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# Rate of decline of residual renal function is associated with all-cause mortality and technique failure in patients on long-term peritoneal dialysis

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## Abstract

**Background.** Residual renal function (RRF) at the initiation of peritoneal dialysis (PD) therapy can predict patient outcome. However, RRF declines with time at variable rates in different patients. This study was performed to compare the impact of baseline RRF and the rate of RRF decline on patient survival and on death-censored technique survival after initiation of long-term PD.

**Methods.** We enrolled 270 patients with sufficient urine amount (daily urine volume >100 mL) from a medical centre in North Taiwan who began PD between January 1996 and December 2005 and followed them until December 2007. The study population was stratified by the decline rate of RRF into a fast, intermediate and slow decline group. The Kaplan–Meier survival analysis was used to determine patient survival and technique survival. The Cox regression model was used to identify factors associated with patient outcome. The proportional odds polychotomous logistic regression model was used to identify variables associated with rapid decline of RRF.

**Results.** During an average follow-up period of 45 months, 50 (18.5%) deaths, 67 (24.8%) death-censored technique failures (transfer to haemodialysis) and 43 (15.9%) renal transplantations occurred. The median rate of RRF decline was 0.885 mL/min/1.73 $m^2$ per year. Survival analysis showed that patients with fast RRF decline had worse survival and increased risk of technique failure. The multivariate Cox regression model confirmed that the rate of RRF decline was an independent factor associated with patient and technique survival and was a more powerful prognostic factor than basal RRF. Variables associated with a rapid decline of RRF were larger body mass index, presence of diabetes, prior history of congestive heart failure, use of diuretics, peritonitis episodes and hypotensive events.

**Conclusions.** Our data indicate that the rate of decline of RRF is a more powerful prognostic factor than baseline RRF associated with all-cause mortality and technique failure in patients on long-term PD. To prevent accelerated loss of RRF, it is imperative that every effort be made to avoid overdiuresis, peritonitis and hypotensive episodes, especially in those with diabetes, obesity and congestive heart failure.

**Keywords:** peritoneal dialysis; residual renal function; survival; technique failure

## Introduction

Preservation of residual renal function (RRF) is associated with better survival in patients with end-stage renal disease (ESRD) who are undergoing long-term peritoneal dialysis (PD). Presumably, this is because RRF has beneficial effects on blood pressure control, left ventricular hypertrophy, sodium and fluid removal, nutritional status, haemoglobin and bicarbonate maintenance, and β2-microglobulin clearance [1–3]. This has been confirmed by several recent studies, which showed that RRF, but not peritoneal clearance, was closely associated with patient survival and, to a lesser extent, technique survival during PD therapy [4–8]. Thus, it is clear that therapeutic strategies that preserve RRF are associated with more favourable PD outcomes [9].

Many PD studies emphasize the importance of RRF at the initiation of PD. However, baseline RRF tends to decline after initiation of long-term dialysis [10], and numerous causal factors have been identified [11–14]. Given the progressively deteriorating nature of RRF, we hypothesized that the rate of RRF decline, rather than baseline RRF, would be a better prognostic factor associated with patient and technique survival. In this retrospective cohort study, we compared the effects of baseline RRF and the rate of RRF decline on PD outcome for patients at a single medical centre in northern Taiwan.

## Subjects and methods

### *Study population*

This study was approved by the National Taiwan University Hospital (NTUH) research ethics committee (No. 200804058R). Four hundred and twenty-one patients who started PD at the NTUH during January 1996 and December 2005 were screened for eligibility. Among these patients, 81 patients were excluded due to lack of initial biochemical data ($n = 10$), failed renal transplant ($n = 8$) and discontinuation of PD treatment within 6 months ($n = 63$). The reasons for discontinuation of PD included death (28 patients), shift to haemodialysis (18 patients), transfer to other hospitals (10 patients), renal transplantation (5 patients) and recovery of renal function (2 patients). In addition, 70 patients were excluded due to the anuric status at the start of PD (daily urine amount <100 mL). Most of them had undergone preceding acute haemodialysis before changing to long-term PD therapy. Finally, a total of 270 patients were included in this study.

