

Original Article

Effect of previously failed kidney transplantation on peritoneal dialysis outcomes in the Australian and New Zealand patient populations

Sunil V. Badve^{1,2}, Carmel M. Hawley^{1,2}, Stephen P. McDonald¹, David W. Mudge^{1,2}, Johan B. Rosman^{1,3}, Fiona G. Brown^{1,4} and David W. Johnson^{1,2} for The ANZDATA Registry PD Working Committee

¹Australia and New Zealand Dialysis and Transplant Registry, Adelaide, ²Department of Renal Medicine, Princess Alexandra Hospital, Brisbane, ⁴Department of Nephrology, Monash Medical Centre, Clayton, Victoria, Australia and ³Renal Department, Middlemore Hospital, Otahuhu, Auckland, New Zealand

Abstract

Background. There is limited information about the outcomes of patients commencing peritoneal dialysis (PD) after failed kidney transplantation. The aim of the present study was to compare patient survival, death-censored technique survival and peritonitis-free survival between patients initiating PD after failed renal allografts and those after failed native kidneys.

Methods. The study included all patients from the ANZDATA Registry who started PD between April 1, 1991 and March 31, 2004. Times to death, death-censored technique failure and first peritonitis episode were examined by multivariate Cox proportional hazards models. For all outcomes, conditional risk set models were utilized for the multiple failure data, and analyses were stratified by failure order. Standard errors were calculated by using robust variance estimation for the cluster-correlated data.

Results. In total, 13 947 episodes of PD were recorded in 23 579 person-years. Of these, 309 PD episodes were started after allograft failure. Compared with PD patients who had never undergone kidney transplantation, those with failed renal allografts were more likely to be younger, Caucasian, New Zealand residents and life-long non-smokers with lower body mass index (BMI), poorer initial renal function and a longer period from commencement of the first renal replacement therapy to PD. On multivariate analysis, PD patients with failed kidney transplants had comparable patient mortality [weighted hazards ratio (HR) 1.09, 95% confidence interval (CI) 0.81–1.45, $P=0.582$], death-censored technique failure (adjusted HR 0.91,

95% CI 0.75–1.10, $P=0.315$) and peritonitis-free survival (adjusted HR 0.92, 95% CI 0.72–1.16, $P=0.444$) with those PD patients who had failed native kidneys. Similar findings were observed in a subset of patients ($n=5496$) for whom peritoneal transport status was known and included in the models as a covariate.

Conclusion. Patients commencing PD after renal allograft failure experienced outcomes comparable with those with failed native kidneys. PD appears to be a viable option for patients with failed kidney allografts.

Keywords: failed renal allograft; patient survival; peritonitis; technique survival; transplantation; treatment modality

Introduction

Although efforts are being made to improve the long-term survival of renal allografts, the success of kidney transplantation is limited by a finite half-life. In 2003, 196 kidney transplant recipients returned to dialysis following loss of functioning grafts in Australia and New Zealand [1]. In the USA, ~20% of all the patients waiting for kidney transplantation had a previously failed transplant [2]. As the number of people with a functioning transplant is increasing, it is expected that the proportion of patients returning to dialysis after failed grafts would increase commensurately.

It has previously been observed that patients returning to dialysis after graft failure are at increased risk of death after graft loss [3] and constitute a unique group with specific risk factors, including a longer duration of end-stage renal disease (ESRD), concomitant immunosuppression and possibly more rapid loss of residual renal function [4,5]. More importantly,

Correspondence and offprint requests to: Professor David Johnson, Department of Renal Medicine, Level 2, Ambulatory Renal and Transplant Services Building, Princess Alexandra Hospital, Ipswich Road, Woolloongabba, Brisbane, Qld 4102, Australia.
Email: david_johnson@health.qld.gov.au

the optimal modality of dialysis for these patients is not yet clearly defined. Three previous studies involving small numbers of patients have reported conflicting findings regarding whether patients with failed renal allografts experience comparable [5,6] or worse [4] outcomes on peritoneal dialysis (PD) compared with individuals with failed native kidneys. However, these investigations were limited by small sample sizes (≤ 42 subjects), inadequate statistical adjustment for differences in baseline characteristics and restriction to single-centre observations.

The aim of the present study was to compare patient survival, death-censored technique survival and peritonitis-free survival in patients initiating PD after failed allografts *vs* native kidneys, using data from the Australia and New Zealand Dialysis and Transplant (ANZDATA) Registry.

