Dialysis Adequacy and Nutrition Determine Prognosis in Continuous Ambulatory Peritoneal Dialysis Patients¹

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Abstract

Peritoneal membrane function was assessed in patients undergoing continuous ambulatory peritoneal dialysis (CAPD) using parameters derived from urea kinetic modeling and the peritoneal equilibration test (PET). Their relationships with other nutritional markers and overall morbidity were determined. Data regarding the patients' nutritional status as determined by total body nitrogen (TBN) measurements, hospital admissions, and infectious complications within the last 12 months were reviewed. Total dialysate clearance (Kt/V) delivered was highly dependent on residual renal function (P < 0.0001). Kt/V derived from peritoneal clearance diminished with increasing age (P < 0.05). A higher delivered total Kt/V was associated with higher normalized protein catabolic rates (P < 0.002), which in turn were associated with improved TBN (P < 0.05). Hospital admissions decreased with improved normalized protein catabolic rates (P < 0.05), and higher serum albumin and total protein levels (P < 0.01 and P < 0.002, respectively). Infectious complications correlated positively with time on dialysis (P < 0.01), and correlated negatively with TBN measurements (P = 0.05). No correlations were found between infectious complications and serum albumin level or peritoneal protein loss. However, the total duration of hospitalization was shortened with higher serum albumin and total protein levels (P < 0.0001 and P < 0.002, respectively). Although Kt/V determinations did not correlate with clearances determined by the PET, the PET-determined creatinine transport rate correlated with TBN (P < 0.05) but not with infectious complications. In conclusion, nutritional parameters correlate with outcome on continuous ambulatory peritoneal dialysis. An integral relationship exists between nutritional status and dialysis delivery, which is best assessed by urea kinetic modeling.

Key Words: CAPD, Kt/V, TBN, dialysis adequacy and morbidity

The accumulated experience and significant improvement in technology over the past decade have established continuous ambulatory peritoneal dialysis (CAPD) as a successful replacement therapy in the management of patients with ESRD. However, what constitutes adequate dialysis in CAPD is, as yet, ill-defined. Following the National Cooperative Dialysis Study (NCDS), urea kinetic modeling (UKM) has become a valuable tool in assessing and prescribing hemodialysis therapy (1,2), as well as for determining the protein catabolic rate (PCR) and thus the dietary protein intake (DPI) in stable patients. These parameters have been found to correlate with morbidity and mortality in hemodialysis patients (3,4). However, attempts to apply these parameters to assess the adequacy of CAPD prescription have yielded conflicting results (5–8).

The peritoneal equilibration test (PET) was developed by Twardowski et al. (9) in 1987 to monitor the adequacy of the peritoneum as a dialytic membrane. The test was designed to determine the membrane-transport characteristics of CAPD patients. Although patients with low peritoneal-transport characteristics may have good ultrafiltration with low-dialysate glucose concentration, they are likely to develop symptoms of inadequate dialysis when undergoing standard CAPD treatment when their residual renal function becomes negligible. However, the usefulness of the PET in determining ultimate prognosis has not been evaluated.

The study presented here was thus designed to assess the relevance of UKM and the PET in CAPD patients in relation to nutritional markers and overall morbidity.

Patients and Methods

Thirty-one patients (15 men, 16 women) were recruited from 33 patients undergoing CAPD at the time of the study at Royal North Shore Hospital, Sydney, Australia. Two patients were excluded because of social or demographic reasons. The patients were otherwise unselected. The ages for the male and female patients were 64.2 ± 3.5 and 58.8 ± 4.2 (mean ± SE) yr, respectively. At the time of the study, these patients had been undergoing CAPD for 14.7 ± 2.4 months (range, 1 to 50.2 months), and all had used this form of dialysis as their only mode of renal replacement therapy.

Thirty-two percent of the patients had end-stage renal failure because of glomerulonephritis, 22% because of analgesic nephropathy, 18% because of renovascular disease, 13% because of hypertensive nephrosclerosis, and 7% be-
cause of diabetic nephropathy. A further 10% of patients had renal failure as a result of miscellaneous causes. Three major comorbid diseases were assessed—diabetes mellitus, cardiovascular disease, and congestive heart failure. For statistical analysis, these comorbid conditions were quantified according to previously described methods (5). A value of 2 was given if only one disease was observed. However, this value would be squared or cubed if two or three concurrent conditions were present, respectively. These patients were free from any major illnesses, such as infection and peritonitis, for the preceding month, and were thus considered stable at the time of assessment.

