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Original Article

Association between residual renal function, inflammation and patient survival in new peritoneal dialysis patients

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Abstract

Background. The recent ADEMEX study (Paniagua R, Amato D, Vonesh E *et al. J Am Soc Nephrol* 2002; 13: 1307–1320) indicates that peritoneal small solute clearance is not as critical for the survival of peritoneal dialysis (PD) patients as thought previously. On the other hand, low residual renal function (RRF), inflammation and an increased peritoneal transport rate (PTR) as evaluated by the peritoneal equilibration test (PET) are reported to be associated with increased mortality in PD patients, but the relationships between these factors and their separate and combined impact on the survival of PD patients are not clear. In this retrospective analysis, we evaluated possible relationships between RRF, inflammation and initial PTR in patients starting PD and the impact of these factors on patient survival.

Methods. A total of 117 patients with initial assessments for RRF, serum C-reactive protein (CRP) and PET at a mean period of 0.4 ± 0.2 months (range 0.1–1.0 months) after start of PD were included in this study. Based on RRF (cut-off point, 4 ml/min/1.73 m^2), serum CRP (cut-off point, 10 mg/l), and the dialysate to plasma creatinine ratio at 4-h of dwell (mean +1SD), the patients were divided into different groups: low RRF and high RRF group, high CRP and normal CRP group and high PTR and other PTR group, respectively.

Results. Of 117 patients, 54 patients (46%) were in low RRF (<4 ml/min/1.73 m^2) group, 36 patients (31%) were in high serum CRP ($\geqslant 10$ mg/l) group and 17 patients (15%) were in high PTR group. Forty-nine patients (42%) had one of these characteristics, 26 patients (22%) had two of these characteristics, two patients (2%) had three, and 40 patients (34%) had none of these characteristics. Patients with low RRF were older and had a higher prevalence of high CRP, lower normalized protein equivalent of total nitrogen appearance (nPNA), lower total Kt/V_{urea} and lower total creatinine clearance (CCr) whereas patients with high CRP were older and had a higher proportion of men, lower serum albumin, lower nPNA, lower RRF and lower total CCr. Patients with high PTR had lower serum albumin, higher RRF and higher total CCr compared with patients with other PTR. Upon logistic multiple regression analysis, age and RRF were identified as factors affecting inflammation. Overall patient survival was significantly lower in the patients with low RRF, with high CRP, and in patients with more than two of the following: low RRF, high CRP and high PTR. In contrast, in patients with none of the discriminators low RRF, high CRP and high PTR, the 5-year survival was 100%. A high PTR was associated with decreased survival during the initial year on PD, but not thereafter. Patients who died during the follow-up period had a higher prevalence of high CRP and lower serum albumin, lower RRF, lower Kt/V_{urea} and lower total CCr. Upon Cox proportional hazards multivariate analysis, age and RRF were predictors of mortality.

Conclusions. These results indicate that in patients starting PD, low initial RRF is associated with inflammation, and low RRF and inflammation are both associated with high overall mortality. A high PTR was associated with higher mortality, but only during the initial year on PD, whereas Kt/V_{urea} did not predict mortality. These results indicate the importance of RRF and inflammation as predictors of mortality in PD patients whereas the predictive power of PTR as such may lose its significance if these two parameters are taken into consideration.

Keywords: inflammation; mortality; peritoneal transport rate; residual renal function

Introduction

The recent ADEMEX study [1] shows that peritoneal small solute clearance is not as critical for patient

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survival as thought previously. On the other hand, there has been an increasing focus in recent years on the roles of residual renal function (RRF) [2], inflammation [3] and peritoneal transport rate (PTR) [4–6] as predictors of mortality in peritoneal dialysis (PD) patients. However, the relative importance of these factors for patient survival and the relationships between these factors are not clearly established.

A low RRF at start of PD has been reported to predict mortality [2]. The reason for this may be an adverse effect of low RRF on nutritional status before initiation of dialysis, and this in turn may be associated with a decreased probability of survival. On the other hand, inflammation has recently been reported to be associated with malnutrition [7] and to predict outcome in dialysis patients [8]. However, the origin of inflammation in these patients has not been clearly identified. Reduction in renal function may play a role, considering the high prevalence of inflammation in pre-dialysis patients [9] and a significant increase in C-reactive protein (CRP) and serum cytokine levels in patients developing chronic renal failure [10].