Materials and methods

Study population

The ANZDATA Registry collects information every 6 months from all renal units throughout Australia and New Zealand, concerning all patients receiving chronic renal replacement therapy (RRT). Complete details of the structure and methods of the ANZDATA Registry have been reported elsewhere [7]. In summary, the collection is complete from the first RRT procedure in Australasia in 1963 and includes all patients from all renal units in both countries. The data collected consist of information on the underlying cause of ESRD, demographic details, a limited range of co-morbidities (the presence of coronary artery disease, peripheral vascular disease, cerebrovascular disease, chronic lung disease, diabetes, hypertension and smoking), the type and dose of dialysis treatment, details about kidney transplantation and, from April 1, 1991, measurements of height and dialysate-plasma creatinine ratio at 4 h (D-P Cr 4h). Peritoneal equilibration tests (PETs) were requested to be performed at least 4 weeks apart from any peritonitis episodes for all patients after April 1, 1991.

The present study included all 13 947 episodes of PD in all 11 979 patients in the ANZDATA registry, who started an episode of PD treatment for ESRD between April 1, 1991 and March 31, 2004. For this study, PD included continuous ambulatory PD, automated PD using cyclers and tidal PD. Height and weight records were available for 13 666 episodes (98%) to calculate body mass index (BMI). BMI was calculated from the quotient of the weight and the square of the height at the commencement of RRT and was analysed as a continuous variable. Peritoneal transport status was analysed as a categorical variable according to the four groupings of D-P Cr 4h values defined by Twardowski *et al.* (low, <0.50 ; low average, $0.50\text{--}0.64$; high average, $0.65\text{--}0.80$; and high, ≥ 0.81) [8]. In adults, the estimated glomerular filtration rate (eGFR) at the time of initiation of PD was calculated by using the abbreviated (four variable) MDRD formula [$\text{eGFR (ml/min/1.73 m}^2\text{)} = 186 \times (\text{serum creatinine in mg/dl})^{-1.154} \times (\text{age})^{-0.203} \times (0.742 \text{ if female}) \times (1.210 \text{ if African-American)}$]. In children, the eGFR was calculated by using the Schwartz equation [$\text{eGFR (ml/min)} = \text{K} \times \text{height in cm/serum creatinine in mg/dl}$; K varies with age and gender

(0.33 pre-term infants; 0.45 full-term infants; 0.55 both sexes 2–12 years; 0.55 girls 13–21 years; 0.70 boys 13–21 years)]. For patients with failed native kidneys, the duration of ESRD prior to PD was defined as the total duration of dialysis (PD and haemodialysis) before commencement of the current episode of PD. For the patients in the failed allograft group, the duration of ESRD prior to post-transplant PD was calculated by adding the total duration of dialysis (PD and haemodialysis) before transplantation to the duration of any dialysis between loss of the allograft and starting PD. If the patient had received a pre-emptive kidney transplant, the pre-transplant duration of ESRD was assigned zero time. The duration of ESRD before starting PD was expressed in months and was analysed as a continuous variable.

The outcomes examined were patient death, technique failure and occurrence of the first episode of peritonitis. If a patient died within 60 days after transfer to haemodialysis, then the death was attributed to PD, because such early deaths were considered to reflect the health status of patients during the period of failing PD therapy. In contrast, deaths that occurred in <60 days after cessation of PD due to renal transplantation were not attributed to PD, and such episodes were censored at the end of PD treatment. Death-censored technique failure was defined as a transfer from PD to haemodialysis for >1 month and was examined without counting death during treatment as a failure. The date of the first episode of peritonitis was recorded in all patients. For these three outcomes, survival time was calculated from the date of commencement of each PD episode to the date of death, transfer to haemodialysis, occurrence of first episode of peritonitis, transplantation, loss to follow-up or March 31, 2004.

