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Association between initial and pretransplant dialysis modality and graft and patient outcomes in live- and deceased-donor renal transplant recipients

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Summary

The association between pretransplant dialysis modality and transplant outcomes remains inconsistent. The aim of this study is to address the association between alteration in dialysis modality and post-transplant outcomes. Using Australia and New Zealand Dialysis and Transplant Registry, primary live- and deceased-donor renal transplant recipients (RTR) between 1997 and 2009 were examined. Pre-emptive and multiple-organ transplants were excluded. The association between initial and pretransplant dialysis modality and transplant outcomes were examined. Of the 6701 RTR, 18.6% were initiated-maintained on peritoneal dialysis pretransplant (PD-PD), 9.2% were initiated on PD, but maintained on haemodialysis (HD) pretransplant (PD-HD), 63.3% were HD-HD and 8.9% were HD-PD. PD-HD [odds ratio(OR)1.44, 95% CI 1.21,1.72] and HD-HD (OR1.25, 95% CI 1.12,1.41) were associated with a significantly greater risk of slow graft function compared with the overall mean of the groups, whereas a change in initial dialysis modality from HD to pretransplant PD was associated with higher risk of overall graft failure [hazard ratio(HR)1.19, 95% CI 1.04,1.36) and recipient death (HR1.34, 95% CI 1.13,1.59). Our registry analysis suggest that dialysis modality pretransplant may affect transplant outcomes and future studies evaluating patient selection, choice of modality and/or potential interventions in the pre and post-transplant period may have a beneficial effect on post-transplant outcomes.

Introduction

The effect of pretransplant dialysis modality on renal transplant outcomes has been a subject of considerable interest over the years with conflicting findings over the past decades. Several studies have shown that pretransplant peritoneal dialysis (PD) is associated with a higher risk of early graft failure [1], but other large registry studies have demonstrated pretransplant haemodialysis (HD) may be associated with greater risk of graft failure and

death [2,3]. However, the association between pretransplant dialysis modality and renal transplant outcomes remains debatable [4,5]. The biological rationale for these observed findings remains unclear as the majority of the studies did not consider the effects of varying dialysis modality and the risk of post-transplant mortality and morbidity. Previous studies have shown that dialysis duration prior to kidney transplantation negatively influence the overall graft and patient survival, implying it may be the effects of the prolonged exposure to uraemia rather than the treatment itself poses significant impact on longer term clinically relevant outcomes [6,7].

In this study, we aimed to determine the association between alteration in dialysis modality and post-transplant graft and patient mortality and morbidities independent of dialysis duration and transplant era.

Patients and methods

Study population

Using the Australia and New Zealand Dialysis and Transplant (ANZDATA) Registry, all primary live- and deceased-donor renal transplant recipients in Australia and New Zealand between 1997 and 2009 were included. Pre-emptive and multiple-organ transplant recipients were excluded from the study. Less than 2% of renal transplant recipients had missing clinical outcome data and were excluded for analysis.

Renal transplant recipients were categorized into four groups depending on their initial (at commencement of renal replacement therapy) and pretransplant dialysis modality – PD-PD (initiated and maintained on PD pretransplant), PD-HD (initiated on PD and maintained on HD pretransplant), HD-HD (initiated and maintained on HD pretransplant) and HD-PD (initiated on HD and maintained on PD pretransplant). PD included both automated peritoneal dialysis and continuous ambulatory peritoneal dialysis.

Data collection

Recorded baseline data included donors' characteristics such as age (categorized as <50 and ≥50 years), type [live (LD) and deceased donor (DD), the latter categorized into four groups according to total ischaemic time of ≤6 h, >6–12 h, >12–18 h and >18 h] and gender; recipients' characteristics including age (categorized as ≤19, >19–30, >30–50 and >50 years), gender, race (Indigenous and non-Indigenous), cause of end-stage kidney disease (ESKD; categorized as diabetic nephropathy, glomerulonephritis, cystic disease, vascular/hypertensive disease or others), peak panel reactive antibody (PRA; categorized as 0–10%, 11–50% and >50%), dialysis duration pretransplant (categorized as 0–1 year, >1–3 years, >3–5 years and >5 years on dialysis), diabetes, coronary artery disease (CAD) and smoking history (categorized as current smokers, former smokers or nonsmokers); and transplant-related characteristics including the use of induction therapy (including interleukin-2 receptor antibody or T cell depleting agents), transplant era and transplant state or country. Transplant era was divided into four groups for analysis (i.e. 1997–2000, 2001–2003, 2004–2006, 2007–2009) and transplant state or country into six groups (i.e. South Australia/Northern Territory, Victoria/Tasmania, New South Wales/Australia Capital Territory, Western Australia, Queensland and New Zealand). The number of HLA-mismatches (0–6 mismatches) was modelled as a continuous variable in the analysis.

