Peritoneal solute transport predicts survival on CAPD independently of residual renal function

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Abstract

Background. Loss of residual renal function has a profound effect on the survival of peritoneal dialysis patients. Less is known of the impact of peritoneal function. The purpose of this study was to investigate the influence of solute transport on clinical outcome in CAPD patients.

Methods. Two hundred and ten consecutive patients commencing CAPD since 1990 were enrolled into a single centre prospective longitudinal observational study of urea, protein, and peritoneal kinetics. On entry, and at 6-monthly intervals, estimations were made of weight, body mass index (BMI), plasma albumin, Kt/V, residual renal function (RRF), NPCR, low-molecular-weight solute transport (D/Pcreat), and peritoneal protein losses. All patients were censored in 1996, regardless of treatment modality.

Results. During the 6-year follow up period (median 22 months) there were 51 deaths, and the actuarial survival was 58% at 5 years. Urea, protein and peritoneal kinetics varied with time on dialysis: as anticipated there was a reduction in Kt/V, attributable to loss of RRF, whereas plasma albumin was stable for the first 2 years of treatment, but subsequently started to decline, a trend that became significant at 42 months. Peritoneal kinetics stabilized within the first 6 months of treatment and then showed a trend of increased solute transfer with time on treatment, which became significant by the end of the study.

Comparing survivors with non-survivors Kt/V and RRF were similar at the start of treatment, but loss of RRF occurred significantly earlier in non-survivors than survivors (0.37 vs 0.68, P = 0.02 at 6 months, 0.19 vs 0.54, P = 0.01 at 12 months). D/Pcreat was also identical at commencement of treatment, but subsequently whilst survivors had stable solute transfer, non-survivors had consistently higher solute transfer beyond 6 months that reached increasing significance after 18 months, (0.70 vs 0.67, P = 0.05 at 18 months, 0.72 vs 0.66, P = 0.03 at 24 months).

A Cox proportional hazard model constructed for the variables age, sex, BMI, albumin, Kt/V and D/Pcreat at 6 months of treatment indicated that low Kt/V (P = 0.004), high D/Pcreat (P = 0.013) and age (P = 0.028) were independent predictors of death.

Conclusion. There is good reason to believe that high peritoneal solute transport is an independent marker of poor outcome in CAPD patients.

Key words: peritoneal solute transport; Kt/V; residual renal function; survival; albumin; peritoneal dialysis

Introduction

Several factors are now known to be related to clinical outcome in patients treated with continuous ambulatory peritoneal dialysis (CAPD). Adverse factors include age, comorbid disease, poor nutritional state and low plasma albumin at onset of treatment, and the dialysis dose (Kt/V), particularly as manifested by the loss of residual renal function [1–7]. There is also growing evidence that peritoneal function, as assessed by low-molecular-weight solute transport and ultrafiltration capacity can influence outcome, both in relation to technique failure and certain types of comorbidity [8–10]. Defining an independent role for peritoneal function as a predictor, let alone determinant, of patient survival is complicated by two factors: firstly the interrelationships between these predictive markers, and secondly their tendency to change with time on treatment. For example, both solute transport and peritoneal protein losses are proportional to the effective peritoneal surface area, such that D/Pcreat will co-vary with plasma albumin [2,11]. Furthermore, the impact of poor peritoneal ultrafiltration (which is associated with high transport) will be masked by the presence of good residual renal function, which in turn is lost with time on CAPD, whilst progressive changes in peritoneal function might be occurring [12]. A fuller understanding of how these factors interact with each other, and thus play a deterministic role in clinical outcome is clearly desirable if this treatment modality is to be optimized.

The purpose of this observational study was to...
establish how urea, protein and peritoneal kinetics develop over the first 4 years of CAPD in a homogeneous group of patients in whom there were no systematic attempts to alter or maintain \( \text{Kt/V} \), in order to establish if solute transport is related to clinical outcome.

**Subjects and methods**

**Patient population and study design**

This was a single-centre, prospective, longitudinal observational study. All of 210 patients commencing on the CAPD programme between 1990 and 1995 inclusive, regardless of aetiology of renal failure and comorbid diseases, were enrolled into the study. Patient data was collected at 6-monthly outpatient assessments which included a biochemical profile, full 24-h dialysate collection, and peritoneal equilibration test from which the \( \text{Kt/V} \), RRF, low-molecular-weight solute transport (\( \text{D/P}_{\text{creat}} \)), 24-h protein losses, and protein catabolic rate (PCR) were calculated. Patient demographics including age, height, body mass index (BMI), and sex were recorded on entry to the study, and patient death was the clinical end-point.