Statistical analysis

Results were expressed as frequencies and percentages for categorical variables, mean \pm SD for continuous variables, and median and interquartile range for non-parametric data. The patients were divided into two groups, (i) with failed native kidneys (non-Tx group); and (ii) with failed allografts (fTx group). Distributions of categorical variables across the two groups were compared by means of χ^2 test, continuous variables by *t*-test if parametric, and Mann-Whitney test if non-parametric. Multivariate Cox proportional hazards models with backward stepwise elimination processes utilizing the likelihood ratio test were used to determine independent predictors of survival outcomes. The covariates included in the Cox models were failed allograft or native kidneys, gender, age, race, coronary artery disease, peripheral vascular disease, cerebrovascular disease, chronic lung disease, diabetes mellitus, smoking, BMI (continuous variable), time from commencement of first RRT to the first episode of PD in months (continuous variable) and country of residence. In contrast to our previous analyses where BMI was used as a categorical variable, in the present study BMI was used as continuous variable so that Cox proportional hazards assumptions were met. The effect of duration of a functioning allograft on subsequent PD outcomes was also examined. For all outcomes examined, we utilized the conditional risk set model for the multiple failure data, and analysis was stratified by failure order according to the episode number [9]. Standard errors were calculated by using robust variance estimation for the cluster-correlated

Table 1. Patient characteristics at commencement of PD

Characteristic	All patients	Non-Tx group	fTx group
No. of observations	13 947	13 638 (97.8%)	309 (2.2%)
Female gender	6678 (47.9%)	6520 (47.8%)	158 (51.1%)
Age (years) ^a	56.9 ± 16.8	57 ± 16.5	37.6 ± 16.6
Racial origin ^b			
Caucasians	10 050 (72.1%)	9802 (71.9%)	248 (80.3%)
Aboriginal, Torres Strait Islander	868 (6.2%)	862 (6.3%)	6 (1.9%)
Maori, Pacific Islander, Cook Islander, Samoan, Tongan	1813 (13%)	1783 (13.1%)	30 (9.7%)
Asian	988 (7.1%)	966 (7.1%)	22 (7.1%)
Others	228 (1.6%)	225 (1.6%)	3 (1%)
Chronic lung disease ^a	2011 (14.4%)	2001 (14.7%)	10 (3.2%)
Coronary artery disease ^a	5404 (38.7%)	5377 (39.4%)	27 (8.7%)
Peripheral vascular disease ^a	3855 (27.6%)	3834 (28.1%)	21 (6.8%)
Cerebrovascular disease ^a	2124 (15.2%)	2111 (15.5%)	13 (4.2%)
Diabetes mellitus ^a	4884 (35%)	4837 (35.5%)	47 (15.2%)
Smoking status ^a			
Never	6887 (49.4%)	6698 (49.1%)	189 (61.2%)
Former	5316 (38.1%)	5242 (38.4%)	74 (23.9%)
Current	1744 (12.5%)	1698 (12.5%)	46 (14.9%)
eGFR (months) (median, IQR) ^b	6.2 (4.7–8.3)	6.3 (4.8–8.3)	5.3 (4.1–8.4)
Body mass index (kg/m ²) ^a	25.4 ± 5.8	25.5 ± 5.3	22.8 ± 4.6
D-P Cr 4h ^b	0.69 ± 0.12	0.69 ± 0.12	0.66 ± 0.12
Peritoneal membrane transport status			
Low	279 (5.1%)	269 (5%)	10 (7.3%)
Low average	1621 (29.5%)	1572 (29.3%)	49 (35.8%)
High average	2740 (49.9%)	2679 (50%)	61 (44.5%)
High	856 (15.6%)	839 (15.7%)	17 (12.4%)
Duration of ESRD prior to PD (months) ^a	0 (0–2.2)	0 (0–1.9)	17 (8–30.4)
Residence in New Zealand ^b	3371 (24.2%)	3280 (24.1%)	91 (29.4%)
Duration of follow-up of PD (months) (median, IQR) ^b	15 (6.3–28.9)	15 (6.3–28.9)	12.4 (5.3–25.4)
End-points: per 100 person-years (95% CI)			
Death ^a	16.9 (16.3–17.4)	17 (16.5–17.5)	10.8 (8–14.2)
Death-censored technique failure ^b	24.2 (23.6–24.9)	24.1 (23.5–24.8)	28.9 (24.2–34.2)
Occurrence of first episode of peritonitis ^b	51.6 (50.4–52.9)	51.8 (50.6–53.1)	40 (32.1–49.3)

Values in italics are representative of model B.

Non-Tx group = native kidney failure group; fTx group = allograft failure group; eGFR = estimated glomerular filtration rate; D-P Cr 4h = dialysate–plasma creatinine ratio at 4h; IQR = interquartile range; ESRD = end-stage renal disease; 95% CI = 95% confidence interval.

^a*P* < 0.001.