One possible explanation for the association between low initial RRF and decreased patient survival could therefore be an association between low RRF and inflammation at start of dialysis [11]. Furthermore, a high PTR at the start of PD has been shown to be associated with inflammation [12], comorbid diseases [6] and high mortality [4–6], and inflammation and low RRF are linked to increases in PTR during the initial year on PD [11]. Thus, it is possible that a low RRF at start of PD might be linked to inflammation, which in turn may be associated with a high PTR, and these three factors may be associated with increased mortality in PD patients.

The aim of the present study was to test this hypothesis. For this purpose we evaluated possible relationships between RRF, inflammation and initial PTR in patients starting PD and the impact of these factors, alone or in combination on patient survival.

Subjects and methods

Patients and study design

A total of 117 patients who were started on PD at the Home Dialysis Unit at the Department of Renal Medicine, Huddinge University Hospital, Stockholm, Sweden, were analysed retrospectively. The inclusion criterion was that patients underwent assessment of RRF, inflammation and PTR within 1 month of PD start of therapy. All patients therefore underwent assessments of RRF, serum CRP and nutritional status and peritoneal equilibration test (PET) at a mean period of 0.4 ± 0.2 months (range 0.1–1.0 months) after beginning PD. Based on RRF (cut-off point, 4 ml/min/1.73 m^2, see below), serum CRP (cut-off point, 10 mg/l, see below), and the dialysate to plasma creatinine ratio at 4 h of dwell (D/P Cr, cut-off point 0.86, see below) the patients were divided into different groups; low RRF and high RRF group, high CRP and normal CRP group, and high PTR and other PTR group, respectively. Their mean age was 56.5 years (range 24–85 years).

Of the 117 patients, 70 patients were male, 28 patients had a history of cardiovascular disease (CVD; defined as previous myocardial infarction, angina, peripheral vascular disease or cerebrovascular disease), and 42 patients had diabetes. The causes of renal failure in the 117 patients were chronic glomerulonephritis ($n = 37$), diabetic nephropathy ($n = 31$), interstitial nephritis ($n = 11$), polycystic kidney disease ($n = 9$) and other diseases of unknown aetiology ($n = 29$).

The endpoint of the study was the patient status (dead or alive) at termination of the follow-up period (mean 20.7 ± 14.3 months, range 1.6–75.2 months). The patients were censored at renal transplantation, transfer to HD or at the end of the observation period.

Residual renal function

RRF was estimated by calculating the average residual renal clearance of urea and creatinine. The median value of RRF was 4.3 ml/min/1.73 m^2 (0–11.2 ml/min/1.73 m^2). The classification of low and high RRF group was based on the receiver operating characteristics (ROC) curve for RRF *vs* inflammation, which yielded a cut-off point of 4 ml/min/1.73 m^2 (sensitivity 63.0% and specificity 63.9% for prediction of CRP $\geqslant 10$ mg/l). The area under the ROC curve was 0.67 with standard error 0.06 and 95% confidence interval 0.56–0.78; $P = 0.002$.

Peritoneal equilibration test

The PET was performed according to Twardowski [13]. Briefly, a standard 4-h dwell period was used, using a 2.27% glucose concentration for a 2-l volume exchange. As glucose interferes with the assay for creatinine, the corrected value for creatinine was obtained by subtracting the glucose concentration multiplied by a correction factor (0.35) derived in our laboratory. The mean $\pm$ SD of D/P Cr was 0.70 ± 0.16 and 0.86 (mean + 1 SD) was used as cut-off point for high PTR and other PTR group. This value is higher than that reported by Twardowski [13] and others. The reason for this discrepancy may be due to differences in methodology and differences in patient characteristics.

Estimated protein intake

Dietary protein intake was estimated from the protein equivalent of nitrogen appearance (PNA) using the equation PNA = 15.1 + 0.195 urea appearance (mmol/24 h) + protein losses (g/24 h) [14]. Urea appearance rate and protein losses were determined from the measured urea and protein excretion rate in dialysate and urine. PNA was normalized to desirable body weight obtained from the Metropolitan height and weight table [15].