### *Decline of RRF and patient outcomes*

RRF for the 270 patients was calculated as the arithmetic mean of 24-h urea nitrogen and creatinine clearance, which were measured within 3 months following initiation of PD, and thereafter at 3- to 6-month intervals. RRF was normalized to body surface area using the Du Bois formula and the patient's dry weight [15]. The study population was categorized as the 'fast' ($n = 90$), 'intermediate' ($n = 90$) and 'slow' ($n = 90$) decline groups according to the tertiles of the calculated RRF decline rate.

All patients were followed until death, transfer to HD, kidney transplantation or transfer to other institutions. The primary outcomes were death from any cause and technique failure. Technique failure was defined as discontinuation of PD and transfer to haemodialysis. Patients remaining on long-term PD were censored at the end of the study in December 2007. For the analysis of patient overall survival, the event was death, and kidney transplantation, transfer to HD or transfer to another institution was the censored observation. For the analysis of technique survival, transfer to HD was the event, and censored observations included death, kidney transplantation and transfer to another institution. For the analysis of combined patient and technique survival, death or technique failure was the event of interest, and kidney transplantation or transfer to other institutions were the censored observations.

Other patient-specific data such as demographics, dialysis adequacy, peritoneal transport and laboratory results were recorded at the time of enrolment. Use of antihypertensive drugs and diuretics from the start of PD therapy, hypotensive events (defined as systolic blood pressure <100 mmHg requiring nursing interventions) and episodes of peritonitis were also documented by reviewing medical charts.

### *Statistical analysis*

The data were expressed as mean ± standard deviation (SD) for normally distributed continuous variables, median and range for non-normally distributed continuous variables, and frequency with percentage (%) for categorical variables. Group differences were assessed by the two-sample *t*-test or one-way analysis of variance (ANOVA) for normally distributed continuous variables, the Mann–Whitney *U*-test or the Kruskal–Wallis test for non-normally distributed continuous variables, and the chi-square test for categorical variables. The Kaplan–Meier estimate of the survival curve and the log-rank test were performed for descriptive analysis of survival data.

To investigate the association of the rapidity of RRF decline with patient outcome, the multivariate time-dependent Cox regression model was used to determine statistically significant factors associated with patient overall survival, death-censored technique survival, as well as combined patient and death-censored technique survival. RRF and the decline rate of RRF were treated as time-dependent variables in the Cox regression model using the so-called counting process approach. The time-dependent decline rate of RRF was defined as the number of units of RRF decline per month from baseline to each time at which an outcome event occurred. The non-time-dependent variables considered in the regression analysis were age, sex, mode of PD, peritoneal transport status, underlying diabetes mellitus (DM), hypertension (HTN), coronary artery disease (CAD), congestive heart failure (CHF) and the baseline data of body mass index (BMI), serum albumin, normalized protein nitrogen appearance rate (nPNA), haematocrit, as well as the dialysis indices (total KT/V, peritoneal KT/V and RRF). On the other hand, the polychotomous proportional odds logistic regression model was performed to identify statistically significant risk factors that were associated with a rapid decline of RRF.