**Dialysis dose (\( \text{Kt/V} \))**

The dialysis dose was assessed by calculating the weekly \( \text{Kt/V}_{\text{urea}} \) from the 24-h urinary and dialysate clearance, by direct measurement of urea in urine and from each dialysate exchange. The volume of distribution for urea was estimated as 58% of the body dry weight. Results are expressed as the total weekly \( \text{Kt/V}_{\text{urea}} \) (peritoneal and renal components), or for the residual renal function (RRF) alone.

**Protein catabolic rate (PCR)**

This was calculated using the equation derived from detailed nitrogen balance studies in CAPD patients: \( \text{PCR} \) (g/day) = (0.261·UA (mmol/day)) + 13 + TPL (g/day), where UA is the total (urine plus dialysate) urea appearance and TPL is the total (urine plus dialysate) protein loss over 24 h. PCR was normalized for dry body-weight (NPCR) [13].

**Analytical methods**

Plasma and dialysate concentrations of urea, creatinine and glucose were determined on an automated discrete random access analyser (DAX 72, Bayer Instruments, Basingstoke, UK). Urine and dialysate total protein estimations were made using the Biuret method. Plasma albumin levels were measured using the bromocresol green method.

**Peritoneal equilibration test (PET)**

The peritoneal equilibration test was used to measure peritoneal kinetics, and this was performed as described previously [12,14,15]. Briefly, a standard 4-h dwell period was used (first exchange of the day), using a 2.27% glucose concentration 2-litre volume exchange. The patients used their usual overnight dialysis regime, and both the overnight and test drainage volumes were measured. Net ultrafiltration (UF) was calculated as the difference between the 2 litres of instilled dialysate and the volume drained after the 4-h dwell. The dialysate/plasma ratio of creatinine at the completion of the 4-h dwell period, (\( \text{D/P}_{\text{creat}} \)), was used as the estimate of low-molecular-weight solute transfer. As glucose interferes with the assay for creatinine in a linear fashion, concentrations for both these solutes are measured at 4 h and the true value for creatinine obtained by subtracting the glucose concentration multiplied by a correction factor derived locally by our laboratory (0.47). Using this method the 4-h \( \text{D/P}_{\text{creat}} \) is a highly reproducible measure of low-molecular-weight solute transfer across a wide range of values (0.45–0.9), in the short term (3 months or less provided there has been no clinical event such as peritonitis or surgery), with a coefficient of variation of 3–5%. Normal ranges ±95% CI, 0.635 ±0.25 for \( \text{D/P}_{\text{creat}} \) and 498 ±409 ml for net ultrafiltration.

**Statistical analysis**

Actuarial survival following entry to the study was performed using the Kaplan–Meier method. Cox’s proportional hazard regression model was used in the multivariate analyses, utilising chi-squared for significance testing, adopting a manual stepwise approach for the six variables, age, \( \text{Kt/V} \), plasma albumin, solute transport, sex, and BMI [16]. Comparisons between \( \text{Kt/V} \), RRF, plasma albumin, and peritoneal function in survivors versus non-survivors at different time-points were made using non-paired Student \( t \) test, whereas longitudinal changes were analysed using an ANOVA.

**Results**

The mean age of the patient population was 52.8 years, (median 57, range 14–80), with a mean height of 1.67 m, and male:female sex ratio of 58:42. The Kaplan–Meier actuarial survival plot for the whole population is shown in Figure 1, along with numbers of patients at risk. Of 210 patients who entered, 51 died during the study period, and the actuarial survival at 5 years was 58% (see Figure 1). All patients were censored at the end of the study period regardless of
the treatment modality at that point, and a total of 102 patients were not on CAPD for various reasons, although the median time spent on CAPD was 22 months (mean 27 months). Of the 51 patients who had died, 25 died on CAPD, five following transplantation and 21 following transfer to unit haemodialysis. There were 45 renal transplants and 28 CAPD technical failures (in addition to the deaths), 17 due to recurrent peritonitis, 11 due to ultrafiltration failure. Of these patients transferring to haemodialysis, 65% with recurrent peritonitis and 54% with ultrafiltration failure died before the close of the study. Four patients requested transfer to haemodialysis out of choice, three of whom survived. Because of the relatively high number of endpoints occurring after transfer from CAPD an analysis of these patients was carried out. Of these deaths, 81% occurred within 6 months of transfer, and when the statistical analyses were performed excluding those patients with longer that 6 months survival on a different treatment modality there was no difference in the overall findings (see below).