A standard CAPD regimen of 2 L of dialysate exchanged four times a day was developed. This prescription was modified on the basis of the general clinical status and biochemical parameters of the patient. At the time of the study, 24 patients had the standard regimen, four patients were using a 2.5-L bag four times a day, and three patients each receiving one of the following prescriptions (1.5 L four times a day, 2.5 L three times a day, and 3.0 L four times a day).

On the day before their regular clinic follow-ups, patients were instructed to collect both 24-h dialysate (noting the concentration of glucose in the bags instilled) and urine. The dialysate and urine samples were assayed for urea, creatinine, and total protein levels, and the dialysate sample for glucose on a Beckman ASTRA 8 analyzer (Brea, CA). During their clinic visits, all patients underwent a 4-h Fast PET as previously described (10), and blood was taken for the measurement of urea, creatinine, glucose, total protein, albumin, total serum cholesterol, and triglyceride levels by using standard laboratory techniques. Total urea and creatinine clearance rates, peritoneal protein losses, renal and peritoneal urea generation rates, and ultrafiltration rates were determined. The daily caloric intake, derived from the peritoneal glucose absorption, was determined by subtracting the total amount of glucose present in the 24-h dialysate from the known quantity of glucose instilled.

In these stable CAPD patients, PCR was considered to be equal to DPI. Hence, PCR was derived from the urea generation rate (UGR) by using the following two methods. For the purposes of comparison, the first is designated as PCR1 and the second as PCR2. First, the formula introduced by Sargent and Gotch (11) and later validated for CAPD patients by Randerson et al. (12):

\[
PCR_1 = \frac{[UGR \text{ (mmol/d)}] \times 0.028}{0.154 + 1.7} + \text{peritoneal and urinary protein}
\]

Second, the equation proposed in the recent nitrogen balance study conducted by Bergstrom et al. (13) to yield a protein equivalent of total nitrogen appearance that reflects the DPI:

\[
PCR_2 = 13 + 0.261 \times [UGR \text{ (mmol/d)}] + \text{peritoneal and urinary protein}
\]

The normalized protein catabolic rate (NPCR) was computed by dividing the PCR result by the ideal body weight (IBW) of the patient:

\[
NPCR_1 = \frac{\text{PCR}_1}{\text{IBW (kg)}}
\]

\[
NPCR_2 = \frac{\text{PCR}_2}{\text{IBW (kg)}}
\]

For the total Kt/Vurea (Kdt/Vurea), the contribution of residual renal function (Kt/Vurea) was included. The dialytic Kt/Vurea (Kdt/Vurea) was calculated by obtaining the 24-h solute clearance as the quotient of total solute removal rate in dialysate and plasma concentration. This clearance was then divided by solution distribution volume (Vd), which was assumed to be 0.58 of body weight for urea. To equate this index with the thrice-weekly schedule of HD patients, it was then multiplied by 2.33 (14): Thus:

\[
K_{urea} = 24\text{-h urine volume} \times \text{urinary [urea]/plasma [urea]}
\]

\[
Kt/V_{urea} = 2.33 K_{urea}/V_d
\]

\[
K_{d}t/V_{urea} = 24\text{-h dialysate volume} \times \text{dialysate [urea]/plasma [urea]}
\]

\[
K_{d}t/V_{urea} = K_{d}t/V_{urea} + K_{dt}/V_{urea}
\]

Peritoneal solute transfer rates were further determined by the Fast PET, which was modified from the original PET developed by Twardowski et al. in 1987 (9,10). All patients undergoing a 4-h Fast PET were instructed to come to the clinic early in the morning. Their overnight dwell fluids were then drained over 20 min with the patient in the upright position. Subsequently, 2 L of 2.5% dextrose dialysate was infused over 10 min and kept inside the peritoneum for 4 h. At the end of this time, the peritoneum was emptied over 20 min with the patient in the same posture as in the last exchange. The drained dialysate volume was noted and a sample of dialysate was sent for glucose and creatinine estimation. A blood sample was also taken for the measurement of plasma glucose, creatinine, and other biochemical parameters.