Clinical outcomes

The primary clinical outcomes of this study were slow graft function (SGF; defined as requiring dialysis within the first 72-h post-transplantation), acute rejection occurring in the first 6 months post-transplant, overall graft failure, death-censored graft failure (DCGF) and death. Data on acute rejection was collected from 1997. The reporting of acute rejection is voluntary, with the majority being biopsy-proven and coded according to Banff classification. For the purpose of this study, outcome data of all recipients were censored at 31st December 2009. Effect modification between changes in dialysis modality with covariates and outcomes were examined.

Statistical analyses

Comparisons of baseline characteristics between dialysis modality groups were made by chi-square test. Predictors of SGF and acute rejection at 6 months were modelled by adjusted and unadjusted logistic regression. Graft and patient survival were examined using Cox proportional hazard regression. In the absence of a standard comparator, the association between dialysis modality groups and outcomes in regression models was examined using dummy/indicator coding, where the effect of each group is defined as a deviation from the overall 'grand mean' of all groups. Results were expressed as hazard ratio (HR) or as odds ratio (OR) with 95% confidence interval (95% CI). The covariates included in the logistic regression and Cox regression models were donors' characteristics (including age, gender and type), recipients' characteristics (including age, race, gender, cause of ESKD, peak PRA, dialysis duration pretransplant, diabetes, smoking history and CAD) and transplant-related characteristics (including induction therapy, transplant era and transplant state/country). Statistical evaluation was performed

using SPSS V10 statistical software program (SPSS Inc., North Sydney, NSW, Australia). A *P*-value of less than 0.05 was considered statistically significant.

Results

Baseline characteristics

Of the 6701 renal transplant recipients included in this study, 1244 (18.6%) were PD-PD, 619 (9.2%) were PD-HD, 4241 (63.3%) were HD-HD and 597 (8.9%) were HD-PD. Baseline characteristics according to initial and pretransplant dialysis modality are shown in Table 1. Renal transplant recipients in the PD-PD group were younger, more likely to receive live-donor transplants and have spent less time on dialysis prior to transplantation compared with other dialysis modality groups. The reasons for the change in modality from PD to HD are usually attributed to social reasons/patient preference (42%),

Table 1. Baseline characteristics of renal transplant recipients stratified by initial and pretransplant dialysis modality.

	PD-PD % (*n* = 1244)	PD-HD % (*n* = 619)	HD-HD % (*n* = 4241)	HD-PD % (*n* = 597)	*P*-value
Donor type*					
LD	40.9	29.4	36.0	33.8	0.001
DD ≤6 h	2.9	2.5	2.3	2.9	
DD >6–12 h	18.9	25.4	22.3	19.7	
DD >12–18 h	26.5	31.2	28.5	30.8	
DD >18 h	10.8	11.5	10.9	12.8	
Donor age ≥50 years	35.7	42.0	39.8	39.5	0.071
Donor male	51.2	51.9	53.1	54.8	0.453
Recipient age					
≤19 years	16.4	7.4	2.8	5.9	<0.001
>19–30 years	8.6	9.5	12.6	14.2	
>30–50 years	37.1	38.4	42.6	39.0	
>50 years	37.9	44.7	42.0	40.9	
Recipient male	50.1	56.4	67.6	53.4	<0.001
Indigenous recipients	7.1	11.8	8.3	8.9	0.006
ESKD cause					
Diabetic nephropathy	10.6	10.2	8.4	8.0	<0.001
Glomerulonephritis	39.5	42.2	48.2	46.4	
Cystic	13.8	16.0	15.6	7.5	
Vascular/hypertension	4.7	5.7	4.2	6.4	
Time on dialysis					
0–1 year	34.5	7.9	25.3	21.6	<0.001
>1–3 years	45.3	31.0	36.0	46.2	
>3–5 years	13.4	24.9	18.4	18.8	
>5 years	6.8	36.2	20.3	13.4	
Recipient BMI >30 kg/m^2*	18.5	16.5	18.6	16.6	0.008
HLA-MM*					
0	6.5	5.5	6.1	5.9	0.018
1–2	34.3	27.1	30.9	33.2	
Peak PRA >50%*	7.2	14.9	9.6	9.6	<0.001
Recipients diabetes (yes)	12.1	13.2	11.7	11.4	0.719
Recipient nonsmoker*	65.9	59.8	55.1	56.5	<0.001
Recipient CAD (yes)*	7.4	10.2	10.2	9.7	0.028
Transplant era*					
1997–2000	27.3	21.3	27.2	26.1	0.013
2001–2003	22.7	20.2	23.1	22.1	
2004–2006	22.3	26.3	24.0	25.0	
2007–2009	27.7	32.2	24.7	26.8	
Received induction (yes)*	46.6	53.2	46.0	48.2	0.009

