in extended hour and conventional haemodialysis patients

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Running title: Post-transplant outcomes in extended hour HD

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1111/nep.13221

ABSTRACT

Aim: Differences in early graft function between kidney transplant recipients previously managed with either haemodialysis (HD) or peritoneal dialysis are well described. However, only two single-centre studies have compared graft and patient outcomes between extended hour and conventional HD patients, with conflicting results.

Methods: This study compared the outcomes of all extended hour (≥24 hours/week) and conventional HD patients transplanted in Australia and New Zealand between 2000 and 2014. The primary outcome was delayed graft function (DGF), defined in an ordinal manner as either a spontaneous fall in serum creatinine of less than 10% within 24 hours, or the need for dialysis within 72 hours following transplantation. Secondary outcomes included the requirement for dialysis within 72 hours post-transplant, acute rejection, estimated glomerular filtration rate at 12 months, death-censored graft failure, all-cause and cardiovascular mortality, and a composite of graft failure and mortality.

Results: A total of 4,935 HD patients (378 extended hour HD, 4,557 conventional HD) received a kidney transplant during the study period. Extended hour HD was associated with an increased likelihood of DGF compared with conventional HD (adjusted proportional odds ratio 1.33; 95% confidence interval 1.06–1.67). There was no significant difference between extended hour and conventional HD in terms of any of the secondary outcomes.

Conclusion: Compared to conventional HD, extended hour HD was associated with DGF, although long-term graft and patient outcomes were not different.

Keywords: Delayed graft function, extended hour haemodialysis, graft function, graft survival, renal replacement therapy, renal transplantation.

INTRODUCTION

Delayed graft function (DGF) continues to pose a significant challenge to the practice of kidney transplantation and has important implications for graft and patient outcomes. Despite advances in transplantation practice, the incidence of DGF has increased from 14.7% in 1992[1] to 27.0% in 2012[2], which corresponds to the increasing utilisation of higher risk kidneys from expanded criteria donors (ECD)[3] and donation after circulatory death (DCD)[4]. The pathophysiological mechanisms underlying the development of DGF are not entirely understood, but it is thought to relate to a combination of ischaemic, inflammatory, microcirculatory and immunological insults which culminate in tissue injury and impaired early function[5]. Although the definition of DGF varies widely[6], from failure of creatinine to fall within a defined period to requirement for post-transplant dialysis, the clinical impact of DGF on graft outcomes has been clearly established[1,7–9]. Epidemiological studies have indicated that DGF is associated with a 41% increased risk of graft loss, as well as a 38% increase in the risk of acute rejection, highlighting that interventions aimed at reducing the incidence of DGF may potentially lead to improved graft outcomes[8,9].

Several donor, graft and recipient characteristics are associated with a higher incidence of DGF, including greater donor age or terminal creatinine, longer duration of cold or warm ischaemia, higher immunological risk, and recipient male sex, indigenous race, higher body mass index [BMI], diabetic status and longer waiting time[6,10,11]. A number of large observational studies have examined the interaction between pre-transplant dialysis modality and post-transplant graft and patient outcomes[12–22]. Although a clear association has not been established, several studies have shown that recipients maintained on peritoneal dialysis prior to transplant were less likely to experience DGF compared to those maintained on

haemodialysis (HD), possibly due to differences in residual renal function, extracellular fluid volume, peripheral vascular resistance and complement and leukocyte activation[19,23–25].

It remains uncertain whether a similar disparity in early graft function exists between patients treated with extended hour and conventional HD. In observational studies, extended hour HD has been associated with improvements in survival[26], blood pressure control[27], biochemical profile[28–30], and cardiac structure and function[31]. It is plausible that differences in extravascular fluid volume and haemodynamic parameters between extended hour and conventional HD patients could affect allograft function in the early post-transplant period. Two single-centre observational studies have examined this effect, by comparing nocturnal and conventional HD patients[32,33]. Both studies were limited by small patient numbers, short follow-up duration, and lack of multivariable adjustment for differences in characteristics between the groups. With increasing interest in the use of extended hour HD in suitable patients, it is important to explore the potential implications of this therapy in patients who are transplant candidates, especially if early graft function may differ. Therefore, this study was conducted to examine the effect of pre-transplant HD modality on graft and patient outcomes using data from the Australia and New Zealand Dialysis and Transplant (ANZDATA) Registry.