The goal of regression analysis is to find parsimonious regression models that fit the observed data well. To ensure the quality of analysis results, the basic model-fitting techniques for (1) variable selection, (2) goodness-of-fit assessment and (3) regression diagnostics were used in our regression analyses whenever applicable. Specifically, in the stepwise variable selection procedure, all the univariate significant and non-significant covariates were considered and the significance levels for entry (SLE) and for stay (SLS) were set to 0.15 or larger. Both the GOF measures, including percentage of concordant pairs, estimated area under the receiver operating characteristic (ROC) curve, adjusted generalized $R^2$ (for logistic regression model) and adjusted generalized $R^2$ (for Cox's proportional hazards model) and the GOF tests, including the deviance GOF test, Pearson's chi-squared GOF test, the Hosmer–Lemeshow GOF test (for logistic regression model) and the Grønnesby–Borgan GOF test (for Cox's proportional hazards model), were examined to assess the GOF of the fitted regression model. Yet, the values of the adjusted generalized $R^2$ for the logistic regression model and for Cox's proportional hazards model are usually low. Larger $P$ values of the deviance GOF test, Pearson chi-squared GOF test, Hosmer–Lemeshow GOF test (for logistic regression model) and Grønnesby–Borgan GOF test (for Cox's proportional hazards model) indicate better fit. Finally, the statistical tools for regression diagnostics such as verification of model assumption (e.g. proportional odds assumption and proportional hazards assumption), residual analysis, detection of influential cases and check for multicollinearity were applied to discover model or data problems. Two-sided $P \leq 0.05$ was considered statistically significant. All statistical analyses were performed using the SPSS software, version 13.0 (SPSS Inc., Chicago, IL, USA) and SAS software (Version 9.1.3, SAS Institute Inc., Cary, NC, USA).

## Results

### *Study population*

The baseline characteristics of the 270 patients are shown in Table 1. The most common primary aetiologies of ESRD included chronic glomerulonephritis (43.7%), diabetic nephropathy (17.4%) and hypertensive nephrosclerosis (8.1%). Among the 270 enrolled patients, the overall initial dialysis indices were total (peritoneal plus renal) Kt/V 2.38 ± 0.50, peritoneal Kt/V 1.77 ± 0.39 and renal Kt/V 0.61 ± 0.40. The total Kt/V among the fast decline group (2.44 ± 0.47), the intermediate decline group (2.39 ± 0.51) and the slow decline group (2.32 ± 0.50) did not differ significantly from one another ($P = 0.18$). Patients in the fast decline group were more likely to be male, older and diabetic, and more likely to have prior CHF, larger BMI, higher baseline RRF and higher residual urine volume.

### *Factors associated with patient and technique survival after start of chronic PD*

During the average follow-up time of 45 months, 50 patients (18.5%) died, 67 (24.8%) experienced death-censored technique failure (i.e. transfer to haemodialysis) and 43 (15.9%) received renal transplantation. Infection (52%) and cardiovascular disease (32%) were the most common causes of death, and peritonitis (41.8%) and inadequate small solute clearance (29.9%) were the most common causes of death-censored technique failure.

The Kaplan–Meier estimate of the survival curve and the log-rank test showed that patients with fast RRF decline were likely to have worse patient survival (Figure 1A), technique survival (Figure 1B), as well as combined patient and

**Table 1.** Comparisons of baseline demographic and clinical characteristics among patients with fast, intermediate and slow decline of residual renal function