^b*P* < 0.05.

data [10,11]. Proportional hazards assumptions were checked by Schoenfeld residuals and scaled Schoenfeld residuals, examined by formal hypothesis test and graphically. First-order interaction terms between the significant covariates were examined for all models. Where interaction terms were significant, weighted hazard ratios (HRs; following stratification by the significant interaction term) are given. When there were no significant first-order interactions, adjusted HRs are given.

The primary analysis examined all the above covariates and included all 13 947 episodes of PD recorded in the Registry. Henceforth, this primary model is referred to as 'model A'. In view of the possible importance of D-P Cr 4h with respect to influencing PD outcomes, a secondary analysis was performed which included this covariate. This secondary analysis included 5496 episodes of PD. Henceforth, this secondary model is referred to as 'model B'. An alternative analysis was performed by adding the continuous covariate eGFR in model B (complete data available in 4893 subjects). Since the alternative analysis (data not shown) did not alter the results of model B, it was not considered for final presentation. *P*-values < 0.05 were considered statistically significant. Statistical analyses were performed using Stata 8.0 (College Station, TX) statistical software.

Results

Patient characteristics

Between April 1, 1991 and March 31, 2004, a total of 11 979 patients commenced PD, of whom 1617 patients had more than one episode of PD recorded in the Registry. Thus, a total of 13 947 episodes of PD were recorded over 23 579 person-years of follow-up. Of these, 309 episodes (2.2%) were started after allograft failure. As expected, the two groups, namely native kidney failure (non-Tx group) and allograft failure (fTx group), were different in many aspects (Table 1). The patients in the fTx group were more likely to be younger (37.6 ± 16.6 vs 57 ± 16.5 years, *P* < 0.01), Caucasian (80.3 vs 71.9%, *P* < 0.01), residents of New Zealand (29.4 vs 21.4%, *P* = 0.028) and life-long non-smokers (61.2 vs 49.1%, *P* < 0.01) with lower BMIs (22.8 ± 4.6 vs 25.5 ± 5.3 kg/m², *P* < 0.01) and a longer duration of ESRD prior to PD [17 (8–30.4) vs 0 (0–1.9) months, *P* < 0.01]. They also had significantly fewer co-morbid conditions, such as chronic lung disease, cardiovascular disease and diabetes mellitus. Although

Table 2. Risk of patient death by multivariate Cox proportional hazard model

Covariate	Model A		Model B	
	WHR (95% CI)	P	WHR (95% CI)	P
PD after allograft failure	1.09 (0.81–1.45)	0.582	1.32 (0.76–2.31)	0.328
Age	1.04 (1.03–1.04)	<0.001	1.04 (1.04–1.05)	<0.001
Racial origin				
Caucasians	Reference		Reference	
Aboriginal, Torres Strait Islander	1.29 (1.11–1.50)	0.001	1.48 (1.13–1.93)	0.004
Maori, Pacific Islander, Cook Islander, Samoan, Tongan	0.88 (0.79–0.99)	0.037	0.71 (0.57–0.89)	0.003
Asian	0.64 (0.56–0.74)	<0.001	0.68 (0.53–0.86)	0.001
Others	0.70 (0.52–0.95)	0.021		
Chronic lung disease	1.23 (1.13–1.33)	<0.001		
Coronary artery disease	1.49 (1.38–1.60)	<0.001	1.66 (1.44–1.90)	<0.001
Peripheral vascular disease	1.34 (1.24–1.45)	<0.001	1.50 (1.30–1.72)	<0.001
Cerebrovascular disease	1.25 (1.15–1.35)	<0.001		
Diabetes mellitus	1.45 (1.35–1.56)	<0.001	1.60 (1.39–1.83)	<0.001
Body mass index	1.02 (1.00–1.03)	0.016		
Residence in New Zealand	1.18 (1.08–1.29)	<0.001	1.35 (1.14–1.59)	0.001
Peritoneal membrane transport status				
Low				
Low average			Reference	
High average				
High			1.28 (1.07–1.53)	0.006
Duration of ESRD prior to PD (months)	1.02 (1.01–1.02)	<0.001	1.02 (1.01–1.02)	<0.001

WHR = weighted hazard ratio; CI = confidence interval; ESRD = end-stage renal disease.

the proportions of the four peritoneal transport categories were not different between the two groups, the patients in the fTx group had slightly lower D-P Cr 4h values (0.66 ± 0.12 vs 0.69 ± 0.12 , $P = 0.009$). The median duration of prior allograft function was 23.7 months (interquartile range 0.2–62.2 months) and 154 patients (49.8%) had >2 years of graft function.