Body mass index

The body mass index was calculated as weight (in kilograms)/[height (in meters)]^2.

Biochemical analyses

A fasting venous blood sample was taken before the morning exchange. Blood chemistries were analysed by standard techniques. Serum creatinine was determined by the Jaffe method. Serum albumin was determined by the bromcresol purple method.

Serum CRP was measured by using an immunonephelometric method (Tina-quant®; Boehringer-Mannheim/Hitachi Ltd, Tokyo, Japan). The limit for reported values of CRP at the Department of Clinical Chemistry, Huddinge University Hospital was 10 mg/l and this value, which is generally thought to indicate clinically significant inflammation, was chosen as the cut-off point for the classification of high CRP group.

Statistical analysis

Student's *t*-test or Kruskal–Wallis test was used to compare the difference in clinical characteristics between different subgroups. χ^2 test or Fisher's exact test was used to compare the nominal variables between different subgroups. The factors affecting inflammation was determined with logistic regression analysis. Actuarial survival was performed using the Kaplan–Meier method and the log-rank test was used to compare survival between subgroups. Cox proportional hazards model was used to identify the factors predicting patient mortality. Data are presented as mean ± SD. The difference was considered significant when the *P*-value was <0.05.

Results

Prevalence of low RRF, inflammation and high PTR

Figure 1 shows the prevalence of low RRF (46%), inflammation (31%) and high PTR (15%). Of 117 patients, 49 (42%) patients had one of these characteristics, 26 (22%) patients had two of these characteristics, two patients (2%) had three, and 40 (34%) patients had none of these characteristics.

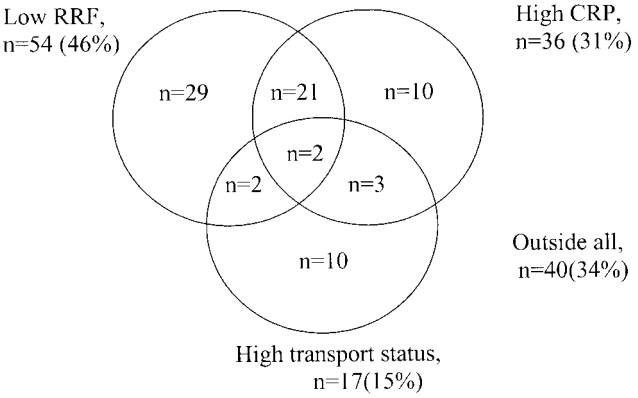

Fig. 1. Prevalence of low RRF, inflammation, and high PTR. Of 117 patients, 40 patients had none of these characteristics.

Clinical characteristics vs RRF

The clinical characteristics in the two RRF groups are shown in Table 1. The mean value of RRF was 5.6 ± 1.4 ml/min/1.73 m^2 (range 4.0–11.2) and 2.3 ± 1.1 ml/min/1.73 m^2 (range 0–3.9) for the high RRF and low RRF group, respectively. Patients with low RRF were older and had a higher prevalence of serum CRP $\geqslant$10 mg/l, lower nPNA, lower total Kt/V_{urea} and lower total creatinine clearance rate (CCr) compared with patients with high RRF.

Clinical characteristics vs CRP

The clinical characteristics in the two CRP groups are shown in Table 2. Patients with serum CRP $\geqslant$10 mg/l were older and had a higher proportion of men, lower serum albumin, lower nPNA, lower RRF and lower CCr compared with patients with serum CRP $<$10 mg/l.

Clinical characteristics vs peritoneal transport rate

The clinical characteristics in the two transport groups are shown in Table 3. The mean value of D/P Cr was 0.65 ± 0.12 (range 0.26–0.86) and 0.94 ± 0.05 (range 0.87–1.00) for other PTR and high PTR group, respectively. Patients with high PTR had lower serum albumin, higher total CCr, and higher RRF, indicating that they had started earlier on dialysis compared with the other patients.