| Variables | Patients with sufficient RRF (daily urine amount >100 mL) | | | | |
|---|---|---|---|---|---|
| | All patients ($n = 270$) | Group 1: fast decline ($n = 90$) | Group 2: intermediate ($n = 90$) | Group 3: slow decline ($n = 90$) | *P*-value |
| Age (years) | 50.4 ± 15.8 | 55.6 ± 17.0 | 46.6 ± 13.2 | 49.0 ± 15.8 | <0.001 |
| Gender (male) | 128 (47.4%) | 57 (21.1%) | 44 (16.3%) | 27 (10%) | <0.001 |
| Body mass index (kg/m$^2$) | 21.6 ± 3.3 | 22.4 ± 3.2 | 21.7 ± 3.3 | 20.8 ± 3.2 | 0.005 |
| Major causes of ESRD | | | | | |
| Chronic glomerulonephritis | 118 (43.7%) | 33 (36.7%) | 46 (51.1%) | 39 (43.3%) | 0.148 |
| Diabetic nephropathy | 47 (17.4%) | 31 (34.4%) | 10 (11.1%) | 6 (6.7%) | <0.001 |
| Hypertensive nephropathy | 22 (8.1%) | 5 (5.6%) | 9 (10.0%) | 8 (8.9%) | 0.526 |
| Major comorbid conditions | | | | | |
| Diabetes | 52 (19.2%) | 32 (35.6%) | 12 (13.3%) | 8 (8.9%) | <0.001 |
| Hypertension | 162 (60%) | 60 (66.7%) | 51 (56.7%) | 51 (56.7%) | 0.287 |
| Coronary artery disease | 19 (7.0%) | 11 (12.2%) | 5 (5.6%) | 3 (3.3%) | 0.053 |
| Congestive heart failure | 33 (12.2%) | 21 (23.3%) | 6 (6.7%) | 6 (6.7%) | <0.001 |
| Laboratory parameters | | | | | |
| Haematocrit (%) | 24.1 ± 5.2 | 25.0 ± 4.6 | 23.8 ± 5.2 | 23.6 ± 5.6 | 0.126 |
| Albumin (g/dL) | 3.6 ± 0.6 | 3.6 ± 0.6 | 3.7 ± 0.6 | 3.6 ± 0.6 | 0.554 |
| nPNA (g/kg/day) | 1.12 ± 0.27 | 1.09 ± 0.29 | 1.14 ± 0.24 | 1.14 ± 0.27 | 0.352 |
| PD-related parameters | | | | | |
| Mode (APD) | 82 (30.4%) | 30 (33.3%) | 27 (30.0%) | 25 (27.8%) | 0.719 |
| H and HA peritoneal transport | 90 (33.3%) | 38 (42.2%) | 26 (28.9%) | 26 (28.9%) | 0.091 |
| Total KT/V urea | 2.38 ± 0.50 | 2.44 ± 0.47 | 2.38 ± 0.51 | 2.31 ± 0.51 | 0.180 |
| Peritoneal KT/V urea | 1.77 ± 0.39 | 1.64 ± 0.32 | 1.80 ± 0.41 | 1.88 ± 0.40 | <0.001 |
| Renal KT/V urea | 0.61 ± 0.40 | 0.81 ± 0.39 | 0.59 ± 0.36 | 0.43 ± 0.31 | <0.001 |
| Total weekly CrCl (L/week/1.73 m$^2$) | 77.86 ± 22.67 | 87.96 ± 22.78 | 76.85 ± 20.23 | 68.78 ± 20.92 | <0.001 |
| Peritoneal weekly CrCl (L/week/1.73 m$^2$) | 39.80 ± 9.20 | 38.97 ± 8.63 | 40.92 ± 10.55 | 39.52 ± 8.25 | 0.341 |
| Renal weekly CrCl (L/week/1.73 m$^2$) | 31.34 ± 21.27 | 43.38 ± 21.80 | 29.45 ± 17.94 | 21.19 ± 17.79 | <0.001 |
| RRF (mL/min/1.73 m$^2$) | 2.75 ± 1.72 | 3.70 ± 1.71 | 2.61 ± 1.53 | 1.93 ± 1.44 | <0.001 |
| Residual urine volume (L/day) | 0.786 ± 0.516 | 0.933 ± 0.528 | 0.765 ± 0.499 | 0.660 ± 0.489 | 0.001 |

APD, automated peritoneal dialysis; CrCl, creatinine clearance; ESRD, end-stage renal disease; H, high; HA, high average; nPNA, normalized protein nitrogen appearance rate; RRF, residual renal function.

technique survival (Figure 1C), when compared to patients with slow and intermediate RRF decline. Further analysis using the Cox regression model, which treated RRF and decline rate of RRF as time-dependent variables, indicated that a more rapid rate of RRF decline was independently associated with increased risk of death-censored technique failure and was more powerful than lower baseline RRF associated with combined death and technique failure (Table 2).