Patient survival

The patients from the fTx group experienced a lower death rate [10.8 per 100 person-years, 95% confidence interval (CI) 8–14.2] than those in the non-Tx group (17 per 100 person-years, 95% CI 16.5–17.5, $P < 0.01$). On univariate Kaplan–Meier analysis of model A, the patients in the fTx group enjoyed lower mortality (unadjusted HR 0.50, 95% CI 0.37–0.68, $P < 0.01$). Other factors that were associated with lower patient mortality included female gender, younger age, Asian and miscellaneous racial origin, non-smoking, lower BMI, shorter duration from the first RRT to commencement of PD and the absence of co-morbid conditions (chronic lung disease, coronary artery disease, peripheral vascular disease, cerebrovascular disease and diabetes). Duration of renal allograft function prior to failure was not significantly associated with subsequent patient survival on PD (<6 months unadjusted HR 1.63, 95% CI 0.87–3.06; 6–24 months HR 1.13, 95% CI 0.46–2.75; >24 months reference). On univariate analysis of model B, peritoneal transport status was additionally found to be associated with mortality; specifically, high average and high transporter statuses were associated with increased mortality.

In the multivariate analyses of model A, the patients in the fTx group had mortality comparable with those in the non-Tx group (weighted HR 1.09, 95% CI 0.81–1.45, $P = 0.582$) (Table 2). Mortality was independently associated with Aboriginal and Torres Strait Islander racial origin, residence in New Zealand, coronary artery disease, peripheral vascular disease, cerebrovascular disease, chronic lung disease and greater length of time between the first RRT and commencement of PD. A significant first-order interaction was observed between age and diabetes, and, when these groups were analysed separately, the older and diabetic patients had worse survival than the younger and non-diabetic ones.

When multivariate analysis of model B was performed by adding D-P Cr 4h, the fTx group was still found to have a mortality that was not significantly different from the non-Tx group (adjusted HR 1.32, 95% CI 0.76–2.31, $P = 0.328$) (Table 2). High transporters and BMI were both independently associated with increased mortality. However, a number of covariates associated with mortality in model A were no longer found to be significant following the inclusion of D-P Cr 4h in model B (including miscellaneous racial origin, chronic lung disease and cerebrovascular disease). Significant interaction was also noted between age and diabetes in model B (data not shown).

Death-censored technique survival

The patients from the fTx group experienced a higher death-censored technique failure rate (28.9 per 100 person-years, 95% CI 24.2–34.2) than those in the non-Tx group (24.1 per 100 person-years, 95% CI 23.5–24.8,

Table 3. Risk of death-censored technique failure by the multivariate Cox proportional hazard model

Covariate	Model A		Model B	
	AHR (95% CI)	<i>P</i>	AHR (95% CI)	<i>P</i>
PD after allograft failure	0.91 (0.75–1.10)	0.315	1.03 (0.75–1.42)	0.856
Female	0.93 (0.89–0.99)	0.016		
Racial origin				
Caucasians	Reference		Reference	
Aboriginal, Torres Strait Islander	1.38 (1.26–1.52)	<0.001	1.37 (1.15–1.62)	<0.001
Maori, Pacific Islander, Cook Islander, Samoan, Tongan				
Asian	0.82 (0.73–0.91)	<0.001	0.81 (0.68–0.95)	0.012
Others				
Chronic lung disease	1.09 (1.01–1.17)	0.023		
Body mass index	1.02 (1.01–1.02)	<0.001	1.03 (1.02–1.04)	<0.001
Residence in New Zealand	0.60 (0.55–0.65)	<0.001	0.66 (0.57–0.77)	<0.001
Peritoneal membrane transport status				
Low			Reference	
Low average				
High average				
High			1.17 (1.02–1.35)	0.028

AHR = adjusted hazard ratio; CI = confidence interval.

