COMPARISON OF THE IMPACT OF “FAST DECLINE” IN RESIDUAL RENAL FUNCTION AND “INITIAL ANURIA” ON LONG-TERM OUTCOMES IN CAPD PATIENTS

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◆ **Background:** Residual renal function (RRF) is pivotal to long-term outcomes, while rapid RRF decline (RRFD) is associated with mortality risk for continuous ambulatory peritoneal dialysis (CAPD) patients. This study was conducted to compare the impact of “initial anuria” and rapid RRFD on the long-term prognosis of CAPD patients.

◆ **Method:** According to the timing of anuria and the slope of RRFD, a total of 255 incident CAPD patients were divided into 3 groups. For the “anuria” group, anuria was detected from CAPD initiation and persisted for > 6 months ($n = 27$). Based on the median of the RRFD slope, the other 228 non-anuric patients were divided into a “slow decliner” group ($n = 114$), and a “rapid decliner” group ($n = 114$). The maximal observation period was 120 months.

◆ **Results:** Logistic regression tests indicated that the “anuria” group was associated with previous hemodialysis > 3 months (odds ratio [OR]: 8.52, 95% confidence interval [CI]: 3.12 – 23.28), and female (OR: 0.29, 95% CI: 0.09 – 0.90), while the “fast decliner” group with higher Davies co-morbidity scores (DCS) (OR: 1.52; 95% CI: 1.08 – 2.14), body mass index (BMI) (OR: 1.12; 95% CI: 1.04 – 1.21), and male (OR: 1.12; 95% CI: 1.04 – 1.21). After adjusting for DCS, the “fast decliner” group (hazard ratio [HR]: 0.37; 95% CI: 0.17 – 0.80) showed a better outcome than that of the “anuria” group (reference = 1). Both baseline RRF ($\beta = -0.24$; $p < 0.001$) and DCS ($\beta = -3.76$; $p < 0.001$) showed inverse linear correlations to the slope of RRFD. From the Cox proportional analyses, higher baseline RRF (HR: 0.92; 95% CI: 0.88 – 0.97) and higher slope of RRFD (slower decline in RRF) (HR: 0.90; 95% CI: 0.85 – 0.96) were independent factors for less mortality risk in patients with DCS = 0. However, only a higher slope of RRFD (HR: 0.97; 95% CI: 0.94 – 0.99) was significant for better survival in CAPD patients with DCS > 0.

◆ **Conclusion:** Compared to the baseline RRF, CAPD patients with co-morbidities that rapidly deteriorate RRFD are more crucially associated with long-term mortality risk.

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Residual renal function (RRF) has been found to play a pivotal role in the long-term survival of continuous ambulatory peritoneal dialysis (CAPD) patients (1–3). Preservation of RRF is crucial to the maintenance of dialysis adequacy in CAPD patients. The CANUSA study also emphasized the mortality prediction of RRF loss in peritoneal dialysis (PD) patients (4,5).

Diabetes, male gender, high transporter, and high body mass index (BMI) have been demonstrated to be risk factors for the rapid decline of RRF (3,6). Liao *et al.* have revealed hypotensive episodes and peritonitis frequencies as other factors that accelerate RRF decline, which resulted in worse outcomes in PD patients (7). However, high baseline renal function was paradoxically reported as a risk factor for rapid decline of RRF (7). The exact association between these clinical characteristics and RRF decline thus remains to be determined.

In an effort to elucidate this association, several questions need to be asked. First, since RRF loss has a detrimental effect on the long-term survival of CAPD patients, are those patients with complete loss of RRF on the initiation of CAPD program associated with worse outcomes? Conversely, is a higher baseline daily urine output a better prognostic factor for long-term survival? What are the accelerating factors to cause fast decline in RRF? Is a high baseline RRF combined with these factors for RRF decline equal to initial anuria in predicting long-term prognosis? Until now, there has been no consensus on the answers to these questions. Our study was thus undertaken to determine whether fast decline in RRF or initial anuria has a greater impact on long-term clinical outcomes of CAPD patients, and also to show how the clinical characteristics differ between these two groups of patients.