### *Factors associated with RRF decline after start of chronic PD*

Among the 270 patients who had RRF at the beginning of PD, 206 patients (76.3%) became anuric during the follow-up. The mean duration from the initiation of PD to anuria was 31 months (median 28 months). At the commencement of chronic PD, RRF and renal Kt/V were 2.75 mL/min/1.73 m$^2$ (± 1.72) and 0.61 (± 0.40), respectively. The median annual rate of RRF decline was 0.885 mL/min/1.73 m$^2$ per year (range: 0–9.49 mL/min/1.73 m$^2$ per year). The fitted multivariate proportional odds polychotomous logistic regression model after adjusting age, baseline RRF and other variables showed that those who were diabetic, had a history of CHF, large BMI, used diuretics, had peritonitis episodes and suffered hypotensive events experienced more rapid decline of RRF (fast versus intermediate decline rate, or intermediate versus slow decline rate) (Table 3). The rates of RRF decline and time to anuria were stratified by these risk factors as shown in Table 4.

Finally, the most frequent causes of hypotensive events included excessive ultrafiltration (41.7%), sepsis (23.8%), heart failure (14.3%), overuse of antihypertensive agents (9.5%), acute blood loss (4.8%), severe diarrhoea (2.4%) and other unspecified causes (3.5%).

## Discussion

This study demonstrated for the first time that the rate of RRF decline is a better prognostic factor than baseline RRF for all-cause mortality and death-censored technique failure in patients on long-term PD. A faster decline of RRF is associated with worse patient and technique survival. Additional analysis indicated that diabetes, large BMI, prior history of CHF, diuretic use, peritonitis and hypotensive episodes are independent prognostic factors for rapid loss of RRF.

Preserved RRF at the initiation of dialysis is of paramount importance for patients on long-term PD [4–8]. In the re-analysis of the CANNUSA study [4] and the NECOSAD-2 study [6], a higher RRF appeared to be associated with a more favourable patient survival [4,6], and combined patient and technique survival [6]. Our study also