Table 4. Risk of developing peritonitis by multivariate Cox proportional hazard model

Covariate	Model A		Model B	
	AHR (95% CI)	<i>P</i>	AHR (95% CI)	<i>P</i>
PD after failed allograft	0.92 (0.72–1.16)	0.444	0.88 (0.60–1.30)	0.522
Age			1.00 (1.00–1.00)	0.044
Racial origin				
Caucasians	Reference		Reference	
Aboriginal, Torres Strait Islander	1.58 (1.44–1.75)	<0.001	1.64 (1.39–1.94)	<0.001
Maori, Pacific Islander, Cook Islander, Samoan, Tongan	1.57 (1.46–1.69)	<0.001	1.70 (1.51–1.92)	<0.001
Asian	0.83 (0.75–0.91)	<0.001	0.87 (0.75–1.00)	0.051
Others	0.82 (0.67–0.99)	0.037		
Coronary artery disease	1.08 (1.02–1.13)	0.008		
Cerebrovascular disease	1.08 (1.01–1.16)	0.032		
Diabetes mellitus	1.09 (1.03–1.15)	0.004	1.11 (1.02–1.21)	0.018
Smoking status				
Never			Reference	
Former				
Current			1.18 (1.04–1.33)	0.009
Body mass index	1.01 (1.00–1.01)	0.034	1.01 (1.01–1.02)	0.001
Peritoneal membrane transport status				
Low			Reference	
Low average				
High average				
High			1.15 (1.02–1.29)	0.027

AHR = adjusted hazard ratio; CI = confidence interval.

$P=0.049$). On univariate analysis of model A, fTx patients had a lower death-censored technique failure rate (HR 0.79, 95% CI 0.65–0.95, $P=0.012$). Predictors of a higher death-censored technique failure rate included Aboriginal and Torres Strait Islander racial origin, Australian residents, chronic lung disease, current smoking status and higher BMI. Duration of renal allograft function prior to failure was not significantly associated with subsequent death-censored PD technique survival (<6 months HR 1.10, 95% CI 0.74–1.61; 6–24 months HR 0.59, 95% CI 0.34–1.03; >24 months reference). On univariate analysis of model B, the patients in the fTx group had technique

survival comparable with the non-Tx group (HR 0.91, 95% CI 0.66–1.25, $P=0.55$), whilst high peritoneal membrane transport status was associated with technique failure.

On multivariate Cox proportional hazards model analyses, no significant differences in technique survival were observed between the fTx and non-Tx groups in either model A (adjusted HR 0.91, 95% CI 0.75–1.09, $P=0.318$) or model B (adjusted HR 1.02, 95% CI 0.74–1.41, $P=0.908$) (Table 3). There were no significant first-order interactions in either model. In model A, death-censored technique failure was independently associated with male gender, Aboriginal and

Torres Strait Islander racial origin, chronic lung disease and higher BMI. In model B, high peritoneal transport status was additionally associated with poor technique survival, whereas male gender and chronic lung disease were not.

Peritonitis-free survival

Median time to the first peritonitis in the fTx group was longer than in the non-Tx group [20.4 months (95% CI 13.9–26.9) vs 15.2 months (95% CI 14.6–15.8), $P=0.02$]. On univariate analyses of models A and B, this difference was not significant (model A, HR 0.82, 95% CI 0.65–1.03, $P=0.083$; model B, HR 0.77, 95% CI 0.53–1.12, $P=0.176$). Poorer peritonitis-free survival was associated in model A with Aboriginal and Torres Strait Islander racial origin, Maori and Pacific Islander racial origin, New Zealand residence, chronic lung disease, coronary artery disease, peripheral vascular disease, cerebrovascular disease, diabetes, life-long smoking and BMI. On univariate analysis of model B, poorer peritonitis-free survival was additionally associated with high peritoneal membrane transport status, but not with chronic lung disease, peripheral vascular or cerebrovascular disease.

After adjusting for all other covariates in multivariate Cox proportional hazard model A, the patients from the fTx group had a peritonitis-free survival comparable with those in the non-Tx group (adjusted HR 0.93, 95% CI 0.73–1.18, $P=0.544$; Table 4). There were no significant first-order interactions. Poorer peritonitis-free survival was independently associated with Aboriginal and Torres Strait Islander racial origin, Maori and Pacific Islander racial origin, coronary artery disease, cerebrovascular disease, diabetes and BMI. The patients of Asian and miscellaneous racial origins had better peritonitis-free survival. On multivariate analysis of model B, fTx was again not independently associated with peritonitis-free survival (adjusted HR 0.88, 95% CI 0.60–1.30, $P=0.520$; Table 4). Poorer peritonitis-free survival was independently associated with high peritoneal membrane transport status, current smoking status and age.

Discussion

The present study demonstrates that patients starting PD after renal allograft failure have mortality, death-censored technique and peritonitis-free survival comparable with patients commencing PD following native graft failure, once adjustments are made for differences in baseline characteristics. To our knowledge, this investigation is the first, large-scale, multi-centre comparison of PD outcomes between patients with failed kidney transplants and those with failed native kidneys.