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MATERIALS AND METHODS

From January 1998 to December 2007, 295 incident end-stage renal disease (ESRD) patients entered the CAPD program at the Chi Mei Medical Center. The exclusion criteria of this study included those with missing data, those with only one check of renal creatinine clearance rate (CCr) and/or suspicion of acute kidney injury ($n = 20$), as well as those who died and/or were transferred to hemodialysis (HD) before performing the first peritoneal equilibrium test (PET) ($n = 7$), who received automated PD and/or intermittent HD ($n = 4$), who transferred from other centers after the first PET had been done ($n = 7$), and who were long-term bed-ridden with difficulties performing the PET and collecting total daily urine volume ($n = 2$). The inclusion criteria included the incident CAPD patients at our center for treatment for more than 6 months with at least 2 PET evaluations. The maximal observation period was 120 months.

We collected the following demographic data from the patients: period of HD prior to CAPD, mean blood pressures, BMI, normalized protein catabolism rate (nPCR) (8), 4th dialysate to plasma creatinine ratio (4th hr D/P Cr), 24-hour urine volume, residual renal and peritoneal CCr, and Kt/V during the first PET evaluation (9). These data were checked about 2 – 3 months after the initiation of the PD program, and repeated again afterwards on a 6-month interval, until either the patient passed away, discontinued CAPD treatment, or until the end of the study, on January 1st, 2009. Renal CCr was calculated from 24-hour urine volume $\times$ urine to plasma Cr concentration ratio. The decline rate of RRF was determined by the “slope of the trend equation” of serial renal CCr, which was checked every half year after the first PET evaluation. The last renal CCr was estimated at either of the following times: when the patients became completely anuric with “nil” urine volume, just before they shifted to HD treatment, received renal transplantation, or at the end of the study. All the patients had at least 2 measurements of renal CCr. Also recorded were prescriptions of diuretics, converting enzyme inhibitors (ACEI) and/or angiotensin receptor blockades (ARB) before the onset of anuria and with a duration of more than 1 month. No patient took cimetidine or analgesics such as non-steroid anti-inflammatory drugs for more than 1 week during the study period. All patients were dialyzed with 4 – 5 shifts of Dianeal PD solution (PD2 and PD4, Baxter Healthcare Corporation, Singapore) per day. No patient was prescribed Physioneal (Baxter Healthcare, Compton, UK) or Balance (Fresenius Medical Care, Bad Homberg, Germany) during the study period. The co-morbidity factors were determined by Davies

co-morbidity scores (DCS) (10) according to the past history recorded in the medical charts at the beginning of study.

STATISTICAL ANALYSIS

Appropriate chi-square and one-way analysis of variance (ANOVA) with post hoc Bonferroni tests were used for comparisons for the respective categorical and continuous variables among each group in Table 1. Comparisons of the percentage of urine output to total fluid removal, percentage of renal to total CCr, and episode numbers of peritonitis before anuria among each group were conducted with a Kruskal-Wallis one-way analysis of variance. Multiple linear regression tests were calculated to determine the independent factors for “slope of RRF decline,” as shown in Table 2. Multivariate logistic regression tests were used to evaluate the predictors associated with the “anuria” and “rapid decliner” groups in Table 3. Actuarial survival rates of the three groups categorized by different slopes of RRF decline were determined with Kaplan-Meier methods. Those patients shifting to HD treatment, transferring to other centers, or receiving renal transplantations during the follow-up were censored. Log rank tests were employed to compare the different survival curves between each group. Multivariate Cox proportional hazard models were divided into two parts, with Table 4A describing patients with DCS = 0 ($n = 156$), while Table 4B describes patients with DCS > 0 ($n = 99$). To analyze the predictive power of “baseline RRF” and “slope of RRF decline” for long-term mortality, the co-variants such as age, gender, BMI and months of HD prior to CAPD were included in the analysis. With the exception of the percentage of urine output to total fluid removal, and percentage of renal to total CCr (median, inter-quartile ranges), all the other data were expressed as mean $\pm$ standard deviation. A p value of less than 0.05 was considered statistically significant. Computations were performed with the SPSS 17.0 package for Windows (SPSS, Chicago, IL, USA).