Correlation between inflammation and peritoneal transport rate

The initial PTR correlated significantly with serum albumin concentration (Rho = −0.48, $P<0.0001$) and initial serum CRP levels (Rho = 0.38, $P=0.02$) in the

Table 1. Comparison of clinical characteristics in the two RRF groups

	High RRF ($\geqslant$4 ml/min/1.73 m^2) ($n=63$)	Low RRF ($<$4 ml/min/1.73 m^2) ($n=54$)	*P* value
Age (years)	53.5 ± 14.7	60.0 ± 13.6	0.02
Follow-up time (months)	20.1 ± 11.4	21.5 ± 17.2	NS
Male, *n* (%)	39 (62%)	31 (57%)	NS
Cardiovascular disease, *n* (%)	13 (21%)	15 (28%)	NS
Diabetes, *n* (%)	24 (38%)	18 (33%)	NS
Serum CRP $\geqslant$10 mg/l, *n* (%)	13 (21%)	23 (43%)	0.02
Serum albumin (g/l)	33.2 ± 5.2	31.9 ± 5.5	NS
nPNA (g/kg/24 h)	1.11 ± 0.21	0.97 ± 0.26	0.003
Body mass index (kg/m^2)	23.8 ± 3.5	23.3 ± 3.3	NS
Total Kt/V_{urea}	2.5 ± 0.5	2.0 ± 0.4	$<$0.0001
Total CCr (l/week/1.73 m^2)	95.1 ± 14.7	65.4 ± 12.7	$<$0.0001
D/P Cr	0.71 ± 0.18	0.68 ± 0.12	NS
High transporter, *n* (%)	13 (21%)	4 (7%)	NS

RRF, residual renal function; CRP, C-reactive protein; nPNA, normalized protein equivalent of total nitrogen appearance; CCr, creatinine clearance; D/P Cr, dialysate to plasma creatinine ratio.

Table 2. Comparison of clinical characteristics in the two serum CRP groups

	sCRP <10 mg/l ($n=81$)	sCRP $\geqslant 10$ mg/l ($n=36$)	P value
Age (years)	53.4 ± 14.9	63.5 ± 10.8	0.0007
Follow-up time (months)	21.0 ± 14.1	20.1 ± 14.9	NS
Male, n (%)	43 (53%)	27 (75%)	0.04
Cardiovascular disease, n (%)	17 (21%)	11 (31%)	NS
Diabetes, n (%)	30 (37%)	12 (33%)	NS
Serum albumin (g/l)	33.3 ± 5.2	30.9 ± 5.5	0.03
nPNA (g/kg/24 h)	1.07 ± 0.25	0.98 ± 0.21	0.04
Body mass index (kg/m^2)	23.4 ± 3.2	23.8 ± 4.0	NS
RRF (ml/min/1.73 m^2)	4.5 ± 2.0	3.2 ± 2.2	0.004
Total Kt/V_{urea}	2.4 ± 0.5	2.2 ± 0.5	NS
Total CCr (l/week/1.73 m^2)	84.9 ± 19.2	74.2 ± 20.8	0.01
D/P Cr	0.69 ± 0.16	0.70 ± 0.14	NS
High transporter, n (%)	12 (15%)	5 (14%)	NS

sCRP, serum C-reactive protein; nPNA, normalized protein equivalent of total nitrogen appearance; RRF, residual renal function; CCr, creatinine clearance; D/P Cr, dialysate to plasma creatinine ratio.

Table 3. Comparison of clinical characteristics in the two peritoneal transport groups

	Other PTR ($n=100$)	High PTR ($n=17$)	P value
Age (years)	56.8 ± 14.5	55.1 ± 14.9	NS
Follow-up time (months)	21.5 ± 14.9	16.0 ± 8.8	NS
Male, n (%)	57 (57%)	13 (77%)	NS
Cardiovascular disease, n (%)	24 (24%)	4 (24%)	NS
Diabetes, n (%)	34 (34%)	8 (47%)	NS
Serum CRP $\geqslant 10$ mg/l, n (%)	31 (31%)	5 (29%)	NS
Serum albumin (g/l)	33.1 ± 5.5	29.9 ± 3.9	0.01
nPNA (g/kg/24 h)	1.03 ± 0.26	1.06 ± 0.16	NS
Body mass index (kg/m^2)	23.5 ± 3.4	23.7 ± 3.4	NS
RRF (ml/min/1.73 m^2)	3.9 ± 2.1	5.4 ± 1.8	0.006
Total Kt/V_{urea}	2.3 ± 0.5	2.4 ± 0.5	NS
Total CCr (l/week/1.73 m^2)	79.0 ± 19.6	97.3 ± 17.0	0.0004

PTR, peritoneal solute transport rate; CRP, C-reactive protein; nPNA, normalized protein equivalent of total nitrogen appearance; RRF, residual renal function; CCr, creatinine clearance. Note that RRF was higher in the patients with high PTR compared to the other patients.