METHODS

STUDY DESIGN

This was a retrospective multi-centre study using patient records from the ANZDATA Registry between 1 January 2000 and 31 December 2014. The ANZDATA Registry collects information annually from all units throughout Australia and New Zealand, concerning all patients receiving chronic renal replacement therapy[34]. All recipients of living or deceased donor kidney transplants who received HD for at least 3 months prior to transplantation were included in this study. Patients aged less than 18 years at commencement of HD and multi-organ transplant recipients were excluded.

DATA COLLECTION

Data on recipient demographics (age, sex, race), recipient comorbidities (cause of end stage kidney disease [ESKD], waiting time, BMI, diabetes, smoking, ischaemic heart disease [IHD], peripheral vascular disease [PVD], cerebrovascular disease [CVD], prior graft), donor characteristics (age, sex, source [live donation, donation after brain death, donation after circulatory death], donor terminal creatinine [for deceased donors]), transplant factors (transplant centre state of Australia or New Zealand, total ischaemia time, human leukocyte antigen [HLA] mismatches, transplant era), and pre-transplant HD modality (extended hour or conventional) were recorded. Extended hour HD was defined as a weekly treatment time greater than or equal to 24 hours. This definition maintains adequate separation in weekly treatment time between conventional and extended hour HD patients and is consistent with that used in randomised controlled trials in this area[35]. Weekly treatment time was derived from the most recent ANZDATA record prior to transplantation.

CLINICAL OUTCOMES

The primary outcome measure was DGF, which was examined as an ordinal outcome. The reference group was immediate graft function, defined as a spontaneous fall in serum creatinine concentration by 10% or more within 24 hours. The definition of DGF included slow graft function (a spontaneous fall in serum creatinine concentration of less than 10% within 24 hours) and delayed graft function requiring dialysis (the need for dialysis within 72 hours following transplantation). Secondary outcomes included: post-transplant dialysis within 72 hours (examined as a binary outcome); acute rejection; estimated glomerular filtration rate (eGFR) at 12 months; death-censored graft failure; all-cause and cardiovascular mortality; and a composite of graft failure and mortality. eGFR was calculated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation[36]. Graft failure was defined as transfer to dialysis or re-transplantation. Cardiovascular mortality included deaths due to myocardial ischaemia, cardiac failure, cardiac arrest, pulmonary oedema, and hyperkalaemia.

STATISTICAL ANALYSES

Baseline characteristics were expressed as numbers and percentages, means (± standard deviation [SD]), or medians (interquartile range [IQR]), as appropriate. Group comparisons were performed using the chi-squared test, unpaired t-test, or Wilcoxon rank sum test, as dictated by data characteristics. Univariable and multivariable ordinal (proportional odds) logistic regression models were used to examine the primary outcome. These models estimate a common odds ratio across each cutoff of the ordered outcome. The Brant Test was used to check the proportional odds assumption. Binary logistic regression was used to examine the impact of dialysis modality on dialysis requirement within the first 72 hours. Negative binomial regression was used to compare acute rejection rates. Graft function (eGFR) at 12 months was compared using a multivariable linear regression model. Graft and patient

survival were evaluated by Kaplan-Meier methods and univariable and multivariable-adjusted Cox regression models. Regression model diagnostics performed to evaluate appropriateness of the models used graphical techniques and formal model fitting tests. A variance inflation factor was calculated to assess multicollinearity. All multivariable models were adjusted for covariates that differed at baseline or were known to be associated with the outcomes of interest. These included recipient characteristics (age, sex, race, BMI, cause of ESKD, waiting time, diabetes, smoking status, IHD, PVD, CVD, prior graft), donor characteristics (age, sex, source) and transplantation factors (transplant centre state, total ischaemia time, HLA mismatches, transplant era). Transplant centre state was examined as a fixed effect variable in the primary analysis, but also as a random effect variable in sensitivity analyses for each outcome of interest.