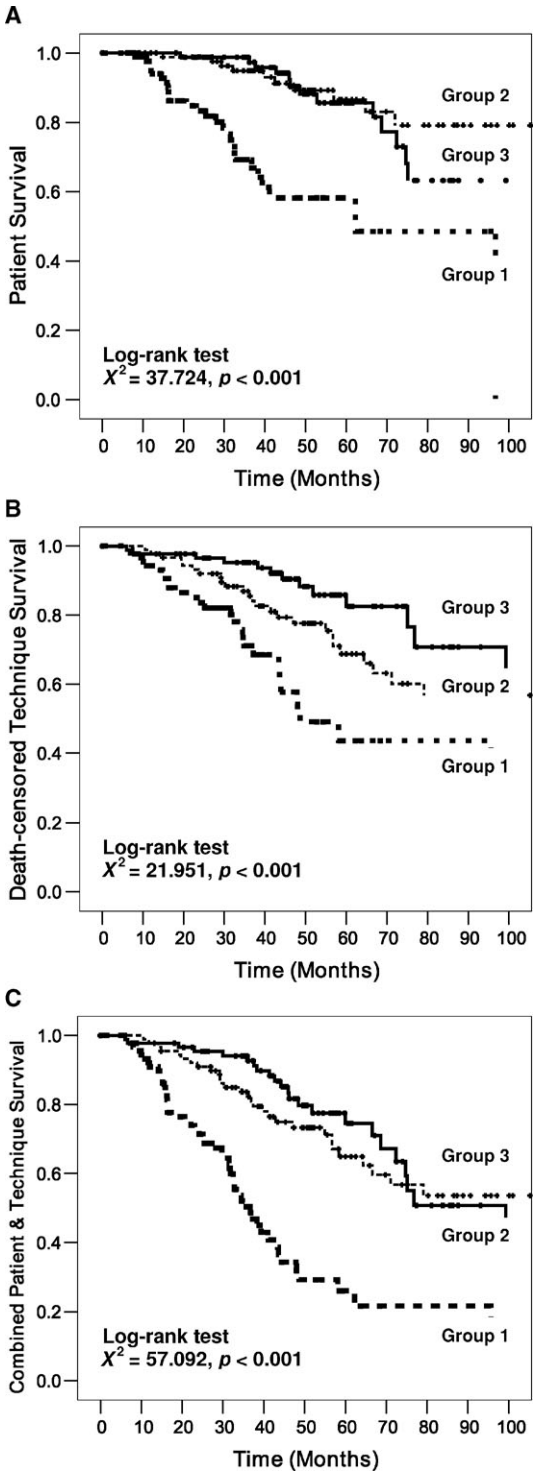


**Fig. 1.** Kaplan–Meier survival analysis demonstrated that patients with a fast decline rate of residual renal function (group 1, $n = 90$) had a worse patient survival (**A**), death-censored technique survival (**B**) as well as combined patient and technique survival (**C**) than the intermediate (group 2, $n = 90$) and slow decline counterparts (group 3, $n = 90$).

demonstrated the same beneficial effect of RRF on patient survival, as well as combined patient and technique survival (Table 2). However, baseline RRF tends to decline at different rates in different patients [10–14] and might not be a reliable factor of PD outcome. Indeed, our Cox model indicated that the rate of RRF decline was a better prognostic factor than baseline RRF for combined patient and technique survival. This suggests that the survival advantage associated with high baseline RRF [16,17] might be offset by a rapid decline of RRF after commencement of PD. In agreement with this, Davies *et al.* [18] found no difference in baseline RRF between survivors and non-survivors

**Table 2.** Independent prognostic factors associated with patient, death-censored technique and combined patient/technique survival using the multivariate time-dependent Cox regression model

| Covariate | Hazard ratio (95% CI) | *P*-value |
|---|---|---|
| Model 1: patient survival | | |
| Age (per year) | 1.053 (1.030–1.076) | <.0001 |
| DM (yes versus no) | 4.323 (2.318–8.062) | <.0001 |
| CHF (yes versus no) | 2.429 (1.233–4.785) | 0.0103 |
| RRF[a] (per mL/min/1.73 $m^2$) | 0.609 (0.408–0.910) | 0.0154 |
| Model 2: death-censored technique survival | | |
| Body mass index (per kg/$m^2$) | 1.090 (1.012–1.174) | 0.0221 |
| DM (yes versus no) | 2.819 (1.581–5.026) | 0.0004 |
| RRF decline rate[a] (per mL/min/1.73 $m^2$/month) | 2402 (16.3–354186) | 0.0022 |
| Model 3: combined patient and technique survival | | |
| Age (per year) | 1.020 (1.005–1.035) | 0.0076 |
| DM (yes versus no) | 3.339 (2.110–5.285) | <.0001 |
| HTN (yes versus no) | 0.631 (0.423–0.943) | 0.0246 |
| CAD (yes versus no) | 2.148 (1.238–3.728) | 0.0066 |
| RRF[a] (per mL/min/1.73 $m^2$) | 0.777 (0.630–0.958) | 0.0182 |
| RRF decline rate[a] (per mL/min/1.73 $m^2$/month) | 693.7 (15.79–30475) | 0.0007 |

DM, diabetes mellitus; CAD, coronary artery disease; CHF, congestive heart failure; RRF, residual renal function; HTN, hypertension.
[a]Time-dependent variables.

**Table 3.** Independent risk factors associated with rapid decline of residual renal function[a]

| Covariate[b] | Odds ratio (95% CI) | *P*-value |
|---|---|---|
| Intercept 2 | | <.0001 |
| Intercept 1 | | 0.0025 |
| Age (per year) | 0.980 (0.962–0.998) | 0.0283 |
| Baseline RRF (per mL/min/1.73 $m^2$) | 1.813 (1.531–2.147) | <.0001 |
| BMI (per kg/$m^2$) | 1.100 (1.017–1.189) | 0.0166 |
| DM (yes versus no) | 3.277 (1.601–6.706) | 0.0012 |
| CHF (yes versus no) | 3.323 (1.392–7.931) | 0.0068 |
| Diuretics use (yes versus no) | 3.638 (1.444–9.166) | 0.0062 |
| Peritonitis episodes (yes versus no) | 2.117 (1.267–3.535) | 0.0042 |
| Hypotensive events (yes versus no) | 2.738 (1.542–4.862) | 0.0006 |