36 patients with CRP $\geqslant 10$ mg/l, i.e. the only group for which individual quantitative CRP values were available.

Factors affecting inflammation

The factors affecting inflammation are shown in Table 4. Old age and low RRF were significantly associated with inflammation.

Table 4. Factors affecting inflammation (Logistic regression analysis)

Variable	B	SE	χ^2	P value
Age	0.046	0.019	5.89	0.02
CVD	0.103	0.269	0.15	NS
Gender (male)	0.444	0.262	0.26	NS
Serum albumin	−0.093	0.050	3.47	0.06
Residual renal function	−0.263	0.120	4.63	0.03
D/P Cr	−1.489	0.880	0.63	NS

B, estimated coefficient; SE, standard error; CVD, cardiovascular disease; D/P Cr, dialysate to plasma creatinine ratio.

Clinical outcome and survival

At the end of the follow-up period (mean 20.7 ± 14.3 months, range 1.6–75.2 months), 29 patients were still on CAPD, 28 had died, 33 transferred to HD, 26 underwent kidney transplantation and one had recovery of RRF. The causes of death were CVD (46%), infection (11%), other (11%) and unknown (32%). CVD was the cause of death in 44% of the low RRF patients, in 60% of the high CRP and 80% of the high PTR patients.

The patient survival according to RRF, serum CRP and PTR at start of PD is shown in Figure 2. Overall patient survival was significantly lower in the patients with low RRF ($P=0.002$), high serum CRP ($P=0.004$) and more than two of the characteristics low RRF, high serum CRP and high PTR ($P=0.0002$). Note that in the patients ($n=40$) who had none of these characteristics, the 5-year survival was 100% whereas the 5-year survival was only 17.5% in patients with two or more of these characteristics (Figure 2). However, in the high PTR group, patient survival rate was significantly lower only at 1 year of PD (1 year survival was