Data expressed as proportion, *$P < 0.05$ chi-square analysis.

PD-PD, initial and pretransplant peritoneal dialysis; PD-HD, initial peritoneal dialysis and pretransplant haemodialysis; HD-HD, initial and pretransplant haemodialysis; HD-PD, initial haemodialysis and pretransplant peritoneal dialysis; LD, live donor; DD, deceased donor (with ischaemic time in hours); ESKD, end-stage kidney disease; BMI, body mass index; HLA-MM, human leucocyte antigen mismatches; PRA, panel reactive antibodies; CAD, coronary artery disease.

followed by infective reasons (25%), technical failure (17%) and dialysis failure (16%, including ultrafiltration failure). The reasons for the change from HD to PD are not available.

Association between initial and pretransplant dialysis modality and slow graft function and acute rejection

In the unadjusted and adjusted models, PD-HD and HD-HD were associated with the greatest risk of SGF, whereas PD-PD was associated with the lowest risk of SGF compared with the mean of the groups. Deceased-donor transplants were associated with at least a fourfold increase in the risk of SGF compared with live-donor transplants, whereas increasing dialysis duration pretransplant was associated with a significantly increased risk of SGF (Table 2). There was no interaction between initial and pretransplant dialysis modality and donor type, transplant era or other covariates and SGF. In a sub-analysis restricted to recipients who had required dialysis beyond 4 days, the results were similar with PD-HD and HD-HD significantly associated with SGF in both unadjusted (PD-PD – OR 0.71, 95% CI 0.43, 1.17; PD-HD OR 2.21, 95% CI 1.15, 4.24; HD-HD OR 1.25, 95% CI 0.88, 1.79; HD-PD OR 0.51, 95% CI 0.31, 0.85) and adjusted models (PD-PD – OR 0.77, 95% CI 0.44, 1.33; PD-HD OR 2.31, 95% CI 1.15, 4.65; HD-HD OR 1.27, 95% CI 0.87, 1.86; HD-PD OR 0.45, 95% CI 0.26, 0.79).

Table 2. Unadjusted and adjusted models of initial and pretransplant dialysis modality and slow graft function and acute rejection.

	Slow Graft Function (OR, 95% CI)	Acute rejection (OR, 95% CI)
Unadjusted model		
PD-PD	0.59 (0.50, 0.69)*	1.01 (0.90, 1.13)
PD-HD	1.69 (1.45, 1.98)*	0.97 (0.84, 1.13)
HD-HD	1.22 (1.10, 1.34)*	1.16 (1.07, 1.27)*
HD-PD	0.83 (0.68, 0.99)*	0.87 (0.75, 1.01)
Adjusted model		
Dialysis modality		
PD-PD	0.69 (0.58, 0.82)*	1.05 (0.92, 1.18)
PD-HD	1.44 (1.21, 1.72)*	0.97 (0.83, 1.13)
HD-HD	1.25 (1.12, 1.41)*	1.14 (1.04, 1.25)*
HD-PD	0.80 (0.65, 0.98)*	0.87 (0.74, 1.01)
Donor type		
LD	1.00	1.00
DD ≤6 h	4.57 (2.85, 7.33)*	0.95 (0.65, 1.38)
DD >6–12 h	4.96 (3.85, 6.40)*	0.91 (0.77, 1.07)
DD >12–18 h	6.86 (5.39, 8.73)*	0.90 (0.78, 1.05)
DD >18 h	10.51 (8.02, 13.78)*	0.95 (0.78, 1.16)
Time on dialysis		
0–1 year	1.00	1.00
>1–3 years	1.39 (1.10, 1.75)*	0.85 (0.73, 0.98)*
>3–5 years	1.55 (1.20, 2.00)*	0.84 (0.70, 1.01)*
>5 years	2.08 (1.61, 2.69)*	1.07 (0.88, 1.30)

