15.19 (1-85)
Gender (male/female)	3,063 (60.93%)/ 1,964 (39.07%)
Ethnicity (white/non-white)	4,061 (80.78%)/ 966 (19%)
Graft number	
1 st	4,278 (85.10%)
2 nd	623 (12.39%)
3 rd	110 (2.19%)
4 th	16 (0.32%)
Immune suppression	
Anti-thymocyte globulin	96 (1.91%)
Muromonab-CD3 (OKT3)	8 (0.16%)
Prednisolone	4,101 (81.57%)
Cyclosporine	1,103 (21.94%)
Tacrolimus	3,739 (74.38%)
Azathioprine	905 (18.00%)
Mycophenolate mofetil	3,357 (66.77%)
Transplant Factors	
HLA mismatch level	
1 (000)	817 (16.25%)
2 (0 DR and 0/1B)	1,665 (33.11%)
3 (0 DR and 2 B or 1 DR and 0/1 B)	2,017 (40.02%)
4 (1 DR and 2 B or 2 DR)	528 (10.50%)
Cold ischaemic time (hours)	17.49+/-5.41 (0.3-46)

Table 3. Unadjusted and adjusted outcomes. Adult recipients of first grafts only, not machine perfused. Early graft function was missing in 5% related to aortic flush and 6% related to kidney packing fluid. HR=Hazard Ratio, OR=Odds Ratio, UW= University of Wisconsin Solution. Odds Ratio presented for delayed graft function and primary non-function, hazard ratio presented for graft survival. Hazard and Odds Ratio <1 favours UW. P-value calculated by Chi-Squared test for categorical variables and log-rank test for graft survival. Graft survival is death censored. Graft survival for DBD and DCD kidneys was modelled separately; hence there is no adjusted Hazard Ratio for kidneys from both donor types together.

Comparing fluid used for initial aortic flush				
	<u>Marshall's Solution (N=1,819)</u>	<u>UW (N=1,440)</u>	<u>Unadjusted (P-Value)</u>	<u>Adjusted (P-Value)</u>
Delayed graft function	521 (28.64%)	440 (30.56%)	OR=1.09 (p=0.23)	OR=0.96 (p=0.70)
Primary non-function	56 (3.08%)	35 (2.43%)	OR=0.78 (p=0.27)	OR=0.81 (p=0.37)
Graft survival			HR=0.79 (p=0.03)	DBD: HR=0.89 (p=0.42)
12 months	94.88%	96.63%		DCD: HR=1.38 (p=0.27)
24 months	93.09%	94.84%		
36 months	91.15%	92.96%		
Comparing preservation fluid used for kidney storage				
	<u>Marshall's Solution (N=2,781)</u>	<u>UW (N=724)</u>	<u>Unadjusted (P-Value)</u>	<u>Adjusted (P-Value)</u>
Delayed graft function	699 (25.13%)	278 (38.40%)	OR=1.82 (p<0.01)	OR=1.22 (p=0.11)
Primary non-function	78 (2.80%)	19 (2.62%)	OR=0.92 (p=0.74)	OR=0.82 (p=0.50)
Graft survival			HR=0.63 (p<0.01)	DBD: HR=0.71 (p=0.12)
12 months	95.07%	97.27%		DCD: HR=0.99 (p=1.00)
24 months	93.11%	95.59%		
36 months	90.97%	94.42%		