The patients' long-term nutritional status was assessed by the total body nitrogen (TBN). This measurement was performed by prompt neutron activation analysis using methods previously described (15,16). The TBN was assessed when the patient was in stable condition for at least 1 month before the test and within the preceding 6 months of the UKM study. TBN results were compared with sex-, age-, and height-matched control subjects drawn from the general population, and expressed as both nitrogen index, i.e., observed nitrogen/predicted normal nitrogen and as nitrogen in g/kg lean body mass.

Clinical outcomes, including hospital admissions, number of hospitalization days, peritonitis, and infectious episodes in the 12-month period preceding the UKM studies were reviewed. Eighteen patients had been on CAPD for less than 12 months (mean time on CAPD, 6.4 ± 0.9 months). Of these 18 patients, seven patients had had 15 admissions during this period. Hence, uncorrected outcome values were used for analysis, because extrapolating these results as recorded over such a short period of time was considered to be misleading. Patients were considered to have a morbid event if an infectious episode (defined as an infectious illness requiring therapy) or hospitalization occurred. As steady-state nutritional balance is unlikely to be achieved within a few months of the commencement of peritoneal dialysis, data collected from patients who had undergone CAPD for more than 6 months (N = 22) was subanalyzed.

Unless otherwise stated, data are reported as mean ± SE. Statistical analyses were made using the commercially available Statview® IV software package (Abacus Concepts, Inc., Berkeley, CA). Correlations were made by using simple linear and multiple regressions, whereas differences between
groups were measured by unpaired t test. A P value of less than 0.05 was considered to be statistically significant.

RESULTS

Biochemical data and dialysis and nutritional parameters derived from UKM are detailed in Tables 1 and 2. As illustrated in Figure 1, the \( K_{nt}/V_{urea} \) was highly dependent on the \( K_{tv} \) (\( r = 0.67, P < 0.0001 \)). The mean \( K_{nt}/V_{urea} \) was 0.69 ± 0.03, but ranged from 0.40 to 1.32. As shown in Figure 2, ten patients (32%) had a \( K_{nt}/V_{urea} \) value of less than 0.6, with the modal value being between 0.6 and 0.7. The \( K_{nt}/V \) correlated positively with the total urea and the total creatinine clearance rates (\( r = 0.64, P < 0.0001 \) and \( r = 0.69 \), \( P < 0.0001 \), respectively), but not with peritoneal urea clearance nor peritoneal creatinine clearance rates. The two methods of determining PCR yielded significantly different results (\( P < 0.0001 \)). However, as expected, the two values were highly correlated (\( r = 0.99, P < 0.0001 \)). The relationship between the \( K_{nt}/V_{urea} \), NPCR1, and NPCR2 are depicted graphically in Figure 3. As shown, a higher delivered \( K_{nt}/V_{urea} \) was associated with improved NPCR1 (\( r = 0.54, P < 0.0002 \)), which in turn was positively correlated with TBN (\( r = 0.39, P < 0.05 \) and nitrogen index (\( r = 0.56, P < 0.002 \)). Similarly, \( K_{nt}/V_{urea} \) was correlated with NPCR2 (\( r = 0.57, P < 0.001 \)), which in turn correlated with TBN and nitrogen index (\( r = 0.38, P < 0.05 \) and \( r = 0.55, P < 0.002 \), respectively).

Serum urea and creatinine levels decreased as a higher \( K_{nt}/V_{urea} \) was delivered (\( r = -0.36, P < 0.05 \) and \( r = -0.61, P < 0.0005 \), respectively). NPCR1 and NPCR2 were found to positively correlate with serum urea (\( r = 0.54, P < 0.002 \) and \( r = 0.50, P < 0.005 \), respectively), but not with serum creatinine levels. The \( K_{nt}/V_{urea} \) had no correlation with the serum albumin or total protein levels and the normalized protein catabolic rates (NPCR1 and NPCR2) tended to be associated with higher total serum protein levels (\( P = 0.05 \) and \( P = 0.07 \), respectively), but not with serum albumin, serum cholesterol, or triglyceride levels. Despite the fact that the \( K_{V}/V_{urea} \) derived from the peritoneal clearance diminished with increasing age (\( r = -0.42, P < 0.02 \)), independently of time on dialysis, the \( K_{nt}/V_{urea} \) had remained stable with increasing age and time on dialysis. No correlation was found between NPCR1 and NPCR2 and the peritoneal protein loss or peritoneal glucose absorption.