Due to baseline differences between the groups, two different matching techniques were applied and are presented as sensitivity analyses: coarsened exact matching (CEM) and propensity score matching (PSM). CEM involves the temporary coarsening of data followed by exact matching, with analyses run on uncoarsened data[37,38]. It has many advantages in this setting, including a reduced sensitivity to measurement error, control over the degree of imbalance between groups, and the ability to alter balance on covariates independently. In both CEM and PSM models, patients were matched on demographic and clinical characteristics that differed between extended hour and conventional HD patients. These included recipient age, sex, diabetic status, waiting time, donor age, donor source and total ischaemia time. An additional sensitivity analysis including donor terminal creatinine in the multivariable models was performed for recipients of deceased donor kidneys. The multivariable models included all other covariates that were different at baseline, as well as those associated with the outcome of interest in univariable analyses (S1-S5 Tables). Data

were analysed using the software package Stata/SE version 14.0 (StataCorp College Station, TX). Two-sided P values <0.05 were considered statistically significant.

RESULTS

STUDY POPULATION

Between 1 January 2000 and 31 December 2014, 5,098 HD patients underwent renal transplantation in Australia and New Zealand (Figure 1). Of these, 4,935 (97%) patients had complete records detailing HD treatment time and DGF status and were included in the analysis. There were 378 (8%) extended hour and 4,557 (92%) conventional HD patients. The median duration of follow up was 4.6 years (IQR 2.2 – 6.8) for extended hour HD and 5.1 years (IQR 2.4 – 8.4) for conventional HD patients. Baseline characteristics of the study population are displayed in Table 1. Compared to conventional HD, patients who received extended hour HD were more likely to be male, obese, and to have had a longer waiting time. They were less likely to be Aboriginal or Torres Strait Islander, to have diabetic nephropathy and to have received a kidney transplant in the earliest transplant era.

DELAYED GRAFT FUNCTION

Pre-transplant HD modality was associated with a disparity in the rate of DGF, categorised as slow graft function (SGF) or delayed graft function requiring dialysis (DGF-D) (Figure 2, Tables 2-3). A total of 1,979 patients developed DGF (191 extended hour HD, 1,788 conventional HD). Extended hour HD was associated with a higher likelihood of DGF in univariable (proportional odds ratio [OR] 1.47; 95% confidence interval [CI] 1.21 – 1.79, P <0.001) and multivariable adjusted models (adjusted proportional OR 1.33; 95% CI 1.06 – 1.67, P = 0.01).

POST-TRANSPLANT DIALYSIS

Overall, 1,249 patients received dialysis after transplant (114 extended hour HD, 1,135 conventional HD) (Table 2). Examined as a binary outcome, post-transplant dialysis was

required more frequently in extended hour HD patients in the univariable analysis (OR 1.30; 95% CI 1.03 – 1.64, P = 0.02) (Figure 2, Table 3), but not following multivariable adjustment (adjusted OR 1.23; 95% CI 0.94 – 1.61, P = 0.12).

ACUTE REJECTION

During the study period, 1,373 patients had at least one episode of acute rejection (103 extended hour HD, 1,270 conventional HD). There was no difference in the number of episodes or rate of acute rejection between extended hour and conventional HD patients (adjusted incident rate ratio 0.95, 95% CI 0.77 – 1.17, P = 0.61) (Tables 2-3).

GRAFT FUNCTION

Mean eGFR at 12 months was not significantly different between transplant recipients who were maintained on extended hour or conventional HD prior to transplantation (52.3±18.9 vs 54.1±18.9 ml/min/1.73m2, P = 0.10) (Figure 3). The unadjusted and adjusted beta coefficients comparing extended hour and conventional HD patients were -1.77 (95% CI -3.89 – 0.35, P = 0.10) and -1.40 (95% CI -3.32 – 0.53, P = 0.16), respectively.

GRAFT FAILURE

A total of 618 patients developed graft failure (36 extended hour HD, 582 conventional HD). The two groups did not differ significantly with respect to the cause of graft failure (Table 4). Time to death-censored graft failure was comparable between extended hour and conventional HD patients in unadjusted (hazard ratio [HR] 0.88; 95% CI 0.63 – 1.23, P = 0.45) and multivariable adjusted models (adjusted HR 0.89; 95% CI 0.63 – 1.26, P = 0.51) (Figure 4, Figure 5(a)).