*$P < 0.05$, data expressed as odds ratio (OR) with 95% CI.
PD-PD, initial and pretransplant peritoneal dialysis; PD-HD, initial peritoneal dialysis and pretransplant haemodialysis; HD-HD, initial and pretransplant haemodialysis; HD-PD, initial haemodialysis and pretransplant peritoneal dialysis; LD, live donor; DD, deceased donor (with ischaemic time in hours). Adjusted model included donor age, donor gender, recipient age, recipient gender, race, cause of end-stage kidney disease, recipient body mass index, human leucocyte antigen mismatches, panel reactive antibodies, smoking history, diabetes, coronary artery disease, use of induction therapy, transplant state/country and transplant era.

For acute rejection, HD-HD was associated with higher risk of acute rejection occurring in the first 6 months post-transplant compared with the mean of the groups in both unadjusted and adjusted models. There was no association between donor type and the risk of acute rejection; whereas dialysis duration between >1 and 5 years was associated with a lower risk of acute rejection compared with dialysis duration of 0–1 year. The type and severity of rejection episodes occurring in the first 6 months post-transplant was similar (data not shown). There was no interaction between initial and pretransplant dialysis modality and donor type, dialysis duration or other covariates and acute rejection.

Association between initial and pretransplant dialysis modality and graft failure and death

In the unadjusted model, PD-HD and HD-PD were associated with the greatest risk of overall graft failure, whereas PD-PD was associated with the lowest risk of overall graft failure compared with the mean of the groups. Only HD-PD group was associated with a higher risk of overall graft failure in the adjusted model (Table 3 and Fig. 1). The proportion of graft loss in PD-PD was 19.8%, PD-HD 23.9%, HD-HD 21.7% and HD-PD 26.5% (chi-square $P < 0.01$); whereas mean ± SD graft years were 5.09 ± 3.64, 4.42 ± 3.41, 5.11 ± 3.62 and 4.79 ± 3.56 respectively (ANOVA $P < 0.01$. Compared with live-donor transplants, deceased-donor transplants with ischaemic time of >6 h were associated with greater risk of overall graft failure in the adjusted model. Dialysis duration was associated with an incremental increase in the risk of overall graft failure in the adjusted model (Table 3). For DCGF, there was no association between dialysis modality or dialysis duration and DCGF, but deceased-donor transplants were associated with a significantly higher risk of DCGF compared with live-donor transplants. The proportion of graft failure attributed to acute rejection, chronic allograft nephropathy and de novo/recurrent glomerulonephritis were similar in all groups (acute rejection: PD-PD 9%, PD-HD 10%, HD-HD 9% and HD-PD 5%; chronic allograft nephropathy:

Table 3. Unadjusted and adjusted models of pretransplant dialysis modality and graft and patient survival.

	Overall graft failure (HR, 95% CI)	Death-censored graft failure (HR, 95% CI)	Death (HR, 95% CI)
Unadjusted model			
PD-PD	0.83 (0.74, 0.92)*	0.85 (0.71, 0.99)*	0.81 (0.70, 0.94)*
PD-HD	1.14 (1.01, 1.30)*	1.25 (1.03, 1.52)*	1.07 (0.90, 1.28)
HD-HD	0.90 (0.83, 0.98)*	0.90 (0.79, 1.02)	0.91 (0.81, 1.01)
HD-PD	1.17 (1.03, 1.33)*	1.05 (0.86, 1.29)	1.28 (1.08, 1.50)*
Adjusted model			
Dialysis modality			
PD-PD	0.89 (0.79, 0.99)*	0.84 (0.71, 1.01)	0.91 (0.78, 1.06)
PD-HD	0.99 (0.86, 1.14)	1.15 (0.94, 1.42)	0.89 (0.73, 1.07)
HD-HD	0.96 (0.88, 1.04)	0.99 (0.87, 1.12)	0.93 (0.83, 1.04)
HD-PD	1.19 (1.04, 1.36)*	1.04 (0.85, 1.29)	1.34 (1.13, 1.59)*
Donor type			
LD	1.00	1.00	1.00
DD ≤6 h	1.06 (0.72, 1.58)	1.33 (0.77, 2.32)	0.87 (0.49, 1.53)
DD >6–12 h	1.35 (1.15, 1.59)*	1.38 (1.09, 1.76)*	1.30 (1.04, 1.62)*
DD >12–18 h	1.30 (1.12, 1.51)*	1.25 (1.01, 1.56)*	1.32 (1.08, 1.62)*
DD >18 h	1.54 (1.29, 1.83)*	1.48 (1.13, 1.93)*	1.55 (1.23, 1.95)*
Time on dialysis			
0–1 year	1.00	1.00	1.00
>1–3 years	1.23 (1.05, 1.43)*	1.16 (0.93, 1.44)	1.32 (1.05, 1.64)*
>3–5 years	1.33 (1.11, 1.59)*	1.15 (0.88, 1.51)	1.52 (1.18, 1.96)*
>5 years	1.42 (1.16, 1.72)*	1.15 (0.85, 1.55)	1.71 (1.31, 2.23)*