**Longitudinal changes in clinical parameters**

The longitudinal changes in urea kinetics (Kt/V, RRF, and NPCR), protein kinetics (plasma albumin, total protein losses) and peritoneal kinetics (D/Pcreat ratios and ultrafiltration volumes) are summarized for the whole study population in Table 1.

During the first 18 months of dialysis treatment there was a rapid and significant decline in the total Kt/V, due entirely to the loss of residual renal function. Loss of residual renal function was also responsible for the early reduction in total protein losses that occurred following 6 months of treatment. Subsequently the total protein losses remained constant over the 48 months of observation, whereas at 42 and 48 months of treatment there was a significant drop in the plasma albumin. This reduction in the plasma albumin occurred at the same time that there was an increase in the LMW solute transfer, and was associated with a rise in the calculated protein clearances, although this did not reach statistical significance.

The comparison of the longitudinal changes in plasma albumin in survivors with non-survivors is illustrated in Figure 2. It can be seen that plasma albumin at the commencement of treatment is significantly lower in non-survivors, but that this difference disappears subsequently until the later stages of treatment, although it does not reach statistical significance. Figure 3 shows a similar representation for the total Kt/V and RRF with time in survivors and non-survivors. Whilst Kt/V was similar in at the commence-

**Table 1. Mean (± SD) longitudinal values for urea, protein and peritoneal kinetics on CAPD**

<table>
<thead>
<tr>
<th>Months on treatment</th>
<th>1</th>
<th>6</th>
<th>12</th>
<th>18</th>
<th>24</th>
<th>30</th>
<th>36</th>
<th>42</th>
<th>48</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight (kg)</td>
<td>65.3</td>
<td>66.0</td>
<td>69.3†</td>
<td>68.9‡</td>
<td>67.7</td>
<td>69.5</td>
<td>71.1</td>
<td>69.3</td>
<td>73.6</td>
</tr>
<tr>
<td>±13.6</td>
<td>±13.2</td>
<td>±15.4</td>
<td>±15.5</td>
<td>±14.2</td>
<td>±15.5</td>
<td>±16.4</td>
<td>±17.3</td>
<td>±11.4</td>
<td></td>
</tr>
<tr>
<td>Albumin (g/l)</td>
<td>37.4</td>
<td>36.9</td>
<td>37.1</td>
<td>37.7</td>
<td>37.3</td>
<td>36.8</td>
<td>36.7</td>
<td>34.8</td>
<td>35.7</td>
</tr>
<tr>
<td>±5.8</td>
<td>±5.0</td>
<td>±5.8</td>
<td>±5.4</td>
<td>±4.7</td>
<td>±4.9</td>
<td>±5.1</td>
<td>±4.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total Protein loss</td>
<td>9.53†</td>
<td>8.3</td>
<td>8.18</td>
<td>8.03</td>
<td>7.62</td>
<td>7.64</td>
<td>7.35</td>
<td>8.28</td>
<td>8.97</td>
</tr>
<tr>
<td>±4.6</td>
<td>±3.1</td>
<td>±3.0</td>
<td>±3.2</td>
<td>±2.5</td>
<td>±2.75</td>
<td>±2.56</td>
<td>±2.25</td>
<td>±6.7</td>
<td></td>
</tr>
<tr>
<td>Albumin Clearance</td>
<td>0.26</td>
<td>0.23</td>
<td>0.21</td>
<td>0.22</td>
<td>0.204</td>
<td>0.21</td>
<td>0.20</td>
<td>0.24</td>
<td>0.25</td>
</tr>
<tr>
<td>±0.23</td>
<td>±0.14</td>
<td>±0.11</td>
<td>±0.12</td>
<td>±0.08</td>
<td>±0.12</td>
<td>±0.09</td>
<td>±0.09</td>
<td></td>
<td></td>
</tr>
<tr>
<td>D/Pcreat</td>
<td>0.62</td>
<td>0.68</td>
<td>0.68</td>
<td>0.67</td>
<td>0.67</td>
<td>0.67</td>
<td>0.69</td>
<td>0.70†</td>
<td>0.738</td>
</tr>
<tr>
<td>±0.13</td>
<td>±0.10</td>
<td>±0.11</td>
<td>±0.11</td>
<td>±0.10</td>
<td>±0.12</td>
<td>±0.11</td>
<td>±0.15</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ultrafiltration</td>
<td>445</td>
<td>434</td>
<td>407</td>
<td>390</td>
<td>372</td>
<td>394</td>
<td>376</td>
<td>378</td>
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<td>±281</td>
<td>±261</td>
<td>±261</td>
<td>±194</td>
<td>±220</td>
<td>±178</td>
<td>±252</td>
<td>±236</td>
<td>±248</td>
<td></td>
</tr>
<tr>
<td>Total Kt/V</td>
<td>2.3</td>
<td>2.05†</td>
<td>1.84‡</td>
<td>1.84‡</td>
<td>1.84‡</td>
<td>1.69†</td>
<td>1.98</td>
<td>1.56‡</td>
<td>1.43‡</td>
</tr>
<tr>
<td>±0.6</td>
<td>±0.53</td>
<td>±0.57</td>
<td>±0.54</td>
<td>±0.54</td>
<td>±0.5</td>
<td>±0.72</td>
<td>±0.30</td>
<td>±0.20</td>
<td></td>
</tr>
<tr>
<td>RRF (Kt/V)</td>
<td>0.8</td>
<td>0.63§</td>
<td>0.45‡</td>
<td>0.46†</td>
<td>0.4†</td>
<td>0.36†</td>
<td>0.58‡</td>
<td>0.21‡</td>
<td>0.055</td>
</tr>
<tr>
<td>±0.58</td>
<td>±0.52</td>
<td>±0.54</td>
<td>±0.52</td>
<td>±0.53</td>
<td>±0.49</td>
<td>±0.77</td>
<td>±0.34</td>
<td>±0.11</td>
<td></td>
</tr>
<tr>
<td>NPCR (g/kg/day)</td>
<td>1.27</td>
<td>1.23</td>
<td>1.15§</td>
<td>1.14§</td>
<td>1.13§</td>
<td>1.05§</td>
<td>1.11§</td>
<td>1.03§</td>
<td>1.02§</td>
</tr>
<tr>
<td>±0.34</td>
<td>±0.29</td>
<td>±0.30</td>
<td>±0.28</td>
<td>±0.26</td>
<td>±0.25</td>
<td>±0.25</td>
<td>±0.39</td>
<td>±0.22</td>
<td>±0.17</td>
</tr>
</tbody>
</table>