Our findings are similar to those of two previous smaller, single-centre studies [5,6]. Duman *et al.* [6] reported that previous renal transplantation did not significantly adversely affect patient and technique survival in 116 prevalent PD patients (34 failed allografts, 82 failed native kidneys). Although the failed transplant group did experience a higher frequency of peritonitis episodes, these results were questionable in view of the study's retrospective design (thereby potentially introducing recall bias), use of prevalent patients (thereby potentially introducing informative censoring bias) and lack of statistical adjustment for differences in baseline characteristics between the two groups. Davies [5] similarly demonstrated in a prospective, single-centre study of 28 PD subjects with failed allografts that patient and technique survival rates were not significantly different from those of 469 incident PD patients with failed native kidneys following multivariate Cox proportional hazards model analysis. Peritonitis-free survival was not examined and the sample size was too small to exclude a type 2 statistical error with confidence.

In contrast, Sasal and associates [4] noted significantly worse survival, technique survival and peritonitis rates in 42 PD patients with failed renal allografts compared with a randomly selected cohort of 43 never-transplanted PD patients matched for age and the presence of diabetes. These findings may represent confounding, because all statistical analyses were univariate and the results were therefore unadjusted for differences in baseline characteristics (other than age and diabetes). Moreover, the vintage of the cohort (1989–1996) may not have been generalizable to contemporary PD practice. Recently, Guo and co-workers [12] have reported better 1-, 2- and 3-year survival in patients with failed grafts on PD, when compared with the patients who were new to dialysis in the USA. In this study, the groups were not adjusted for age and co-morbid conditions.

The obvious confounder in the present study was the duration of ESRD before starting PD, as the patients returning to dialysis after allograft failure are likely to have been on dialysis prior to transplantation. Similarly, not all the patients commencing PD after native kidney failure started PD as their first renal replacement therapy option. However, when the duration of ESRD was adjusted for in the multivariate analyses, the survival outcomes were not significantly different between the two groups. Interestingly, it was found that a longer duration of ESRD before commencing PD (i.e. a longer duration between first RRT of any type and starting PD) was also associated with increased mortality (adjusted HR 1.02, $P<0.01$). In contrast, the duration of renal allograft function did not appear to impact significantly on subsequent PD outcomes in this study. Whether grafts functioned for <6 months, between 6 and 24 months or for >24 months, no significant differences were observed for patient mortality or death-censored technique failure on either univariate or multivariate analyses.

Earlier studies have also shown that PD patients with high transport status are more prone to faster loss of residual renal function, development of ultrafiltration failure and mortality [13–16]. Hence, we performed a secondary analysis on 5496 PD episodes where D-P Cr 4h measurements were available. High peritoneal membrane transport status was consistently associated with increased patient mortality, technique failure and shorter time to first peritonitis. However, the inclusion of D-P Cr 4h in the multivariate Cox proportional hazards model did not alter the principal findings of our study that patient, technique and peritonitis-free survival were not significantly different between PD patients with failed allografts and those that had never been transplanted.

The strengths of this study lie in its large sample size and the rigorousness and the robustness of the statistical analyses performed. Owing to the coverage of the ANZDATA registry, we were able to analyse the outcomes of relatively large numbers of PD patients both with and without failed renal transplants. Since we included all centres across both countries, we could avoid the bias associated with reports from single centres, which may have had particular interest and expertise in PD that may influence outcome. There were 1617 patients with more than one episode of PD. To analyse such cluster-correlated and multiple failure data, we used the conditional risk set model and robust variance estimator. Thus, not only all the patients but also all the PD episodes recorded in the Registry were included in the study. The patients in the post-transplant group were significantly different in most of the characteristics; hence, all of these characteristics were adjusted for in the multivariate Cox proportional hazards models. D-P Cr 4h data were available in only 39.3% of patients. This subgroup of patients had different demographic features from the rest of the population. Hence, instead of extrapolating results from this subset to a larger population, we decided to analyse this subgroup of patients separately and found that it did not alter the conclusions drawn in this study. Our cohort also consisted solely of incident patients, thereby avoiding the potentially confounding factor of survivor bias associated with prevalent population studies.