*$P < 0.05$, data expressed as hazard ratio (HR) with 95% CI.

PD-PD, initial and pretransplant peritoneal dialysis; PD-HD, initial peritoneal dialysis and pretransplant haemodialysis; HD-HD, initial and pretransplant haemodialysis; HD-PD, initial haemodialysis and pretransplant peritoneal dialysis; LD, live donor; DD, deceased donor (with ischaemic time in hours). Adjusted model included donor age, donor gender, recipient age, recipient gender, race, cause of end-stage kidney disease, recipient body mass index, human leucocyte antigen mismatches, panel reactive antibodies, smoking history, diabetes, coronary artery disease, use of induction therapy, transplant state/country and transplant era.

PD-PD 46%, PD-HD 53%, HD-HD 52% and HD-PD 57%; de novo/recurrent glomerulonephritis: PD-PD 7%, PD-HD 9%, HD-HD 9% and HD-PD 8%).

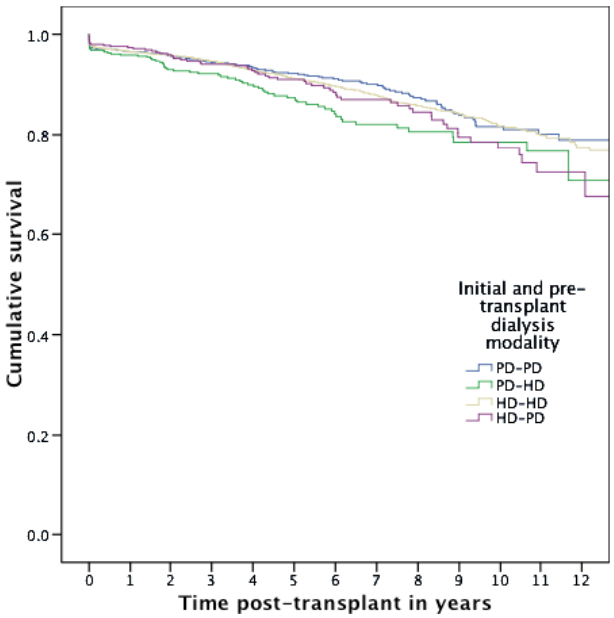
In the unadjusted and adjusted models, HD-PD was associated with a higher risk of recipient death compared with the mean of the groups (Table 3 and Fig. 2). Compared with live-donor transplants, deceased-donor transplants with ischaemic time of >6 h were associated with greater risk of death in the adjusted model. Dialysis duration was associated with an incremental increase in the risk of death in the adjusted model (Table 3). The proportion of deaths attributed to cardiac and infective causes was similar in all groups (cardiac: PD-PD 29%, PD-HD 30%, HD-HD 31% and HD-PD 33%; infective: PD-PD 21%, PD-HD 21%, HD-HD 24% and HD-PD 22%).

There was a significant interaction between dialysis modality with dialysis duration and overall graft failure and recipient death and when stratified by dialysis duration ($P = 0.02$ for interaction), HD-PD was associated with a significantly higher risk of overall graft failure and death in recipients who have spent >3 years on dialysis, but not in those who have spent ≤3 years on dialysis (Table 4). There was no interaction between initial and pretransplant dialysis modality and donor type, transplant era or other covariates and graft failure and death.