RESULTS

BASELINE DEMOGRAPHIC DIFFERENCES AMONG THE 3 GROUPS OF PATIENTS

A total of 255 ESRD incident patients (mean age at the initiation of PD treatment: 49 ± 15 years; range: 11 – 83 years; male: 40%) fulfilled the criteria and were enrolled in this prospective cohort study. The renal etiologies were attributed to chronic glomerulonephritis in 66%

TABLE 1
Basic Characteristics of the 3 Groups of Patients at the Initiation of Peritoneal Dialysis

	"Anuria" group (n=27)	"Slow decliner" group (n=114)	"Rapid decliner" group (n=114)
Demographic data			
Age at initiation of study, years	53±14	49±13	48±16
DM, %	15	11 ^g	26
Male, %	19 ^h	30 ^h	54
sCr, mg/dL	10.1±4	9.7±3	8.5±3
BMI, kg/m ²	21.9±4.2	21.3±3.2 ^c	23.0±4.1
nPCR, g/kg/day	1.08±0.32	1.15±0.29	1.15±0.27
4th hrs D/P Cr	0.61±0.1	0.63±0.12	0.64±0.13
Mean blood pressures, mmHg	91±23	101±17 ^{a,c}	109±16 ^b
Hemodialysis > 3months, %	44	12 ^f	9 ^f
Clearance and fluid balance			
Total fluid output, mL/24hrs	988±613	1293±713	1449±765 ^a
Peritoneal UF, mL/24hrs	988±613	721±670	508±800 ^a
Daily urine output, mL/24hrs	0	571±453 ^{b,d}	941±590 ^b
% Urine output to total fluid removal, median, (Q1–Q3)	0	40 ^{i,j} (19–67)	65 ⁱ (31–87)
CCr, L/week			
Total CCr	46±8	66±20 ^{a,d}	84±31 ^b
Peritoneal CCr	46±8	46±12	46±11
Renal CCr	0	20±16 ^{b,d}	44±28 ^b
% Renal to total CCr, median (Q1–Q3)	0	28 ^{i,j} (14–40)	46 ⁱ (35–55)
Slope of RRF decline	0 ^d	−0.96±3.00 ^d	−14.28±16.68
Number of RRF evaluation (range)	6.1±5.4 (2–19)	6.4±3.9 (2–17)	4.1±2.3 (2–14)
Davies co-morbidity score, %			
0	59	72	51
1	33	21	28
≥ 2	7	7	21
Peritonitis episodes before anuria, median (Q1–Q3)	0 (0–1)	0 (0–1)	0 (0–1)
Prescriptions			
Dialysate infuse volume, L/day	9.5±1.4	9.1±1.6	9.5±1.4
Diuretics, %	17	22	28
ARB and/or ACEI, %	9	32 ^e	31 ^e

DM = diabetes; sCr = serum creatinine level; BMI = body mass index; nPCR = normalized protein catabolism; 4th D/PCr = 4th dialysate to plasma creatinine ratio; UF = ultrafiltration; CCr = creatinine clearance; RRF = residual renal function; ARB = angiotensin receptor blockade; ACEI = angiotensin converting enzyme inhibitor.