Men and women in this study had been on dialysis for a similar period of time (16.7 ± 4.0 versus 12.9 ± 2.9 months, \( P = \) not significant [NS]). The results of TBN measurements are shown in Table 3. As ex-

### TABLE 1. Biochemical data of the population (N = 31)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mean ± SE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum Urea (mmol/L)</td>
<td>23.7 ± 1.2</td>
</tr>
<tr>
<td>Serum Creatinine (mmol/L)</td>
<td>0.75 ± 0.03</td>
</tr>
<tr>
<td>Serum Protein (g/L)</td>
<td>64.2 ± 1.0</td>
</tr>
<tr>
<td>Serum Albumin (g/L)</td>
<td>36.2 ± 0.7</td>
</tr>
<tr>
<td>Serum Glucose (mmol/L)</td>
<td>6.5 ± 0.5</td>
</tr>
<tr>
<td>Serum Cholesterol (mmol/L)</td>
<td>6.3 ± 0.2</td>
</tr>
<tr>
<td>Serum Triglyceride (mmol/L)</td>
<td>3.4 ± 0.3</td>
</tr>
</tbody>
</table>

### TABLE 2. Nutritional and urea kinetic modeling parameters (N = 31)*

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mean ± SE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peritoneal Protein Loss (g/d)</td>
<td>6.0 ± 0.3</td>
</tr>
<tr>
<td>Peritoneal Caloric Absorption (Kcal/day)</td>
<td>395 ± 27</td>
</tr>
<tr>
<td>Total Creatinine Clearance (mL/min)</td>
<td>7.3 ± 0.7</td>
</tr>
<tr>
<td>( K_{urea} )</td>
<td>2.18 ± 0.54</td>
</tr>
<tr>
<td>( K_{V}/V_{urea} )</td>
<td>0.55 ± 0.02</td>
</tr>
<tr>
<td>( UGR (mmol/day) )</td>
<td>0.69 ± 0.03</td>
</tr>
<tr>
<td>NPCR1 (g/kg per day)</td>
<td>0.65 ± 0.04</td>
</tr>
<tr>
<td>NPCR2 (g/kg per day)</td>
<td>1.35 ± 0.06</td>
</tr>
</tbody>
</table>

*\( K_{urea} \) = residual renal function clearance; \( K_{V}/V_{urea} \) = dialytic urea clearance; \( UGR \) = urea generation rate; NPCR1 and NPCR2, normalized protein catabolic rates (computed by two methods).

**Figure 1. Correlation between \( K_{nt}/V \) and \( K_r \).**

**Figure 2. Distribution of \( K_{nt}/V \) (count = number of patients).**
expected, men had higher TBN values. However, the nitrogen index was similar in both men and women (88.5 ± 2.8 versus 89.7 ± 4.1%; P = NS, respectively). Women were observed to have a lower peritoneal glucose absorption (471 ± 49 versus 631 ± 54, P < 0.05), lower PET-determined creatinine transport rate (D/P Cr) (0.65 ± 0.02 versus 0.72 ± 0.01, P < 0.05), and a lower serum albumin level (34.6 ± 1.0 versus 38.0 ± 0.7, P < 0.02).

A higher TBN value was obtained in patients with increased KNt/Vurea (r = 0.40, P < 0.05) and higher peritoneal glucose absorption rates (r = 0.36, P = 0.05) and tended to be associated with higher KNt/Vurea and higher total creatinine clearance rates (P = 0.09 and P = 0.09, respectively). The nitrogen index further correlated with the ultrafiltration rate (r = 0.45, P < 0.05). No correlation was found between TBN measurements and serum urea, serum creatinine, serum albumin, total serum protein, or creatinine clearance values.