Discussion

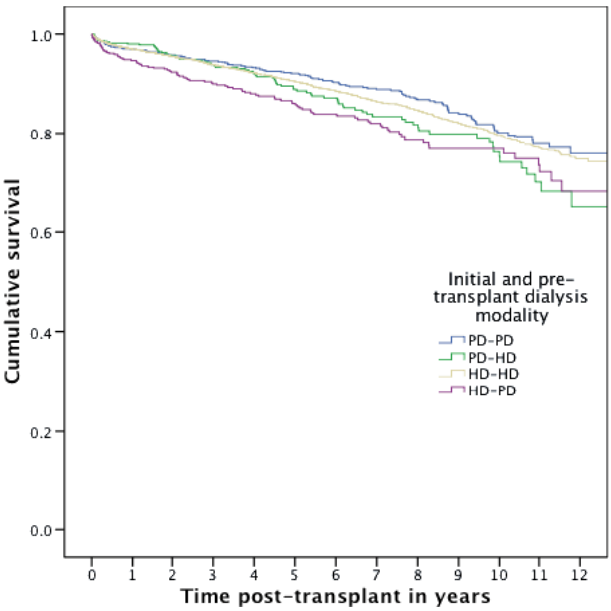
Our study has demonstrated that pretransplant HD was associated with a significantly greater risk of SGF compared with pretransplant PD, whereas a change in initial dialysis modality from HD to pretransplant PD was associated with higher risk of overall graft failure and recipient death, but not DCGF.

We found that pretransplant HD, irrespective of initial dialysis modality was associated with a greater risk of SGF, but this effect had no impact on graft or patient survival. The association between pretransplant HD and SGF persisted even when restricted to recipients who had required dialysis beyond 4 days post-transplant, therefore



Years	PD-PD	PD-HD	HD-HD	HD-PD
0	1107	538	3717	498
1	952	456	3217	438
3	727	316	2508	325
5	560	210	1864	234
8	287	101	980	121
12	39	10	135	16

Figure 1 Kaplan–Meier survival curve of death-censored graft failure with corresponding numerical table of the number at risk post-transplant (Log-rank *P*-value = 0.037).



Years	PD-PD	PD-HD	HD-HD	HD-PD
0	1203	617	4240	596
1	1086	543	3734	517
3	844	392	2931	390
5	660	220	2236	287
8	353	138	1226	156
12	50	15	182	23

Figure 2 Kaplan–Meier survival curve of recipient death with corresponding numerical table of the number at risk post-transplant (Log-rank *P*-value = 0.002).

potentially excluding those who may have had dialysis post-transplant for hyperkalaemia rather than for SGF. Although there was only a trend towards a higher risk of SGF in HD-HD recipients, we believe that this is still clinically relevant and may reflect a reduced number of events (episodes of SGF decreased from 1107 to 775). Nevertheless, the finding that PD-HD patients having the highest frequency of SGF may be related to residual confounding as this group of patients had the highest proportion of deceased-donor transplants (70.6%) and highest proportion of patients who have spent >3 years on dialysis pretransplant (61.1% vs. <40% in other groups), both factors have been strongly associated with SGF [8]. Similar finding has been observed in a small single centre study of 306 nonpre-emptive renal transplant recipients showing pretransplant HD patients had a significantly greater risk of SGF compared with PD patients (37% vs. 13%, $P = 0.037$), but with similar graft and patient survival [9]. Although SGF has been shown to be associated with a greater risk of rejection and poorer graft survival [1,10], these studies have focused predominantly on the earlier transplant eras with limited availability of the more potent immunosuppressive agents. The mechanism of why pretransplant HD is associated with a greater risk of SGF compared with PD remains unclear, possibly related to the better preservation of residual renal function in PD patients [11,12]. However, this possibility cannot be accurately explored using registry data.

In our study, the finding of a greater risk of acute rejection in the first 6 months post-transplant in HD-HD recipients was surprising. It is plausible that compared with PD, HD process may be associated with a greater inflammatory response ± exacerbated by the use of more bio-incompatible membrane during earlier eras may have contributed to this finding [13,14].