[a]Polychotomous proportional odds logistic regression model: $n = 270$, the score test of the proportional odds assumption $P$-value $= 0.0901 > 0.05$ (df = 8), percentage of concordant pairs = 79.6%, percentage of discordant pairs = 20.2%, adjusted generalized $R^2 = 0.4090$, deviance goodness-of-fit test $P$-value $= 0.9703 > 0.05$, and Pearson's goodness-of-fit test $P$-value $= 0.4015 > 0.05$.
[b]Other covariates without statistical significance included sex, mode of PD, peritoneal transport status, hypertension, history of coronary artery disease, baseline serum albumin, normalized protein nitrogen appearance rate and haematocrit.
RRF, residual renal function; BMI, body mass index; DM, diabetes mellitus; CHF, congestive heart failure.

**Table 4.** Rates of RRF decline and time to anuria stratified by variables accrued from the logistic regression model

| | Rate of RRF decline (mL/min/1.73 $m^2$/year) | | Time to anuria (months) | |
|---|---|---|---|---|
| Variables | No. | Median (range) | No. | Mean ± SE |
| Total | 270 | 0.89 (0–9.49) | 206 | 30.9 ± 19.3 |
| BMI ($kg/m^2$) | | | | |
| >25 | 34 | 1.09 (0–9.49)* | 27 | 23.5 ± 14.9* |
| 18–25 | 208 | 0.87 (0–7.78) | 158 | 31.3 ± 19.6 |
| <18 | 28 | 0.59 (0.04–2.58) | 21 | 38.1 ± 19.6 |
| DM | | | | |
| Yes | 52 | 1.95 (0.24–7.78)* | 44 | 21.3 ± 10.9* |
| No | 218 | 0.77 (0–9.49) | 162 | 33.6 ± 20.3 |
| CHF | | | | |
| Yes | 33 | 1.97 (0.04–6.75)* | 22 | 22.0 ± 13.2# |
| No | 237 | 0.83 (0–9.49) | 184 | 32.0 ± 19.7 |
| Diuretics use | | | | |
| Yes | 28 | 1.94 (0.01–9.49)* | 20 | 18.2 ± 10.7* |
| No | 242 | 0.82 (0–7.78) | 186 | 32.3 ± 19.5 |
| Hypotension | | | | |
| Yes | 84 | 1.61 (0.01–7.37)* | 73 | 26.3 ± 15.0* |
| No | 186 | 0.76 (0–9.49) | 133 | 33.5 ± 20.9 |
| Peritonitis | | | | |
| Yes | 107 | 1.09 (0–7.37)# | 89 | 29.1 ± 16.4 |
| No | 163 | 0.76 (0–9.49) | 117 | 32.3 ± 21.2 |

No., patient number; SE, standard error of the mean; RRF, residual renal function; BMI, body mass index; DM, diabetes mellitus; CHF, congestive heart failure.
*$P < 0.01$; #$P < 0.05$, versus each respective counterparts.

among long-term PD patients, but that loss of RRF occurred significantly earlier in non-survivors. We identified additional factors associated with all-cause mortality as older age, diabetes and CHF. All of these are all well-known prognostic factors for death in patients on long-term PD [4,6].

Other than diabetes, we also showed that rapid decline of RRF was a significant factor associated with death-censored technique failure in our cohort. The reason for this is not clear, but rapid loss of RRF had been previously linked with peritonitis [13] and inadequate small solute clearance [5,6], and these accounted for the majority (~66%) of technique failure that we observed. We also identified elevated BMI as an independent prognostic factor associated with death-censored technique failure. This is consistent with an analysis based on the Australian and New Zealand PD population, which showed that patients with BMI >25 $kg/m^2$ were more likely to experience technique failure than those with a BMI of 18–25 $kg/m^2$ [19]. The possible explanation for this finding could be that patients with a large body size were subject to inadequate small solute clearance when their RRF declined to minimal amount.