ALL-CAUSE MORTALITY

There were 652 deaths during the study period (23 extended hour HD, 629 conventional HD) (Table 2). There was no significant difference in cause of death between the two groups (Table 4). In unadjusted models, time to all-cause mortality was significantly longer in patients treated with extended hour HD compared to those treated with conventional HD (HR 0.55, 95% CI 0.36 – 0.83, P = 0.004) (Table 3, Figure 4, Figure 5 (b)). However, this difference was no longer statistically significant following multivariable adjustment (adjusted HR 0.82, 95% CI 0.53 – 1.25, P = 0.35).

CARDIOVASCULAR MORTALITY

Cardiovascular death accounted for 178 deaths in the study (8 extended hour HD, 170 conventional HD) (Table 2). Time to cardiovascular mortality did not differ between the two groups in unadjusted (HR 0.71, 95% CI 0.35 – 1.44, P = 0.34) or multivariable models (adjusted HR 1.15, 95% CI 0.56 – 2.40, P = 0.70) (Table 3, Figure 4, Figure 5(c)).

COMPOSITE OF DEATH OR GRAFT FAILURE

Graft failure or death occurred in 1,099 patients (52 extended hour HD, 1,047 conventional HD). Extended hour HD was associated with a favourable time to the composite outcome in the unadjusted analysis (HR 0.71, 95% CI 0.54 – 0.94, P = 0.02) (Table 2, Figure 4, Figure 5(d)). However, following multivariable adjustment, there was no statistically significant difference between extended hour and conventional HD patients (adjusted HR 0.83, 95% CI 0.63 – 1.11, P = 0.22).

SENSITIVITY ANALYSES

The coarsened exact matched analysis included 2,357 patients (352 extended hour HD, 2,005 conventional HD). In the extended hour HD cohort, patients were more likely to be obese, to smoke and to have received a prior kidney transplant. Other baseline characteristics were similar (S6 Table). Extended hour HD was associated with an increased risk of DGF compared to conventional HD (adjusted proportional OR 1.28, 95% CI 1.02 – 1.61, P = 0.03). There was no difference in any of the secondary outcomes between the two groups (S7 Table).

In the propensity score matched analysis of 1,491 patients, there were 378 extended hour HD patients and 1,113 conventional HD patients. Extended hour HD patients were more likely to be obese, Caucasian, have a longer waiting time, and to have received a prior kidney transplant (S8 Table). Compared to conventional HD, there was an increased likelihood of DGF in extended hour HD patients (adjusted proportional OR 1.35, 95% CI 1.06 – 1.71, P = 0.02). There was also a trend towards a lower eGFR at 12 months in patients previously managed with extended hour HD (adjusted coefficient -2.48, 95% CI -4.96 – 0.01, P = 0.05). Otherwise, secondary outcomes did not differ (S9 Table).

The primary analysis was repeated including state of transplantation as a random effect and results were comparable (S10 Table). There were no differences in findings when donor terminal creatinine was included in the multivariable models for recipients of deceased donor kidneys.

DISCUSSION

In this large cohort of HD patients from Australia and New Zealand, compared with conventional HD, extended hour HD was associated with an increased risk of DGF post-kidney transplant, defined categorically as either a spontaneous fall in serum creatinine concentration of less than 10% within 24 hours, or the need for dialysis within the first 72 hours following transplantation. However, acute rejection, renal function (eGFR) at 12 months, death-censored graft failure, all-cause and cardiovascular mortality, and a composite of graft failure and mortality were comparable.

These findings contrast with those of two previous small, short-duration, single-centre observational studies which examined DGF, defined as post-transplant dialysis requirement, in nocturnal HD patients[32,33]. McCormick et al[32] reported no significant differences in DGF (64% vs 41%, P = 0.15), 1-year graft function (eGFR 53±6 vs. 59±5ml/min, P = 0.43) or graft survival (92% vs 95%, P = 0.75) between 15 nocturnal HD and 29 conventional HD patients between 1994 and 2002. Similarly, Pauly et al[33] observed similar rates of post-transplant dialysis requirement (42.9% vs. 36.8%, P = 0.43), graft survival and patient survival between 36 nocturnal HD and 68 conventional HD patients between 1994 and 2006. The sample sizes and follow-up durations of these studies were considerably smaller than those of the present investigation, which reduced their power to detect a difference in outcomes between the groups. Minimal information on patient characteristics was provided and neither study examined outcomes in multivariable analyses. Their single-centre design and examination of cohorts from an earlier transplant era also limited the generalisability of their results.