A large number of studies have evaluated the association between pretransplant dialysis modality and graft and patient outcomes. In a retrospective cohort analysis of 60 008 primary deceased-donor renal transplant recipients recorded in the Collaborative Transplant Study during the time period between 1998 and 2007, Schwenger V *et al.*. demonstrated that pretransplant PD was associated with significantly better 5-year overall graft and patient survival compared with recipients maintained on pretransplant HD, primarily attributed to lower rates of cardiovascular death. There was no difference between dialysis modality and death-censored graft survival [4]. In an analysis of the Scientific Registry of Transplant

Table 4. Interaction between dialysis modality and dialysis duration for overall graft failure and recipient death.

	Overall graft failure (HR, 95% CI)	Death (HR, 95% CI)
Adjusted model		
Dialysis duration		
0–1 year		
PD-PD (*n* = 424)	0.98 (0.74, 1.29)	1.03 (0.68, 1.57)
PD-HD (*n* = 46)	0.97 (0.55, 1.74)	0.75 (0.31, 1.79)
HD-HD (*n* = 1063)	0.79 (0.61, 1.02)	0.81 (0.55, 1.20)
HD-PD (*n* = 127)	1.32 (0.94, 1.86)	1.58 (0.96, 2.61)
>1–3 years		
PD-PD (*n* = 555)	0.83 (0.69, 0.99)*	0.80 (0.63, 1.01)
PD-HD (*n* = 190)	1.04 (0.82, 1.33)	1.04 (0.75, 1.45)
HD-HD (*n* = 1511)	1.00 (0.87, 1.15)	0.98 (0.82, 1.18)
HD-PD (*n* = 270)	1.15 (0.94, 1.41)	1.23 (0.94, 1.60)
>3 years		
PD-PD (*n* = 243)	0.88 (0.71, 1.10)	0.97 (0.74, 1.25)
PD-HD (*n* = 366)	0.97 (0.81, 1.17)	0.82 (0.63, 1.04)
HD-HD (*n* = 1599)	1.00 (0.88, 1.15)	0.92 (0.78, 1.09)
HD-PD (*n* = 183)	1.17 (1.01, 1.46)*	1.39 (1.05, 1.82)*

*$P < 0.05$, data expressed as hazard ratio (HR) with 95% CI.
PD-PD, initial and pretransplant peritoneal dialysis; PD-HD, initial peritoneal dialysis and pretransplant haemodialysis; HD-HD, initial and pretransplant haemodialysis; HD-PD, initial haemodialysis and pretransplant peritoneal dialysis; LD, live donor; DD, deceased donor (with ischaemic time in hours). Adjusted model included donor age, donor gender, recipient age, recipient gender, race, cause of end-stage kidney disease, recipient body mass index, human leucocyte antigen mismatches, panel reactive antibodies, smoking history, diabetes, coronary artery disease, use of induction therapy, transplant state/country and transplant era.

Recipients (SRTR) between 2001 and 2006, *Molnar et al.* demonstrated that renal transplant recipients who had been on PD had 62% (HR: 0.34, 95% CI 0.14, 0.88) lower risk of cardiovascular death in the adjusted model compared with HD recipients. There was no association between pretransplant dialysis modality and SGF or DCGF [3]. It is noteworthy that this cohort comprised of 38% diabetics in the HD recipients (27% PD recipients) with over 20% African–American recipients, which may have contributed to the study findings. Similarly, analysis of the United States Renal Data System (USRDS) of 92 844 deceased-donor renal transplant recipients over a 10-year period between 2000 and 2009 demonstrated that pretransplant PD was associated with a significant improvement in overall graft and patient survival compared with recipients maintained on pretransplant HD. In addition, the authors shown that an increase in the number of dialysis modalities during end-stage kidney disease was associated with increased risk of graft failure (HR 1.04 per additional modality used; $P < 0.01$) and recipient death (HR 1.11 per additional modality used; $P < 0.01$) [2]. In contrast, other studies have demonstrated no association between dialysis modality and transplant outcomes [7,9]. The different population and transplant eras may explain the differences in results among studies. Similar to the USRDS study, we have demonstrated that a change in dialysis modality from initial HD to pretransplant PD was associated with a significant increase in overall graft failure and recipient death, but not DCGF, although this association was confined to those who have spent >3 years on dialysis prior to transplantation. In addition, there was a greater proportion of cardiac death in the HD-PD group with 33% of deaths attributed to cardiovascular disease. It is plausible that HD-PD recipients may characterize those with poorer general health and/or vascular access problems necessitating a change in dialysis modality, but this assumption cannot be accurately explored further using registry data. However, it is noteworthy that several studies have demonstrated no association between switching of dialysis modality and patient survival in nontransplant end-stage renal disease patients, and may suggest that early and timely change from one modality to the other in the event of PD or HD-related problems may not necessary lead to poorer outcomes, but this association needs to be explored further in the context of transplant outcomes [15,16].