Our study found factors associated with rapid decline of RRF, after adjusting for age and baseline RRF, included diabetes, large BMI, prior history of CHF, diuretic use, peritonitis and hypotensive episodes. Some of these, such as diabetes, large BMI and prior CHF, are well-recognized prognostic factors for the loss of RRF [10,12]. In contrast, there is still uncertainty in the use of diuretics in PD patients. Medcalf *et al*. [20] reported that long-term use of high dose diuretics (e.g. furosemide 250 mg qd) effectively increased urine volume and augmented salt excretion in PD patients, yet did not jeopardize residual renal creatinine clearance. Our data, however, showed that patients who received diuretic therapy from the start of PD experienced a faster decline of RRF and became anuric more rapidly. Given the retrospective nature of this study, it could be argued that patients with rapid decline of RRF were prescribed diuretics more commonly than those without. Thus, for now, suffice to say that regardless of the reasons for use of diuretics, urine volume and fluid status should be monitored closely to avoid overdiuresis especially in those exhibiting declining RRF.

Previous studies have demonstrated that peritonitis is associated with a more rapid loss of RRF in patients on PD therapy, and that this is presumably due to infection or nephrotoxic renal injury [13,14]. Our data also identified peritonitis as an independent risk factor for rapid decline of RRF, and as shown in Table 3, patients who experienced peritonitis became anuric more rapidly than their counterparts. The underlying mechanisms could be related to systemic inflammation and the potential nephrotoxicity of antibiotics, such as aminoglycosides. On the other hand, other previous reports showed that reduced basal RRF at the initiation of PD therapy was a risk factor for the development of subsequent peritonitis [21,22]. The reason for this is not clear, but it could be related to the presence of compromised immunity that is secondary to renal failure, along with a poor nutritional status [17,23]. Furthermore, in the face of reduced RRF, more exchanges of dialysate would be needed to maintain the dialysis adequacy. This might potentially expose the patients to an increased risk of subsequent peritonitis.

Low blood pressure is a well-known risk factor for all-cause mortality in PD patients. Traditionally, this association was attributed to poor cardiac function, since this association was demonstrated mainly in patients with a history of heart failure [24]. This association also could be explained as an indirect effect of the detrimental influence of low blood pressure on RRF, which then caused adverse outcome. In the current study, we found that patients who experienced hypotensive events exhibited faster decline of RRF and become anuric more quickly than their counterparts. Upon further analysis, we identified excessive ultrafiltration as the most frequent cause (41.7%) of hypotensive events. In this regard, our data coincide with the report by Jansen *et al*. [12], who showed that clinically significant dehydration was one of the most significant factors associated with rapid loss of RRF in patients undergoing PD therapy.

This study was limited by the retrospective nature of the design and by being conducted at a single medical centre. Therefore, our observations might have been affected by confounding factors and not be generalizable to PD patients elsewhere. Future multi-centre, prospective cohort studies are needed to evaluate the external validity of this study, and to investigate whether therapeutic interventions that target the predictors we identified here can help to preserve RRF in patients on long-term PD [9].

In conclusion, this observational study of patients on long-term PD showed that the rate of RRF decline is a more powerful prognostic factor than baseline RRF for all-cause mortality and death-censored technique failure. Given the

adverse impact of rapid RRF decline on patient and technique outcome, we suggest that every effort be made to prevent the accelerated loss of RRF by avoiding overdiuresis, peritonitis and hypotensive episodes, especially in those with diabetes, obesity and CHF.

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*Conflict of interest statement*. None declared.

(See related article by S. Kim *et al.* Benefits of biocompatible PD fluid for preservation of residual renal function in incident CAPD patients: a 1-year study. *Nephrol Dial Transplant* 2009; 24: 2899–2908.)

(See related article by S. J. Davies. Preserving residual renal function in peritoneal dialysis: volume or biocompatibility? *Nephrol Dial Transplant* 2009; 24: 2620–2622.)

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