^a $p < 0.05$, ^b $p < 0.001$ vs "anuria" group (ANOVA with Bonferroni tests)

^c $p < 0.05$, ^d $p < 0.001$ vs "rapid decliner" group (ANOVA with Bonferroni tests)

^e $p < 0.05$, ^f $p < 0.001$ vs "anuria" group (Chi-square test)

^g $p < 0.05$, ^h $p < 0.001$ vs "rapid decliner" group (Chi-square test)

ⁱ $p < 0.001$ vs "anuria" group (Kruskal-Wallis one-way analysis of variance)

^j $p < 0.001$ vs "rapid decliner" group (Kruskal-Wallis one-way analysis of variance)

TABLE 2
Multiple Linear Regression Analyses for Evaluation of the Risk Factors Associated with "Slope of RRF Decline Rate"^a

	β	Model 1 95% CI		<i>p</i>	β	Model 2 95% CI		<i>p</i>
Baseline renal CCr, L/week	-0.24	-0.31	-0.18	<0.001				
Davies co-morbidity score	-3.76	-5.79	-1.73	<0.001	-4.80	-7.04	-2.55	<0.001
BMI, kg/m ²	-0.10	-0.54	0.33	0.64	-0.56	-1.02	-0.10	0.02
Age, year	0.02	-0.09	0.13	0.69	0.02	-0.10	0.14	0.73
Diabetes, y or n	1.28	-3.55	6.11	0.60	2.23	-3.15	7.61	0.41
Male, y or n	0.70	-2.53	3.93	0.67	-2.06	-5.58	1.45	0.25
Hemodialysis prior to CAPD, month	0.00	-0.18	0.19	0.98	0.12	-0.08	0.33	0.24

RRF = residual renal function; CI = confidence interval; CCr = creatinine clearance; BMI = body mass index; CAPD = continuous ambulatory peritoneal dialysis.

^a Dependent variable: slope of RRF decline rate in non initial anuria patients (*n*=228).

TABLE 3
Multivariate Logistic Regression Analyses of the Clinical Associations of "Anuria" Group (A) and "Rapid Decliner" Group (B)

	OR	95% CI		<i>p</i>
		Lower	Upper	
A. Anuria group ^a				
Male, y or n	0.29	0.09	0.9	0.03
Hemodialysis more than 3 months, y or n	8.52	3.12	23.27	<0.001
Davies scores	0.91	0.46	1.81	0.78
B. Rapid decliner group ^b				
Male, y or n	2.40	1.35	4.28	0.003
Davies scores	1.56	1.08	2.25	0.02
BMI, kg/m ²	1.12	1.04	1.22	0.005

CI = confidence interval; OR = odds ratio; BMI = body mass index.

^a Dependent variable: "anuria" group (*n*=27) vs "slow and rapid decliner" groups (*n*=228); adjusted by body mass index, age at initiation of study, diabetes mellitus.

^b Dependent variable: rapid decliner group (*n*=114) vs slow decliner group (*n*=114); adjusted by age at initiation of study.

of patients, diabetic nephropathy in 18%, chronic tubulointerstitial nephritis in 7%, and other etiologies in the remaining 9%. In total, 255 CAPD patients were divided into 3 groups: the "anuria" group consisted of patients with nil daily urine volume for more than half a year (*n* = 27); the other 228 non-anuric patients were stratified into two groups based on the median (β = -3.99) of "the slope of RRF decline equation," with the "slow decliner" group defined as slope > -3.99 (*n* = 114), and the "rapid decliner" group as slope < -3.99 (*n* = 114).

As shown in Table 1, the "rapid decliners" had a higher prevalence of diabetes mellitus and male gender. This group also had a slightly lower serum Cr concentration, as well as a higher mean blood pressure (BP) and BMI than those of the "anuria" group. There were no significant

differences in the levels of 4th D/P Cr ratio, and nPCR among the 3 groups. Furthermore, the "rapid decliners" also had a higher initial daily urine volume, renal CCr and higher DCS. Compared to the other 2 groups, the "anuria" group not only had "nil" urine output and renal CCr at initiation, but also had the least total weekly CCr. However, the levels of weekly peritoneal CCr were similar across the 3 groups. There were also no differences among the 3 groups in the number of peritonitis episodes before anuria development. The prescription rates of diuretics and ARB and/or ACEI were lower in the "anuria" group. The "rapid decliner" group had the steepest slopes of RRF decline, and the "slow decliner" group a gentle one, in contrast to the "anuria" group that persistently had a "0" slope (Figure 1).