NPCR, normalized protein catabolic rate; RRF, residual renal function. †Different from initial value, P < 0.05; ‡different from initial value, P < 0.02; §different from subsequent values, P < 0.05.
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For factors that might be considered to interact with these (age, sex, and BMI), for values obtained at 6 months of treatment. This time-point was chosen for several reasons. Firstly it is evident from the longitudinal changes in solute transport that the values obtained at the commencement of treatment do not reflect subsequent peritoneal performance. Secondly the number of patients at risk at 6 months (148) and the number of remaining deaths (44) represents a sufficient population size and number of end-points to allow the examination of this number of variables [17]. Whilst it is clear from the longitudinal data that further changes in residual renal function, hence Kt/V, and solute transport occur with time, the number of patients at risk at these time points do not permit multivariate analysis.

**Fig. 3.** Longitudinal changes in total KT/V and residual renal function (RRF) in survivors and non-survivors on CAPD. The drop in total KT/V (solid lines) and residual renal function (hatched lines) was significantly (*P<0.05*) faster in non-survivors (□) compared to survivors (■).

**Fig. 4.** Longitudinal low molecular weight solute transfer in survivors and non-survivors on CAPD. After an initial increase in solute transfer during the first 6 months of treatment in both groups, there was a continued increase in D/P_creat in non-survivors (□), whereas peritoneal kinetics remained stable in the survivors (■). *P<0.05, +P<0.02.

ment of treatment, and both groups of patients lost RRF following commencement of CAPD, this was significantly more rapid in the non-survivors, in whom the majority of loss was within the first 6 months of treatment. A similar plot for longitudinal changes in peritoneal solute transfer (D/P_creat) with time in survivors and non-survivors (Figure 4), was rather different in its pattern. D/P_creat was identical for both groups at the commencement of treatment, and increased significantly at 6 months, by which time the solute transfer was higher in non-survivors. Subsequently, whilst solute transfer remained stable in survivors over the next 4 years, there was an increasing disparity due to elevated D/P_creat in the non-survivors.