An increased D/P Cr and the dialysate-to-plasma creatinine ratio correlated with higher TBN value (r = 0.43, P < 0.02) and higher nitrogen expressed as g/kg lean body mass (r = 0.37, P < 0.05). The D/P Cr further correlated with serum triglyceride levels (r = 0.53, P < 0.002), but no correlation was observed between serum triglyceride levels and peritoneal glucose absorption rates. The D/P Cr did not show any relationship with KNt/Vurea, NPCR, serum urea, serum creatinine, serum albumin, or serum cholesterol levels. In addition, D/P Cr remained stable with age and time on dialysis (P = 0.46 and P = 0.21, respectively). As expected, D/P Cr correlated with peritoneal creatinine clearance and peritoneal glucose absorption rates (r = 0.58, P < 0.001 and r = 0.63, P < 0.0001 respectively), and inversely correlated with ultrafiltration rates (r = −0.53, P < 0.005).

Of the 31 patients, 15 had a total of 31 hospitalizations in the 12 months period preceding the study. The hospitalization rate was 1.4 per patient-yr. Despite the fact that KNt/Vurea had no direct correlation with hospitalization rate, an improved NPCR was associated with a reduced number of hospitalizations (r = −0.34, P < 0.05). In addition, hospitalization episodes decreased with higher total serum protein and higher serum albumin levels (r = −0.54, P < 0.002 and r = −0.47, P < 0.01, respectively), but no correlation was observed with time on dialysis. Furthermore, the total duration of hospital stay decreased with higher total serum protein as well as higher serum albumin levels (r = −0.54, P < 0.002 and r = −0.59, P < 0.001, respectively). The number of hospitalizations correlated inversely with age (r = −0.43, P < 0.02).

A total of 44 infectious complications were recorded in 19 patients, representing an infectious rate of 2.0 episodes per patient-yr. Ten episodes of peritonitis, requiring eight admissions, occurred in seven patients; 33 exit-site infections occurred in 16 patients; urinary tract infections occurred in two patients; a skin infection occurred in one patient; chest infection, diarrhea, and herpes zoster infection occurred in each of three patients and required hospitalization in each case. Infectious complications were observed to correlate positively with time on dialysis (r = 0.49, P < 0.005), but not with the age of the patient. A lower incidence of infectious complications was associated with higher TBN (r = 0.35, P = 0.05). However, the infectious complications did not correlate with KNt/Vurea or NPCR. In addition, no correlation was observed between the infectious complications and serum albumin nor peritoneal protein losses.

In patients on CAPD for more than 6 months (N = 22), UKM and nutritional parameters were more strongly associated with outcomes. TBN measurements were more highly correlated with both measures of PCR (r = 0.58, P < 0.004 and r = 0.63, P < 0.002, respectively) and an improved PCR correlated more strongly with reduced hospitalization rates (r = −0.40, P < 0.05). Similarly, the hospitalization episodes were inversely correlated with serum total protein and albumin levels, but at more highly significant values (r = −0.62, P < 0.002 and r = −0.66, P < 0.001, respectively). As expected, a decrease in the total duration of hospital stay was associated with higher total serum protein and higher serum albumin levels (r = −0.64, P < 0.002 and r = −0.74, P < 0.0001, respectively). In these patients, improved nitrogen (expressed as g/kg lean body mass) correlated with lower incidence of infectious complications (r = −0.525, P < 0.02), and the time on dialysis was no longer associated with the infectious complications (P = 0.24).
Differences between patients who suffered a morbid event, defined as either an infectious complication or hospitalization, are detailed in Table 4. As shown, patients who suffered a morbid event were similarly aged, but had been undergoing CAPD for a longer period of time compared with those who remained well. Serum albumin and cholesterol levels as well as other measured biochemical parameters were similar in both groups of patients. Despite having similar values in $K_{\text{D}}/V_{\text{urea}}$ and $K_{\text{D}}/V_{\text{urea}}$, patients who remained well had a higher protein intake, particularly as determined by NPCR2, a higher PET drainage volume, and lower daily peritoneal protein losses. There was no significant difference between the two groups in peritoneal glucose absorption, peritoneal solute transport rate, TBN values, or comorbidity.