TABLE 4
Multivariate Cox Proportional Hazard Methods for Evaluation of the Risk Factors for Long-Term Mortality of CAPD Patients

	A. Davies Score = 0 ^a				B. Davies Score > 0 ^b			
	HR	95% CI		p	HR	95% CI		p
Baseline renal CCr (per L/week)	0.92	0.88	0.97	<0.001	0.98	0.96	1.00	0.10
Slope of RRF trend (per 1 unit)	0.90	0.85	0.96	0.002	0.97	0.94	0.99	0.04
Age (per year)	1.06	1.02	1.10	0.006	1.05	1.01	1.09	0.009
Male (vs Female)	1.85	0.56	6.16	0.32	2.77	1.19	6.49	0.02
BMI (per kg/m ²)	1.03	0.94	1.13	0.55	1.02	0.89	1.17	0.76
HD prior to CAPD (per month)	1.00	0.98	1.03	0.92	1.01	0.99	1.03	0.36

A = "anuria" group; B = "rapid decliner" group; HR = hazard ratio; CI = confidence interval; CCr = creatinine clearance; RRF = residual renal function; BMI = body mass index; HD = hemodialysis; CAPD = continuous ambulatory peritoneal dialysis.

^a n=156.

^b n=99.

Figure 1 — Slope of trend equation of each patient was calculated by serial creatinine clearances (CCr), which were measured every 6 months after first peritoneal equilibrium test evaluation. A total of 255 incident CAPD patients were divided into 3 groups: the "anuria" group had "nil" daily urine volume for more than half a year (■); the other 228 non-anuric patients were stratified into "slow decliner" (Δ) and "rapid decliner" (●) groups according to the median of "the slope of RRF decline." CAPD = continuous ambulatory peritoneal dialysis; RRF = residual renal function.

FACTORS ASSOCIATED WITH THE SLOPE OF RRF DECLINE

By analysis of the multiple linear regression tests in Table 2, the slope of RRF decline was inversely correlated to the baseline renal CCr and DCS. It was observed that the higher the initial urine volumes and/or co-morbidity scores, the more rapid the decline in RRF. After withdrawing "baseline RRF" in the model 2 study, high DCS and BMI became independent factors causing rapid RRF decline.

EVALUATION OF THE CHARACTERISTICS OF "ANURIA" AND "RAPID DECLINER" GROUPS

After performing multivariate logistic regressions, the "anuria" group was correlated to longer HD periods prior to CAPD initiation, and female gender predominance. In contrast, the "rapid decliner" group was associated with higher DCS, BMI, and male gender (Table 3).

LONG-TERM MORTALITY AMONG THE 3 GROUPS OF PATIENTS

From an unadjusted analysis with the Kaplan-Meier method, the "anuria" and "rapid decliner" groups had significantly lower cumulative survival rates than the "slow decliner" group ($p < 0.001$, and $p = 0.004$, respectively), but there was no survival difference between "anuria" and "rapid decliner" groups ($p = 0.13$, Figure 2A). After adjusting for the DCS, the HR for mortality of "slow decliner" (HR: 0.22; 95% CI: 0.10 – 0.50) and "rapid decliner" groups (HR = 0.37, 95% CI: 0.17 – 0.80) was lower than that of the "anuria" group (reference = 1) (Figure 2B).