**Discussion**

This study was designed to observe the natural evolution of urea, protein, and peritoneal kinetics in a population of patients treated in a single centre with conventional CAPD. Evidence from a variety of longitudinal and cross-sectional studies have implicated all these factors as important predictors or even determinants of clinical outcome on CAPD [1–8], but this is the first study to examine all three elements and their interrelationships prospectively over several years. As a result, whilst the importance of loss of residual renal function and a low plasma albumin are clearly apparent, peritoneal kinetics are also seen to be independently linked to survival.

The longitudinal changes observed in urea kinetics are, as would be anticipated, dominated by the loss in residual renal function. This is approximately exponential with time, with a half-life between 18 and 24 months of treatment. The resultant drop in total Kt/V is accompanied by a steady decline in the NPCR, suggesting that the relationship between urea clearance and total urea and protein nitrogen appearance is not simply a mathematical one, a problem that has beset the interpretation of cross-sectional studies [18]. Whilst this cannot be taken as proof that dialysis dose and protein intake are causally related, it does provide
supportive evidence of a longitudinal relationship. The actual values obtained for Kt/V and NPCR during the first 24 months of this study are similar but not identical to the larger, multicentre CANUSA study [6]. These differences, however, are systematic and can be attributed to the different methods used in their calculation. As yet there is still no reliable but simple way of estimating the volume of distribution of urea in CAPD patients, a problem particularly observed in obese patients, and there is a tendency for the Watson formula to give lower estimates for V, resulting in the generally higher values for Kt/V than are seen here [19]. Whichever method used, the influence of residual renal function on the interpatient variability of total Kt/V and subsequent survival was so strong that similar results were obtained. The relatively higher values for NPCR obtained in this study compared to CANUSA reflect the use of an equation derived by Bergstrom et al. [13] from detailed nitrogen balance studies in CAPD patients, which also takes peritoneal protein losses into account. Again, whilst the methods differ [20], the general message that both KL/V and NPCR decline on CAPD due to loss in RRF is the same.

The longitudinal peritoneal kinetics observed in this cohort were, as would be expected, similar to those already described for the first 166 of these patients in overhydration. There is also a gradual decline in ultrafiltration, although the PET is done too early in the course of CAPD that it may not reflect the true effective peritoneal surface area. This is supported by the fact that at 6 months there was a stronger correlation between D/P\textsubscript{\textit{crea}} and body surface area. Subsequently peritoneal kinetics remain stable until 36 months, after which the mean D/P\textsubscript{\textit{crea}} starts to increase. There is also a gradual reduction in ultrafiltration, although the PET is less precise in its quantification of this problem. Both these changes are seen despite a preferential loss of patients with high solute transfer and poor ultrafiltration consequent to frequent peritonitis from both death and technical failure [12]. This would imply that a proportion of patients on CAPD acquire high solute transport with time, that is accelerated by but not conditional on multiple peritonitis episodes.

The longitudinal changes in protein kinetics demonstrated a yet different pattern with time on CAPD. The mean plasma albumin remained stable for the first 36 months of treatment, but subsequently there was a significant fall seen in this patient cohort. Total protein losses, after the small initial drop due to reduced protein losses from RRF, remained remarkably stable over the subsequent 4 years. This is despite the observation that peritoneal permeability to proteins appears to decrease with time on CAPD [21]. The explanation for this is the large influence that molecular size has on the permeability of the peritoneum to proteins. Albumin, a relatively small protein, is in quantitative terms by far the most significant protein present in dialysate effluent, and its losses are therefore more sensitive to changes in size of the effective peritoneal surface area than to peritoneal permeability [11]. The tendency for patients in this study to have increasing D/P\textsubscript{\textit{crea}}, particularly after 30 months of treatment, raises the possibility that the lower plasma albumin levels are due to increased peritoneal protein clearances. Although calculated protein clearances after 3 years tended to be higher, this does not reach statistical significance, suggesting that this is not the only explanation, and raising the possibility that the low plasma albumin levels reflected a degree of overhydration.

In summarizing this part of the study it is apparent that during the first 36 months of CAPD there is a gradual decline in Kt/V due to the loss in RRF, whilst protein and peritoneal kinetics remain stable; there is subsequently a drop in plasma albumin and increase in low-molecular-weight solute transfer. Throughout treatment there a consistent relationship between plasma albumin, dialysate protein losses and peritoneal kinetics, but none of these factors co-vary on cross-sectional analysis with the dialysis dose.