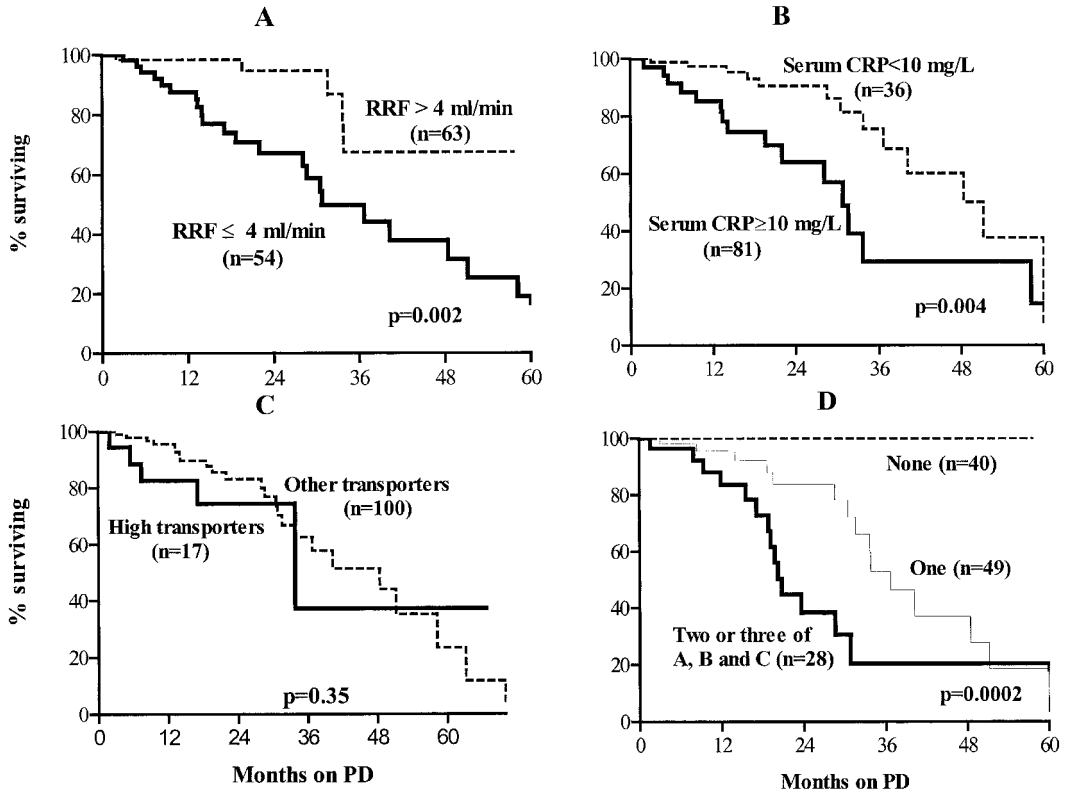

Fig. 2. Probability of patient survival according to RRF (**A**), serum CRP (**B**), PTR (**C**) and presence of A, B and C (low RRF, high CRP, and high PTR) (**D**) at start of PD. Patient survival was significantly lower in the patients with low RRF, high serum CRP, and more than two of these discriminators (low RRF, high CRP and high PTR). However, in the high PTR group, patient survival rates were significantly lower only at 1 year of PD (82.6 *vs* 95.6% for high PTR and other PTR, respectively, $P=0.03$) but not for subsequent years of PD ($P>0.05$).

82.6 *vs* 95.6% for high PTR and other PTR, respectively, $P=0.03$) but not in subsequent years of PD ($P>0.05$). However, the number of high transport patients at risk was low after 1 year.

Clinical characteristics in surviving and deceased patients

The clinical characteristics of surviving and deceased patients are shown in Table 5. Patients who died were older, had more often high serum CRP, lower serum albumin, lower RRF, lower total Kt/V_{urea} and lower total CCr compared to patients who survived.

Predictors of mortality

Upon Cox proportional hazards univariate analysis, age, serum albumin, inflammation and RRF were predictors of mortality whereas CVD ($P=0.05$) and

Table 5. Comparison of clinical characteristics in surviving and deceased patients

	Survived ($n=89$)	Deceased ($n=28$)	*P* value
Age (years)	54.1 ± 14.0	64.2 ± 13.6	0.0009
Follow-up time (months)	24.6 ± 16.9	19.5 ± 13.3	NS
Male, *n* (%)	53 (60%)	17 (61%)	NS
Cardiovascular disease, *n* (%)	19 (21%)	9 (32%)	NS
Diabetes, *n* (%)	28 (32%)	14 (50%)	NS
Serum CRP ⩾10 mg/l, *n* (%)	21 (24%)	15 (54%)	0.005
Serum albumin (g/l)	33.5 ± 5.2	29.8 ± 5.0	0.003
nPNA (g/kg/24 h)	1.05 ± 0.23	0.99 ± 0.28	NS
Body mass index (kg/m^2)	23.5 ± 3.3	23.6 ± 3.9	NS
RRF (ml/min/1.73 m^2)	4.5 ± 2.1	2.8 ± 1.7	<0.0001
Total Kt/V_{urea}	2.4 ± 0.6	2.1 ± 0.4	0.03
Total CCr (l/week/1.73 m^2)	85.0 ± 20.2	70.9 ± 16.6	0.002
D/P Cr	0.69 ± 0.16	0.72 ± 0.13	NS
High transporter, *n* (%)	12 (15%)	5 (14%)	NS

CRP, serum C-reactive protein; nPNA, normalized protein equivalent of total nitrogen appearance; RRF, residual renal function; CCr, creatinine clearance; D/P Cr, dialysate to plasma creatinine ratio.

Table 6. Risk factors for mortality (Cox proportional hazards univariate analysis)

Variable	Relative risk	95% CI	*P* value
Age (per year)	1.05	1.02–1.09	0.0003
Cardiovascular diseases	1.53	1.00–2.28	0.05
Diabetes	1.42	0.97–2.07	0.07
Gender (male)	1.25	0.86–1.86	NS
Serum albumin (per 1 g/l)	0.93	0.86–0.99	0.03
Inflammation (CRP $\geqslant$10 mg/l)	1.69	1.16–2.47	0.007
Residual renal function (per 1 ml/min)	0.81	0.66–0.97	0.03
Total Kt/V_{urea} ($\geqslant$2.0)	0.91	0.61–1.40	NS
D/P Cr (per 0.1 U)	1.24	0.92–1.64	NS

CRP, C-reactive protein; D/P Cr, dialysate to plasma creatinine ratio.