Since dialysis is performed until the time of kidney transplant, there are a number of biologically plausible hypotheses that could explain the observed differences in the rates of DGF between extended hour and conventional HD patients. Extended hour HD is associated with improved blood pressure control[39], reduced peripheral vascular resistance[40], reduced extravascular volume and increased weekly sodium removal[41]. Compounded by the peripheral vasodilatation induced by general anaesthesia, these factors may increase the risk of intraoperative hypotension and allograft hypoperfusion. Although the present study does not include data on these events, this hypothesis is supported by an observational study, in which extended hour HD patients were at greater risk of intraoperative hypotension[32]. The effect of intraoperative hypotension on allograft perfusion may be further amplified by other perioperative vascular changes, including pathologic vasoconstriction within the allograft in response to ischaemic injury, dysregulation of intraglomerular pressure at a microcirculatory level, and calcineurin inhibitor-induced afferent and efferent arteriolar vasoconstriction[42,43]. The vascular effects of calcineurin inhibition may be further worsened by states of salt depletion, which are more likely to be seen in extended hour HD patients[44,45]. It is also plausible that due to a lower pre-operative serum creatinine, extended hour HD patients may have been at greater risk of graft function misclassification, since the definition relies on a spontaneous fall in serum creatinine.

These findings have important clinical implications because hypovolemia and intraoperative hypotension are preventable and modifiable. Consideration should be given to ensuring adequate intravascular volume pre-operatively and intraoperatively, especially in patients having undertaken extended hour HD. Ultrafiltration should be avoided prior to surgery[25]. Intraoperative hypotension should be managed promptly with fluid and vasopressor support to maintain graft perfusion.

The strengths of this study lie in its large size and extended duration of follow up. It included all HD patients who received a kidney transplant in Australia and New Zealand between 2000 and 2014, making the study population representative of a broad range of patient demographics and comorbidities. Limitations of this study include the absence of available data on additional factors that could have affected the risk of DGF, including recipient fluid status at the time of transplantation, blood pressure and use of antihypertensive medications, immunologic variables other than HLA matching, and induction immunosuppression regimen. Additionally, detailed information regarding the timing of the most recent dialysis prior to transplantation, the indication for and number of dialysis sessions required post-transplant, and the duration of DGF was also unavailable. Next, the ANZDATA registry collects data on early graft function in a format that differs from some definitions of DGF. Firstly, the data are recorded categorically (immediate, slow and delayed graft function). Secondly, the requirement for post-transplant dialysis is examined within the first 72 hours rather than within the first 7 days. However, the examination of DGF as an ordinal outcome has several advantages compared to a binary definition of dialysis requirement post-transplant. First, it captures patients with poor graft function who do not receive dialysis; second, it avoids misclassification due to dialysis for reasons other than poor graft function; and third, it minimises centre effect with respect to dialysis practice[2]. To facilitate direct comparison of outcomes from this study to the existing published literature, requirement for post-transplant dialysis was also examined as a secondary outcome. Nonetheless, conclusions from the current study can only be limited to associations, and causal relationships could not be inferred in the setting of an observational study design. Indication bias with residual confounding could not be excluded. Submission of patient data to ANZDATA is voluntary and there is no routine audit of data; therefore, there is a risk of coding or reporting bias.

In conclusion, this study demonstrated an association between extended hour HD and an increased risk of DGF compared with conventional HD, although long-term graft and patient outcomes did not differ. It is plausible that this association arises due to differences in intravascular volume, haemodynamic parameters, and microcirculatory abnormalities in the early post-transplant period. Further studies are required to address this question and explore possible mechanisms. The physiological benefits of extended hour HD are well described; however, this study suggests that when patients receiving extended hour HD undergo renal transplantation consideration should be given to the potentially increased risk of DGF.