The second objective of this study was to establish how these various factors relate to patient survival. Whilst age is a powerful and independent predictor of clinical outcome, this is not the case for sex or patient size, corroborating the findings of other studies. As in the CANUSA study [6], mortality is associated with the failure to maintain the total Kt/V during the first 2 years of CAPD treatment. The loss in residual renal

<table>
<thead>
<tr>
<th>Variables</th>
<th>DF</th>
<th>(\chi^2)</th>
<th>(P)</th>
<th>Relative mortality risk (increment)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kt/V (weekly)</td>
<td>1</td>
<td>8.28</td>
<td>0.004</td>
<td>0.17 (per weekly unit)</td>
</tr>
<tr>
<td>LMW solute transfer (D/P\textsubscript{\textit{crea}})</td>
<td>1</td>
<td>6.17</td>
<td>0.013</td>
<td>2.82 (per 0.1 of ratio)</td>
</tr>
<tr>
<td>Plasma albumin</td>
<td>1</td>
<td>0.05</td>
<td>0.82</td>
<td>0.98 (per g/l)</td>
</tr>
<tr>
<td>Body mass index</td>
<td>1</td>
<td>1.00</td>
<td>0.31</td>
<td>1.08 (unit ratio)</td>
</tr>
<tr>
<td>Sex</td>
<td>1</td>
<td>4.78</td>
<td>0.028</td>
<td>1.07 (years)</td>
</tr>
<tr>
<td>Sex</td>
<td>1</td>
<td>1.72</td>
<td>0.19</td>
<td>3.0 female sex</td>
</tr>
</tbody>
</table>

DF, Degrees of freedom.

Table 2. Cox proportional hazard model for 6 months treatment

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function is considerably more rapid in non-survivors, with the majority of this loss occurring within the first 6 months of treatment. Whilst CANUSA expressed this risk mathematically, it is helpful to see the actual data for Kt/V in survivors and non-survivors in order to appreciate how rapid this change was, particularly when it is taken into context with the changes in peritoneal kinetics that were observed. The reason for this is not clear, but is likely to be due multiple comorbid factors which have a profound affect on clinical outcome [5]. Furthermore it can be seen from this analysis that the dialysis dose (and RRF) at the commencement of treatment was not significantly different between survivors and non-survivors, which lessens the argument that these differences are largely attributable to the late start of dialysis in high risk patients, resulting in what has been termed ‘lead-time bias’. The variation in peritoneal Kt/V was not sufficient to predict survival independent of residual function.

Several longitudinal studies have demonstrated that the plasma albumin at the commencement of CAPD is a powerful predictor of survival [2,3,6,22]. In this study the albumin was also lower at the start of treatment in non-survivors, although it did not predict survival independently at 6 months. This may well be due to the fact that solute transport and albumin co-vary with each other due to the common association with effective peritoneal surface area [2,11].

The single most important finding of this study is that peritoneal function, specifically high solute transfer, is consistently associated with poor clinical outcome, and that this is independent of Kt/V and RRF, age, plasma albumin, body size, and sex of the patient. Several groups have reported recently that increased mortality is associated with high transporter status, indicating that this is not an isolated observation [9,23,24]. It cannot be determined from this analysis whether in individual patients it is the value for solute transport at 6 months or subsequent changes with time which are influencing survival, but Figure 4 does suggest that real increases in solute transport are occurring in those at risk, and that stable peritoneal function is beneficial.

The implications of this finding are considerable. Firstly it supports a growing view, albeit indirectly, that overhydration of the CAPD patient is a significant problem, particularly in those with comorbidity that compromises left ventricular function. Secondly it raises the possibility that the loss of residual renal function influences survival not just through its impact on Kt/V, but also through an inevitable effect on fluid balance. The appropriate therapeutic response to studies such as this one or CANUSA, which show that early loss of Kt/V influences outcome, may not therefore be simply to increase small solute clearances as a single dimension, but rather to combine this with enhanced ultrafiltration. If these implications turn out to be correct then patients with relatively high solute transfer may not be suitable for conventional CAPD, but require either automated PD or alternative osmotic agents that can achieve sustained ultrafiltration.

Acknowledgements. We are grateful to Baxter UK Ltd (Renal Division) for their generous support of Louise Phillips.

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Received for publication: 10.5.97
Accepted in revised form: 11.12.97