The patients with a $K_{\text{D}}/V_{\text{urea}} > 0.6$ (i.e., 1.8 per week) ($N = 21$), were compared with those with a $K_{\text{D}}/V_{\text{urea}} < 0.6$ ($N = 10$). The former group of patients spent fewer days hospitalized (6.4 ± 2.9 versus 44.2 ± 25.3, $P < 0.05$), and showed a tendency to have a lower serum urea level ($P = 0.08$), higher $K_{\text{D}}/V_{\text{urea}}$ ($0.72 ± 0.03$ versus $0.53 ± 0.05$, $P < 0.05$) and a lower hospitalization rate ($0.7 ± 0.2$ versus $2.4 ± 1.1$, $P < 0.05$) when compared with those whose DPI was less than 1.0 g/kg per day. Both groups of patients were similar in age and the amount of time they had been on dialysis ($P = 0.22$ and $P = 0.99$, respectively). There was no significant different in serum albumin level, peritoneal solute transport rate, TBN values, or comorbidity observed between these two groups of patients.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Morbid Events</th>
<th>Number of Morbid Events</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subject</td>
<td>20</td>
<td>11</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>60.4 ± 3.6</td>
<td>63.2 ± 4.2</td>
<td>NS</td>
</tr>
<tr>
<td>Months on CAPD</td>
<td>19.8 ± 3.1</td>
<td>5.6 ± 2.0</td>
<td>&lt;0.005</td>
</tr>
<tr>
<td>Serum Urea (mmol/L)</td>
<td>22.8 ± 1.4</td>
<td>25.5 ± 2.0</td>
<td>NS</td>
</tr>
<tr>
<td>Serum Creatinine (mmol/L)</td>
<td>0.78 ± 0.04</td>
<td>0.70 ± 0.04</td>
<td></td>
</tr>
<tr>
<td>Serum Total Protein (g/L)</td>
<td>62.9 ± 1.3</td>
<td>66.6 ± 1.4</td>
<td>0.08</td>
</tr>
<tr>
<td>Serum Albumin (g/L)</td>
<td>36.1 ± 1.0</td>
<td>36.5 ± 1.0</td>
<td>NS</td>
</tr>
<tr>
<td>Serum Cholesterol (mmol/L)</td>
<td>6.31 ± 0.28</td>
<td>6.39 ± 0.27</td>
<td>NS</td>
</tr>
<tr>
<td>Serum Triglycerides (mmol/L)</td>
<td>3.82 ± 0.53</td>
<td>2.64 ± 0.31</td>
<td>NS</td>
</tr>
<tr>
<td>$K_u$</td>
<td>2.36 ± 0.77</td>
<td>1.85 ± 0.62</td>
<td></td>
</tr>
<tr>
<td>$K_{\text{D}}/V_{\text{urea}}$</td>
<td>0.53 ± 0.02</td>
<td>0.60 ± 0.05</td>
<td>0.10</td>
</tr>
<tr>
<td>$K_{\text{D}}/V_{\text{urea}}$</td>
<td>0.66 ± 0.04</td>
<td>0.73 ± 0.06</td>
<td>NS</td>
</tr>
<tr>
<td>NPCR1 (g/kg per day)$^a$</td>
<td>0.78 ± 0.03</td>
<td>0.98 ± 0.10</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>NPCR2 (g/kg per day)$^a$</td>
<td>1.24 ± 0.04</td>
<td>1.56 ± 0.14</td>
<td>&lt;0.02</td>
</tr>
<tr>
<td>Peritoneal Protein Loss (g/d)</td>
<td>6.6 ± 0.4</td>
<td>5.1 ± 0.4</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Peritoneal Glucose Uptake (mmol)</td>
<td>575 ± 46</td>
<td>499 ± 68</td>
<td>NS</td>
</tr>
<tr>
<td>PET D/P Creatinine</td>
<td>0.70 ± 0.02</td>
<td>0.65 ± 0.02</td>
<td>NS</td>
</tr>
<tr>
<td>PET D/P Glucose</td>
<td>7.11 ± 0.61</td>
<td>7.75 ± 0.62</td>
<td>NS</td>
</tr>
<tr>
<td>PET Drainage Volume (ml)</td>
<td>2404 ± 40</td>
<td>2636 ± 94</td>
<td>&lt;0.02</td>
</tr>
<tr>
<td>Nitrogen (g/kg)</td>
<td>34.0 ± 0.8</td>
<td>34.0 ± 1.3</td>
<td>NS</td>
</tr>
<tr>
<td>Comorbidity</td>
<td>1.4 ± 0.3</td>
<td>1.0 ± 0.4</td>
<td>NS</td>
</tr>
</tbody>
</table>

$^a$ PET D/P Creatinine, peritoneal equilibration test-determined creatinine transport rate; PET D/P Glucose, peritoneal equilibration test-determined glucose transport rate.