Nevertheless, the study also had a number of limitations. The pattern and effect of loss of residual renal function in post-transplant patients on the various outcomes were not studied. Also, the dose and duration of continued immunosuppression after commencing dialysis, dose of dialysis and the centre-size effect were not taken into consideration. We have not studied the outcomes between the patients with failed graft commencing haemodialysis and PD. This may be particularly important if the selection of dialysis modality differs between patients with and without failed renal allografts. Registry data also represent a compromise between the extent and depth of coverage. This was particularly apparent in the reporting of peritonitis where we were unable to ascertain the nature or detailed outcome of individual episodes of

peritonitis. Thus, a serious episode of complicated peritonitis is treated in the same fashion as a quickly resolved issue, which has little impact on long-term outcome. While we were able to adjust for reported co-morbidities on a categorical basis, ANZDATA does not collect information about the severity of co-morbidities, such that it is difficult to exclude entirely the possibility of residual confounding. Finally, since the differences in age and other reported co-morbidities were extremely large, it is possible that even after statistical adjustment there still remains a difference in these baseline characteristics.

In conclusion, the results of our study show that patients commencing PD after allograft failure experience patient survival, death-censored technique survival and peritonitis-free survival comparable with those with native kidney failure. The mortality is determined predominantly by age and co-morbid conditions. PD appears to be a safe and viable option for the patients returning to dialysis after failed graft.

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Conflict of interest statement. None declared.

References

1. Excell L, Chadban S, McDonald SP. *ANZDATA Registry Annual Report 2004*. The ANZDATA Dialysis and Transplant Registry, Adelaide, 2004; 74–91
2. 2004 Annual Report of the U.S. Organ Procurement and Transplantation Network and the Scientific Registry of Transplant Recipients. *Transplant Data 1994–2003*. Ann Arbor, MI, Department of Health and Human Services, Health Resources and Services Administration, Healthcare Systems Bureau, Division of Transplantation, Rockville, MD; United Network for Organ Sharing, Richmond, VA; University Renal Research and Education Association
3. Kaplan B, Meier-Kriesche HU. Death after graft loss: an important late study endpoint in kidney transplantation. *Am J Transplant* 2002; 2: 970–974
4. Sasal J, Naimark D, Klassen J, Shea J, Bargman JM. Late renal transplant failure: an adverse prognostic factor at initiation of peritoneal dialysis. *Perit Dial Int* 2001; 21: 405–410
5. Davies SJ. Peritoneal dialysis in the patient with a failing renal allograft. *Perit Dial Int* 2001; 21 [Suppl 3]: S280–S284
6. Duman S, Asci G, Toz H *et al.* Patients with failed renal transplant may be suitable for peritoneal dialysis. *Int Urol Nephrol* 2004; 36: 249–252
7. Russ GR. *ANZDATA Registry Report 2001*. The ANZDATA Dialysis and Transplant Registry, Adelaide, 2001
8. Twardowski ZJ, Nolph KD, Khanna R. Peritoneal equilibration test. *Perit Dial Bull* 1987; 7: 138–147
9. Prentice RL, Williams BJ, Peterson AV. On the regression analysis of multivariate failure time data. *Biometrika* 1981; 68: 373–379
10. Williams RL. A note on robust variance estimation for cluster-correlated data. *Biometrics* 2000; 56: 645–646

11. Lin D, Wei L. The robust inference for the Cox proportional hazards model. *J Am Stat Assoc* 1989; 84: 1074–1078
12. Guo A, Mujais S. Patient and technique survival on peritoneal dialysis in the United States: evaluation in large incident cohorts. *Kidney Int* 2003; 64 [Suppl 88]: S3–S12
13. Johnson DW, Mudge DW, Sturtevant JM *et al*. Predictors of decline of residual renal function in new peritoneal dialysis patients. *Perit Dial Int* 2003; 23: 276–283
14. Churchill DN, Thorpe KE, Nolph KD, Keshaviah PR, Oreopoulos DG, Page D. Increased peritoneal membrane transport is associated with decreased patient and technique survival for continuous peritoneal dialysis patients. The Canada–USA [CANUSA] Peritoneal Dialysis Study Group. *J Am Soc Nephrol* 1998; 9: 1285–1292
15. Davies SJ, Phillips L, Griffiths AM, Russell LH, Naish PF, Russell GI. What really happens to people on long-term peritoneal dialysis? *Kidney Int* 1998; 54: 2207–2217
16. Davies SJ, Phillips L, Russell GI. Peritoneal solute transport predicts survival on CAPD independently of residual renal function. *Nephrol Dial Transplant* 1998; 13: 962–968

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