ACKNOWLEDGEMENTS

The authors would like to acknowledge the substantial contributions of the Australian and New Zealand nephrology community who provided information to, and maintained, the ANZDATA Registry database. The ANZDATA Registry is funded by the Australian Organ and Tissue Donation and Transplantation Authority, the New Zealand Ministry of Health, and Kidney Health Australia. The interpretation and reporting of these data are the responsibility of the authors and should not be seen as official policy of ANZDATA.

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SUPPORTING INFORMATION LEGENDS

S1 Table. Ordinal logistic regression analysis of the association between delayed graft function and recipient, donor, and transplant characteristics in 4,935 extended hour and conventional haemodialysis patients.

S2 Table. Binary logistic regression analysis of the association between post-transplant dialysis requirement and recipient, donor, and transplant characteristics in 4,935 extended hour and conventional haemodialysis patients.

S3 Table. Negative binomial regression analysis of the association between acute rejection and recipient, donor, and transplant characteristics in 4,935 extended hour and conventional haemodialysis patients.

S4 Table. Linear regression analysis of the association between estimated glomerular filtration rate at 12 months and recipient, donor, and transplant characteristics in 4,935 extended hour and conventional haemodialysis patients.

S5 Table. Log rank analysis of the association between survival outcomes and recipient, donor, and transplant characteristics in 4,935 extended hour and conventional haemodialysis patients.

S6 Table. Baseline characteristics of a coarsened exact matched cohort of kidney transplant recipients previously managed with extended hour (n = 352) or conventional (n = 2,005) haemodialysis.

S7 Table. Regression analyses of post-kidney transplant outcomes in a coarsened exact matched cohort of 352 extended hour haemodialysis (HD) patients compared with 2,005 conventional HD patients.

S8 Table. Baseline characteristics of a propensity score matched cohort of kidney transplant recipients previously managed with extended hour (n = 378) or conventional (n = 1,113) haemodialysis.

S9 Table. Regression analyses of post-kidney transplant outcomes in a propensity score matched cohort of 378 extended hour haemodialysis (HD) patients compared with 1,113 conventional HD patients.

S10 Table. Regression analyses of post-kidney transplant outcomes in 378 extended hour haemodialysis (HD) patients compared with 4,557 conventional HD patients including transplant state as a random effect.

FIGURE LEGENDS

Figure 1. Study flow diagram.

Figure 2. Odds of delayed graft function (DGF) and dialysis requirement (examined as a binary outcome) following kidney transplantation in 378 extended hour haemodialysis (HD) patients compared with 4,557 conventional HD patients.

Figure 3. Estimated glomerular filtration rate (eGFR) at 12 months in 378 extended hour haemodialysis (HD) patients compared with 4,557 conventional HD patients.

Figure 4. Unadjusted and adjusted Cox proportional hazards analyses for death-censored graft failure, all-cause death, cardiovascular death, and a composite of death or graft failure in 378 extended hour haemodialysis (HD) patients compared with 4,557 conventional HD patients.

Figure 5. Kaplan-Meier analysis of (a) graft survival, (b) patient survival, (c) cardiovascular survival and (d) composite of patient and graft survival in 378 extended hour haemodialysis (HD) patients compared with 4,557 conventional HD patients.

Table 1. Baseline characteristics of kidney transplant recipients previously managed with extended hour (n = 378) or conventional (n = 4557) haemodialysis.