$^b$ Value derived from the formula of Sargent and Gotch (11).

$^c$ Value derived from the formula of Bergstrom et al. (13).

**DISCUSSION**

This study illustrates the usefulness of UKM and serum albumin and TBN measurements in determining the clinical outcome of CAPD patients. It demonstrates that the PCR, total serum protein values, and, specifically, serum albumin values can validly be used as markers for predicting the hospitalization rate and duration of hospital stay, and TBN values for predicting infectious complications. Although the PET provides information about the dialysis characteristics of the peritoneum, it yields little further prognostic information concerning the patient. Thus the study provides support for the routine measurement of these parameters as markers of adequacy of dialysis delivery in stable CAPD patients.

The important relationship between adequate dialysis and mortality and morbidity emerged from the National Cooperative Dialysis Study (NCDS) performed in the late 1970s (17). This study used the blood urea level as the single marker of adequate dialysis and determined that increased urea levels, as well as short dialysis times, correlate with poor outcomes. The concept of UKM was developed as being predictive of increased patient morbidity and hospitalizations in the hemodialysis population. However, the conclusions that can be drawn from the NCDS data are limited, as no component of nutritional adequacy was included in the study. Indeed, Lindsay et al. (18) has reinterpreted the NCDS data by assigning a major role in the patient morbidity rate to nutritional status. Additional studies have demonstrated that a poor nutritional state independently portends a poor prognosis in patients with end-stage renal failure (19-24). More recently, the correlation between DPI and dialytic adequacy, particularly in cross-sectional or retrospective studies of hemodialysis patients (4,25,26) and, to a lesser extent, in CAPD patients (27-29) has been demonstrated.
firms the correlation between dialysis delivery and nutritional adequacy, and serves to demonstrate the integral relationship between clinical outcome and nutritional state. as determined by the NPCR and TBN measurement.

Our study indicates that important markers of morbidity, i.e., infectious complications and hospitalizations, were significantly associated with a lower TBN measurement and a lower NPCR, respectively. These two parameters are complementary in their assessment of nutrition. Indeed, TBN measurement has been shown to be a strong predictor of mortality in the dialysis population, which is not predicted by other biochemical or anthropometric data (30). In contrast to our findings, Harty et al. (31) have argued that assessment of the NPCR may not reflect the true nutritional state. Although we would argue that their assessment of anthropometric measurements, subjective global assessment, and visceral protein measurements do not necessarily reflect adequate nutrition, we do agree that the PCR may not reflect the DPI when the patient is not in a steady state. This is particularly likely to occur in the initial months of dialysis, when an anabolic response may be dominant and the PCR may underestimate the protein intake. Hence, we advocate TBN as a longer-term measure of nutrition, and by using this "gold standard," there is a correlation between PCR and TBN. However, once stability is achieved, the PCR should reflect the protein intake. Indeed, the prognostic value of both TBN and PCR in patients on dialysis for more than 6 months was greater than in those who had recently commenced dialysis, as they were more strongly associated with morbid outcomes. This suggests that these parameters are of more value when a steady state with respect to nutrition has been reached.

The PCR derived from the two methods clearly differ significantly with the NPCR derived from the method of Bergstrom et al. (13), which we have designated NPCR1, being on average 58% higher than the method of Randerson et al. (12). The PCR, as determined by Bergstrom et al. (13), has been acknowledged as yielding higher estimates of DPI in CAPD patients in subsequent reports from their group (32). The method used for calculation of PCR1 is the more frequently used method for calculating PCR, and indeed, Harty et al. (31) have demonstrated a high correlation between this method and two additional methods used to calculate PCR, namely that modified from Borah et al. (33) and from Teehan et al. (34). Of these three methods, the Randerson et al. equation (12) yielded the highest value for PCR, and yet the method of Bergstrom et al. (13) is over 50% higher again. In the two methods used in this paper, nitrogen balance studies were used to determine the regression equations for PCR. Eight patients were used by Randerson et al. (12) and these patients were significantly hypoalbuminemic compared with the 12 patients studied by Bergstrom et al. (13). An additional seven patients, in whom prior balance studies were conducted, were included by Bergstrom et al. (13) to strengthen the validity of their fitted regression. A further difference in the methods used to derive regression equations for PCR was that Randerson et al. (12) assumed a volume of distribution of urea of 58% and Bergstrom et al. (13) of 60%. As the majority of the patients in the Bergstrom et al. study were male, this may have overestimated the PCR in this study. Hence differences in calculations of protein metabolism are likely to be evident between the two studies.