EVALUATION OF THE PREDICTIVE VALUES OF "BASELINE RRF" AND "RRF DECLINE RATE" ON CAPD PATIENTS' LONG-TERM MORTALITY

By using multivariate Cox proportional hazard models, for those patients with Davies score = 0 ($n = 156$), both higher "baseline renal CCr" (HR: 0.92; 95% CI: 0.88 – 0.97) and higher "slope" of RRF trend (i.e., slow RRF decline) (HR: 0.90; 95% CI: 0.85 – 0.96) were proven to be independent factors associated with less mortality risk after adjusting for age, gender, BMI, and months of HD

Figure 2 — From an unadjusted analysis with the Kaplan-Meier method, the “anuria” and “rapid decliner” groups had significantly lower cumulative survival rates than the “slow decliner” group ($p < 0.001$, and $p = 0.004$, respectively), but there was no survival difference between the “anuria” and “rapid decliner” groups ($p = 0.13$, Figure 2A). After adjusting for the Davies co-morbidity score, the hazard ratio for mortality of the “slow decliner” (HR: 0.22; 95% CI: 0.10 – 0.50) and “rapid decliner” groups (HR = 0.37, 95% CI: 0.17 – 0.80) was lower than that of the “anuria” group (reference = 1) (Figure 2B). HR = hazard ratio; CI = confidence interval.

prior to CAPD (Table 4A). However, baseline RRF lost the significance in the outcome benefit for those patients with Davies score > 0 ($n = 99$), leaving only the high slope of RRF (i.e., slow decline of RRF) as an independent beneficial prognostic factor for a 3% decrease in death hazard for each unit of RRF slope increase (HR: 0.97; 95% CI: 0.94 – 0.99) (Table 4B).

DISCUSSION

The main finding of this study is that both “baseline RRF” and “rapidity of RRF decline” have an equal predictive power for the long-term outcome in CAPD patients without co-morbidities. However, in those with co-morbid

conditions, rapid RRF decline became a more important risk factor for mortality. Those patients with initial anuria were associated with female gender, and a longer period of HD before starting the CAPD program. On the other hand, rapid RRF decliners were characterized by a high DCS, male gender, and high BMI. Co-morbidity status in CAPD patients was an independent factor causing rapid decline in RRF. Despite having the advantage of highest urine volume at the initiation of the CAPD program, the fast decliners did not have any benefit for long-term outcomes compared to those patients with initial anuria.

The importance of RRF to the survival of dialysis patients was first reported by Maiorca *et al.* in 1995 (11). The CANUSA study also emphasized the mortality prediction of RRF loss in PD patients (4,5). There is now clear evidence that the benefits of RRF in PD extend beyond survival, with beneficial effects on blood pressure control (12) and fluid status maintenance (13). Preservation of RRF has also been observed to decrease circulating inflammatory markers (14), lower the risk of peritonitis (15) and improve quality of life (16). With nil RRF at PD initiation, it was reasonable to expect that the “anuria” group would be associated with a high mortality rate.

We found that about 44% of the “anuria” group patients received more than 3 months of HD before PD initiation. Early onset of RRF loss might have been the result of recurrent intradialytic hypotension after an inappropriate ultrafiltration rate during the HD sessions (17). It can be justifiably asked what allowed the “anuria” group patients to achieve optimal fluid balance on the basis of only about 1000 mL of fluid excretion. Female gender predominance with a smaller body build, tighter fluid adherence and adequate blood pressure control are conjectured to be the major factors responsible for the maintenance of the basic homeostasis.

Although RRF is vital to PD patients, RRF started to be curtailed at various rates after PD initiation (3). This rapidity of decline is a more powerful prognostic factor than baseline RRF associated with all-cause mortality and technique failure in CAPD patients (18). Risk factors for rapid RRF loss have been reported to be associated with high baseline RRF and a high transport membrane (3). Diabetes, high BMI, prior history of congestive heart failure (CHF), use of diuretics, hypotensive events and peritonitis have also been found to be independent prognostic factors for accelerated RRF decline (18). Recently, renal transplant failure, absence of ACEI/ARB treatment, nephrotoxic drugs and intravascular radio-contrast medium were demonstrated to exacerbate rapid RRF decline (19). Left atrial enlargement and left ventricular diastolic dysfunction have also been observed to contribute to RRF decline in CAPD patients (20).