Table 7. Risk factors for mortality (Cox proportional hazards multivariate analysis)

Variable	Relative risk	95% CI	*P* value
Age (per year)	1.05	1.02–1.09	0.002
Inflammation (CRP $\geqslant$10 mg/l)	1.44	0.98–2.13	0.06
Residual renal function (per 1 ml/min)	0.79	0.62–0.99	0.04
D/P Cr (per 0.1 U)	1.42	0.98–2.09	0.07

CRP, C-reactive protein; D/P Cr, dialysate to plasma creatinine ratio.

diabetes ($P=0.07$) did not reach statistical significance (Table 6). In the further multivariate analysis, we included the factors, which were the focus of this study, namely, inflammation (CRP which was more significant than albumin in the univariate analysis), RRF and PTR. Upon Cox proportional hazards multivariate analysis, age and RRF were predictors of mortality whereas inflammation ($P=0.06$) and D/P Cr ($P=0.07$) did not reach statistical significance (Table 7).

Discussion

The present study shows that there were significant relationships between initial RRF and initial serum CRP in this group of patients starting on PD. Both initial RRF and initial serum CRP had an impact on overall patient survival whereas a high PTR was associated with increased mortality only during the initial year on PD. The combined effect of two or more of the three characteristics low RRF, inflammation and high PTR was substantial with 5-year survival of only 17.5% whereas 5-year survival in patients with none of these characteristics was 100%. Upon multivariate analysis age and RRF were found to be independent predictors of mortality and both these factors were associated with inflammation.

In a previous study on 76 of these 117 patients who were still on the therapy after 1 year [11], we found that a decline in RRF was associated with increased PTR and inflammation. In the current study, we could however not demonstrate a relationship between baseline values of RRF and high PTR, whereas inflammation and RRF were indeed related. One reason for this apparent discrepancy is that in our previous study, we analysed changes during the first year (in the 76 patients who had been treated with PD for 1 year) whereas in the current study, we analysed the baseline values in the whole cohort of 117 patients. Thus, the population studied differs between the two studies. Furthermore, the high transporters were started on dialysis earlier and therefore had higher RRF at start, which could obscure the possible relationship between RRF and transport rate.

Although the significant association between initial RRF and initial nPNA as observed in the present study may partly be due to mathematical coupling, it is now well appreciated that RRF may have an impact on protein intake [16,17], no matter whether this is assessed before start of dialysis [16] or later during the course of dialysis [17]. The reason for this could be that toxic middle molecule fractions that are normally excreted in the urine may suppress appetite, resulting in lower protein intake.

In addition to the low nPNA, our study reveals that patients with low RRF also had a higher prevalence of high CRP compared with patients with high RRF at start of dialysis and low RRF was a factor affecting inflammation. These findings are consistent with that of other investigators [18,19] who have reported an association between renal function and inflammatory mediators. Brockhaus *et al.* [18] found that in uraemic non-dialysed patients, plasma levels of soluble tumour necrosis factor (TNF) receptors increased progressively with declining renal function. Memoli *et al.* [19] demonstrated that in uraemic non-dialysed patients, urinary excretion of soluble forms of interleukin (IL)-6 was significantly lower as compared with values obtained in healthy subjects. This suggests that renal failure *per se* may contribute to the inflammatory response with elevated serum levels of pro-inflammatory cytokines. The importance of the kidney in cytokine handling is further underscored by Hession *et al.* [20] who demonstrated that the Tamm–Horsfall glycoprotein might function as a unique renal regulatory glycoprotein that regulates the activity of potent cytokines, such as IL-1 and TNF. Recently, Panichi *et al.* [10] demonstrated that both CRP and IL-6 levels are related to renal function in pre-dialysis patients. Therefore, our finding of a negative correlation between RRF and CRP may perhaps suggest that a reduction in renal function may aggravate the inflammatory state due to decreased renal clearance of cytokines at start of PD.