	All (n = 4935)	Extended hour HD (n = 378)	Conventional HD (n = 4557)	Standardised mean difference	P value
Male	3257 (66.0%)	282 (74.6%)	2975 (65.3%)	0.16	<0.001
Age (years)	49.5 ± 12.9	47.9 ± 11.9	49.6 ± 12.9	0.14	0.01
BMI (kg/m2)					<0.001
<18.5	139 (2.9%)	5 (1.3%)	134 (3.0%)	0.09	
18.5-<25	1757 (36.3%)	118 (31.7%)	1639 (36.7%)	0.09	
25-30	1756 (36.3%)	130 (35.0%)	1626 (36.4%)	0.03	
>30	1183 (24.5%)	119 (32.0%)	1064 (23.8%)	0.15	
Racial origin					<0.001
Caucasian	3889 (78.8%)	317 (83.9%)	3572 (78.4%)	0.11	
ATSI	214 (4.3%)	2 (0.5%)	212 (4.7%)	0.19	
MPI	278 (5.6%)	22 (5.8%)	256 (5.6%)	0.01	
Asian	248 (5.0%)	20 (5.3%)	228 (5.0%)	0.01	
Other	306 (6.2%)	17 (4.5%)	289 (6.3%)	0.06	
Cause of ESKD					0.01
GN	2218 (45.0%)	188 (49.7%)	2030 (44.6%)	0.08	
Diabetes	518 (12.5%)	26 (6.9%)	592 (13.0%)	0.16	
Renovascular	301 (6.1%)	18 (4.8%)	283 (6.2%)	0.05	
Cystic	788 (16.0%)	73 (19.3%)	715 (15.7%)	0.08	
Reflux	376 (7.6%)	28 (7.4%)	348 (7.6%)	0.01	
Other	633 (12.8%)	45 (11.9%)	588 (12.9%)	0.02	
Waiting time (months)	37.4 (20.0-66.0)	47.1 (30.0-75.1)	36.3 (19.5-65.7)	0.23	<0.001
Diabetes	880 (17.8%)	49 (13.0%)	831 (18.2%)	0.12	0.01
Smoking	635 (12.9%)	42 (11.1%)	593 (13.1%)	0.05	0.28
IHD	838 (17.0%)	51 (13.5%)	787 (17.3%)	0.08	0.06
CVD	227 (4.6%)	9 (2.4%)	218 (4.8%)	0.10	0.03
PVD	322 (6.5%)	14 (3.7%)	308 (6.8%)	0.11	0.02

Donor source					0.01
Live	1355 (27.5%)	89 (23.5%)	1266 (27.8%)	0.08	
DBD	3043 (61.7%)	230 (60.9%)	2813 (61.7%)	0.01	
DCD	537 (10.9%)	59 (15.6%)	478 (10.5%)	0.13	
Male donor	2576 (52.2%)	195 (51.6%)	2381 (52.3%)	0.01	0.80
Donor age (years)	46.6 ± 15.7	46.6 ± 15.7	46.8 ± 15.7	0.01	0.80
Donor terminal creatinine (umol/L)†	73 (58-96)	71 (57-94)	73 (58-97)	0.01	0.42
Transplant era					<0.001
2000-2004	1033 (20.9%)	28 (7.4%)	1005 (22.1%)	0.37	
2005-2009	1720 (34.9%)	145 (38.4%)	1575 (34.6%)	0.06	
2010-2014	2182 (44.2%)	205 (54.2%)	1977 (43.4%)	0.18	
Transplant state					<0.001
New South Wales	1273 (25.8%)	117 (31.0%)	1156 (25.4%)	0.10	
Victoria	1304 (26.4%)	120 (31.8%)	1184 (26.0%)	0.11	
Queensland	817 (16.6%)	78 (20.6%)	739 (16.2%)	0.09	
South Australia	523 (10.6%)	4 (1.1%)	519 (11.4%)	0.32	
Western Australia	421 (8.5%)	9 (2.4%)	412 (9.0%)	0.22	
New Zealand	597 (12.1%)	50 (13.2%)	547 (12.0%)	0.03	
Total ischaemia (hours)	10.1 ± 6.1	9.7 ±-5.2	10.1 ± 6.1	0.07	0.23
HLA mismatches					0.01
0	245 (5.0%)	17 (4.5%)	228 (5.0%)	0.02	
1	418 (8.5%)	25 (6.6%)	393 (8.6%)	0.06	
2	1046 (21.1%)	97 (25.7%)	949 (20.8%)	0.09	
3	903 (18.3%)	49 (13.0%)	854 (18.7%)	0.13	
4	856 (17.4%)	59 (15.6%)	797 (17.5%)	0.04	
5	971 (19.7%)	80 (21.2%)	891 (19.6%)	0.03	
6	496 (10.1%)	51 (13.5%)	445 (9.8%)	0.10	
Prior graft	261 (5.3%)	30 (7.9%)	231 (5.1%)	0.10	0.02

ATSI, Aboriginal and Torres Strait Islander; BMI, body mass index; CVD, cerebrovascular disease; DBD, donation after brain death; DCD, donation after circulatory death; ESKD, end stage kidney disease; GN, glomerulonephritis; HD, haemodialysis; HLA, human leukocyte antigen; IHD, ischaemic heart disease; MPI, Maori and Pacific Islander; PVD, peripheral vascular disease. †Deceased donor kidney recipients only.