Our results corroborate and extend previous study findings demonstrating that increasing dialysis duration pretransplant and deceased-donor transplants (especially with ischaemic time beyond 6 h) are associated with poorer graft and/or patient outcomes, perhaps a stronger association compared with the association between dialysis modality pretransplant and graft and/or patient outcomes [17,18]. Dialysis duration pretransplant has been consistently shown to adversely affect patient survival and may in part explain the observed benefit of live-donor versus deceased-donor transplants [6]. In a large single centre study of deceased- donor renal transplant recipients with follow-up period of 84 months, the authors demonstrated that dialysis duration pretransplant of ≥3 years was associated with a 21% greater risk of death compared with dialysis duration pretransplant of <3 years [7]. In a retrospective paired-kidney analysis of 4810 deceased-donor transplants identified from USRDS database (i.e. kidney pairs that were allocated to recipient who had spent <6 months on dialysis and the other kidney to recipient who had been on dialysis for >2 years), the authors demonstrated that increasing duration of dialysis pretransplant was associated with significantly poorer long-term graft survival in both live-donor and deceased-donor transplants [6]. Other studies demonstrating the beneficial effects of live-donor transplantation over deceased-donor transplantation on graft survival may be attributed to shorter dialysis duration

prior to transplantation in the former group, although graft survival of live-donor recipients remained superior compared with deceased-donor recipients for any given dialysis duration [19]. It is difficult to ascertain from registry data why PD-HD patients spent much longer time on dialysis pre-transplant. Possible reasons include that patients in this group may have medical and/or surgical reasons (not adequately captured by registry data) that have prevented them from being on the transplant wait-list, although time from dialysis to listing and time from listing to transplant (not collected by ANZDATA) may have helped to further explore this observation.

The strengths of this study included a large sample size and inclusiveness. We included all renal transplant recipients in Australia and New Zealand during the study period, such that a variety of centres were included with differing approaches to transplantation, which greatly enhanced the external validity of our findings. These strengths should be balanced against the study's limitations, which included limited depth of data collection. ANZDATA does not collect important information, such as patient compliance, individual unit management protocols and have limited data on pretransplant clinical and laboratory data (including residual renal function, albumin level and nutritional parameters), the amount of immunosuppression and other immunological data such as the presence of donor-specific antibodies. Even though we had adjusted for a large number of donor, recipient and transplant-related characteristics, the possibility of residual confounding could not be excluded. In addition, we have not taking into account the possibility of any temporary change in dialysis modalities in the period between commencement of renal replacement therapy and transplantation, although it is unlikely that this would have affected our findings. In addition, there is very limited and inadequate information on the duration of dialysis modality and/or time of modality switch, which may indirectly provide information on the overall health status and/or severity of comorbidities of these patients requiring a switch in dialysis modality. In common with other Registries, ANZDATA is a voluntary Registry and there is no external audit of data accuracy, including the diagnosis of acute rejection and SGF. Consequently, the possibility of coding/classification bias cannot be excluded. Selection bias resulting from clinicians' and patients' preferences for dialysis modality, transplantation (e.g. selection criteria) and immunosuppression type may also occur.

In our contemporary database of 6701 renal transplant recipients between 1997 and 2009, pretransplant HD was associated with a higher risk of SGF, whereas a change from initial HD to PD pretransplant was associated with greater risk of overall graft failure and recipient death. Although this study does not demonstrate causality, future studies should consider whether careful patient selection, choice of dialysis modality and/or interventions in the pre and post-transplant period coupled with more intensive monitoring of at risk recipients may have a favourable effect on post-transplant outcomes. However, it should be stressed that patients who change dialysis modality usually have a problem with their initial modality, which may be for technical reasons and/or the presence of severe comorbidities, all of which are not adequately captured by registry data, but may dictate the choice of dialysis treatment, and therefore should not influence their prospect of receiving a kidney transplant in the future.

Authorship

WHL, PC, GW, GD, SJC, SBC, GRR, KRP, SC and SP McDonald: designed research/study, wrote article. CB and KM: analysed data.

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