High prevalence of CHF, high BMI, diabetes mellitus, and male gender were the major characteristics of the “rapid decliners.” Obesity, or high BMI, is not only a risk factor for the development of chronic kidney disease (21) and ESRD (22), but also a cause for kidney function deterioration after initiation of dialysis therapy (23). CHF tended to decrease cardiac output and to lead to renal hypo-perfusion and deteriorating RRF. Furthermore, certain drugs prescribed in CHF management have been found to worsen RRF and result in earlier anuria (24). Compared to the other two groups, the greater co-morbid condition in the “rapid decliner” group predisposed these patients to frequent admissions and a variety of examinations, which further increased the risk of deteriorating RRF.

It seems paradoxical that rapid RRF decline combined with high baseline RRF should be linked to high mortality risk, since RRF is crucial to long-term prognosis of PD patients. Why was high baseline RRF proven as an independent factor for rapid RRF decline in Table 2? Because of the co-morbidities and high prevalence of diabetes mellitus, the “rapid decliners” were forced to initiate renal replacement therapy under a higher urine volume status, the benefit of which has not been shown to be associated with better prognosis in either CAPD or HD patients (25). All benefit for better outcome in the “rapid decliner” group was completely nullified by a fast RRF decline, which might have resulted from inter-current complications and repeated sub-clinical kidney injuries after PD initiation. This is a floor effect with respect to RRF, insofar as the higher the initial RRF, the greater the drop in amplitude to an anuria state.

Although the frequency of peritonitis episodes has been correlated with the rapid decline of RRF (6), our data failed to support this. In fact, the number of episodes increased proportionally with the duration of the dialysis period. We speculate that the longer “at-risk” period of the RRF slower decliners should lead to a higher number of episodes. In addition, ACEI and ARB have not only been reported to be reno-protective for chronic kidney disease patients before dialysis (26), but have also been suggested to be associated with the delay of RRF decline after the initiation of dialysis (27). However, some studies (3,28), including the present one, have failed to corroborate this observation. Long-term diuretics improve fluid homeostasis in CAPD patients and are associated with better clinical outcomes (29). Due to non-random prescription, the usage of diuretics was not associated with the decline rate of RRF.

This study has two strengths. The first is its long-term observation period of about 10 years’ follow-up. The other is that this study marks the first time that the

cumulative survivals of PD patients has been compared with initial anuria and rapid RRF decline, since both factors contribute to the worsened long-term prognosis in PD patients. However, our study also has certain limitations. Firstly, since the prescription of ACEI and/or ARB was not randomly controlled and began at a later stage of the study, this would result in a lower prescription rate of these medications, and biased results in evaluating the reno-protective effect of these drugs. Secondly, the sample, which consists of relatively younger studied subjects with fewer co-morbidities, may not be generalizable to other populations.

In conclusion, we found that “slow RRF decline rate” and “high initial RRF status” offer an equal survival benefit to PD patients without co-morbidities. However, in those with higher DCS, rapidity of RRF decline is a more important determinant over baseline RRF in predicting long-term outcomes. Owing to the co-morbid conditions and subsequent inter-current kidney injuries, and despite having the advantage of highest baseline urine volume, the fast RRF decliners lost renal function within a short period after initiating PD. Thus, both “initial anuria” and “rapid RRF decline” share a common pathway of “early” RRF loss, which leads to a high mortality risk. Strategies to preserve renal function should be made to reduce the mortality risk of CAPD patients. Careful management of the co-morbid conditions such as CHF and/or hypervolemia is important in influencing their outcomes. Since the “anuria” group had a worse outcome after adjustment for DCS, it is reasonable to ask whether or not anuric patients should start PD. Furthermore, given that patients with “initial anuria” were predominantly females with lower BMI in our data, we do not know whether or not larger, male patients would have done equally well if they started on PD without RRF. Both of these questions still need answers and further clarification.

DISCLOSURES

The authors have no financial conflicts of interest to declare.

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