Table 2. Proportion of patients with delayed graft function, acute rejection, graft failure, all-cause and cardiovascular mortality, and a composite of graft failure or mortality in 378 extended hour haemodialysis (HD) patients compared with 4557 conventional HD patients.

	All (n = 4935)	Extended hour HD (n = 378)	Conventional HD (n = 4557)	P value
Early graft function				<0.001
IGF	2956 (59.9%)	187 (49.5%)	2769 (60.8%)	
SGF	730 (14.8%)	77 (20.4%)	653 (14.3%)	
DGF-D	1249 (25.3%)	114 (30.1%)	1135 (24.9%)	
Acute rejection episodes				0.82
0	3562 (72.2%)	275 (72.8%)	3287 (72.1%)	
1	973 (19.7%)	71 (18.8%)	902 (19.8%)	
2	273 (5.5%)	22 (5.8%)	251 (5.5%)	
≥3	127 (2.6%)	10 (2.6%)	117 (2.6%)	
Graft failure	618 (12.5%)	36 (9.5%)	582 (12.8%)	0.07
All-cause mortality	652 (13.2%)	23 (6.1%)	629 (13.8%)	<0.001
Cardiovascular mortality	178 (3.6%)	8 (2.1%)	170 (3.7%)	0.11
Composite outcome†	1099 (22.3%)	52 (13.8%)	1047 (23.0%)	<0.001

DGF-D, delayed graft function requiring dialysis within 72 hours following transplantation; HD, haemodialysis; IGF, immediate graft function defined as a spontaneous fall in serum creatinine of at least 10% within 24 hours; SGF, slow graft function defined as a spontaneous fall in serum creatinine of less than 10% within 24 hours; †Composite of graft failure or death.

Table 3. Unadjusted and multivariable adjusted regression analyses of post-kidney transplant outcomes in 378 extended hour haemodialysis (HD) patients compared with 4557 conventional HD patients.

	Unadjusted analysis			Adjusted analysis		
	OR, IRR, Coef or HR	95% CI	P value	OR, IRR, Coef or HR	95% CI	P value
Delayed graft function	1.47*	1.21-1.79	<0.001	1.33*	1.06-1.67	0.01
Post-transplant dialysis	1.30*	1.03-1.64	0.02	1.23*	0.94-1.61	0.12
Acute rejection	1.14¶	0.93-1.39	0.20	0.95¶	0.77-1.17	0.61
12 month eGFR	-1.77†	-3.89-0.35	0.10	-1.40†	-3.32-0.53	0.16
Graft failure	0.88§	0.63-1.23	0.45	0.89§	0.63-1.26	0.51
All-cause mortality	0.55§	0.36-0.83	0.004	0.82§	0.53-1.25	0.35
Cardiovascular mortality	0.71§	0.35-1.44	0.34	1.15§	0.56-2.40	0.70
Composite outcome‡	0.71§	0.54-0.94	0.02	0.83§	0.63-1.11	0.22

CI, confidence interval; †Coef, linear regression coefficient; ‡Composite of graft failure or death; eGFR, estimated glomerular filtration rate; §HR, hazard ratio; ¶IRR, incidence rate ratio; *OR, odds ratio.

Table 4. Cause of graft failure and death in 378 extended hour haemodialysis (HD) patients compared with 4557 conventional HD patients.

	Extended hour HD	Conventional HD	P value
Cause of graft failure			0.78
Rejection	21 (67%)	106 (52%)	
Vascular	3 (9%)	24 (12%)	
Technical	2 (6%)	9 (4%)	
Glomerulonephritis	2 (6%)	19 (9%)	
Drug therapy	1 (3%)	28 (14%)	
Other	3 (9%)	19 (9%)	
Cause of death			0.40
Cardiac	8 (35%)	170 (27%)	
Vascular	3 (13%)	52 (8%)	
Infection	4 (17%)	123 (20%)	
Social	4 (17%)	66 (10%)	
Other	4 (17%)	218 (35%)