The inverse correlation of serum CRP with nPNA in the present study is in agreement with previous reports [21,22], suggesting that inflammation may have a direct effect on nutritional intake. Aguilera *et al.* [22] reported that PD patients with anorexia had higher TNF-alpha values than patients without these symptoms. It is probable that pro-inflammatory cytokines inhibit feeding in the central nervous system and by causing a decreasing

gastrointestinal motility, modifying gastric secretion and eliciting taste aversion [21].

In accordance with previous studies [2,3], the present study shows an adverse impact of low RRF and high CRP, respectively, on patient survival. Inflammation is known to be strongly associated with malnutrition and CVD [7]. The predictive value of elevated levels of serum CRP regarding cardiovascular mortality is well documented [8]. However, despite CVD being a common cause of death in the present study, serum CRP lost its predictive power for mortality when the multivariate analysis included RRF. An important finding of the present study is that low RRF was strongly related to malnutrition and high CRP. Thus, the association between low RRF and inflammation may have superseded the predictive role of high CRP on mortality. We could not demonstrate a statistically significant role of inflammation as a predictor of mortality in the multivariate analysis, possibly due to lack of statistical power because of the limited number of patients.

PD patients with initially increased PTR may have higher mortality rates [4–6] as well as signs of inflammation [12]. We confirmed a low patient survival in the patients with initial high transport rate; however, this association was only seen in the 1-year patient survival but not in subsequent years of PD. Although a significant relationship between an initial high PTR and inflammation was not found, in the present study, the initial PTR correlated significantly with initial serum albumin concentrations and initial serum CRP levels (Rho = 0.38, $P = 0.02$) in the 36 patients with CRP $\geqslant 10$ mg/l, i.e. the only group for which individual quantitative CRP values were available. Three of the five high transporters with high CRP died in the first year of PD whereas two of the 12 high transporters with normal CRP died during follow-up period. This underlines the possible importance of inflammation as a contributing factor for the decreased patient survival in high transporters during the initial year on PD although there was not sufficient power to determine the possible impact of inflammation on the survival due to the small number of deceased patients.

However, in the present study, a confounding factor was that patients with high transport rate had a higher initial RRF than the other patients. It is probable that the high RRF in this group may have lessened the impact of high PTR on patient survival. Furthermore, in our previous study [11], high RRF in high transporters was associated with a decrease in PTR during the first year of PD and this change in PTR may have reduced the impact of the predictive role of high initial PTR on mortality during the subsequent years of PD. Although any conclusion is limited by the low number of patients, one may speculate that high transporters with no inflammation and well-maintained RRF may not represent a high risk group.

In contrast to our previous study on incident patients treated for 1 year [4], high peritoneal transport rate was not associated with poorer long-term survival in the present study. Considering that fluid and sodium removal have been shown to predict mortality in PD patients [23], the favourable outcome in high transporters in this study may have been due to improved dialysis management, including fluid restriction, increased use of APD and use of icodextrin-based dialysis fluid. Recent controlled clinical trials of icodextrin have demonstrated significantly greater fluid and sodium removal compared with 2.25% glucose during the long dwell exchanges in both CAPD [24] and APD [25]. In the present study, seven high transporters changed their treatment modality to improve fluid removal during the follow-up period, four patients were treated with APD and three patients were treated with one exchange per day of icodextrin.

Several shortcomings of the present study should be considered. At first, a relatively limited number of patients and therefore a low number of events were retrospectively analysed and we can therefore not exclude a type two statistical error. Secondly, we relied on a single measurement of inflammation, which cannot take into account any variation of inflammation that may have occurred over time. Finally, it is plausible that our findings are limited by the classification of CVD that included only patients with clinically significant disease, which may underestimate the true prevalence of CVD.

In conclusion, our study demonstrates that in patients starting PD, a low initial RRF is associated with inflammation, and low RRF and inflammation are both associated with high mortality. A high PTR was associated with increased mortality, but only during the initial year on PD, whereas Kt/V_{urea} did not predict survival. These results underline the importance of RRF and inflammation as predictors of mortality in PD patients whereas the predictive power of PTR as such may lose its significance if these two parameters are taken into consideration.

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