From the data of Bergstrom et al. (13), the DPI calculated from the dietary nitrogen intakes were almost identical to those obtained in our population (a mean of 1.38 g/kg per day in the earlier studies and 1.26 g/kg per day in the later studies). Similarly, the PCR of our patients, determined by using the Randerson et al. formula (12) was identical to that obtained by Harty et al. (31) when using 147 patients (mean of 0.86 g/kg per day). It is reasonable to assume that Harty et al. (31) would have also found a similar discrepancy had he also used the Bergstrom et al. method (13) in additional calculations. It is impossible to state which formula is "correct" from the available information. Certainly we have demonstrated that anabolism occurs in CAPD patients to a greater extent than in hemodialysis patients, which is reflected in higher TBN values (30). However, as Bergstrom et al. (13) have demonstrated that anabolism in CAPD patients, reflected by a positive nitrogen balance, is possible at DPI of 0.5 g/kg per day, a higher calculated value of PCR need not be implicated in this finding.

Nonetheless, the important prognostic value of PCR is borne out by this study. Because of the variability in methods currently used to determine PCR, extrapolation of data between studies should only be used when identical methods are used to calculate both the Kt/V and PCR.

There has been a longstanding discussion regarding the independence and interdependence of Kt/V and PCR. The physiological versus the mathematical relationship between Kt/V and PCR in hemodialysis has been discussed by Lindsay et al. (4). In addition to the mathematical reasons for their independence, the clinical observations of a dissociation of Kt/V and PCR and maintenance of mass balance, the nonlinear correlation between Kt/V and PCR, and differing values for PCR for the same Kt/V when different membranes are used support their use as independent prognostic variables. Randomized studies assessing this relationship in CAPD patients are limited, but clinical observations suggest that an independent relationship between Kt/V and PCR also exists in CAPD.

A low serum albumin level has been reported as a strong predictor of death in both hemodialysis and CAPD patients (8,22). Our study demonstrates that a higher serum albumin level was associated with a lower incidence of hospitalization and duration of hospital stay. However, it did not correlate with infectious complications and was not different in the overall patient group, which developed morbid events
compared with the patients who did not have complications. Conversely, patients with higher PCR and lower peritoneal protein losses were found to have more favorable outcomes. Men in this study had higher serum albumin levels when compared with women. At least in part, this may be the result of a higher peritoneal glucose absorption rate in men, as Lindholm et al. have shown that nitrogen balance is strongly dependent on energy intake (35). Although Teehan et al. (8) has found a correlation between dialysis adequacy as determined by $K_{\text{tr}}/V_{\text{urea}}$ and serum albumin level, this observation was not confirmed in this study.

The application of $K_{\text{tr}}/V_{\text{urea}}$ in determining the adequacy of dialysis delivery in CAPD is controversial. Although it appears that a $K_{\text{tr}}/V_{\text{urea}}$ in the order of 0.6 to 0.7 is commonly observed in CAPD (14,27), there is little evidence that this delivers adequate dialysis, which translates into an improved prognosis. In the study presented here, the mean $K_{\text{tr}}/V_{\text{urea}}$ value of CAPD patients was thus considered adequate. However, when using this criteria, ten patients (32%) would be underdialyzed, with a $K_{\text{tr}}/V_{\text{urea}}$ value less than 0.6 (14,19). In comparing these two arbitrarily defined groups, it is clear that patients who are underdialyzed, with a $K_{\text{tr}}/V$ of less than 1.8, have a higher morbidity when compared with patients who have a higher $K_{\text{tr}}/V$. This important prognostic difference would not have been determined from any other clinical or biochemical marker. In particular, serum albumin levels were similar in these two groups. The mean $K_{\text{tr}}/V_{\text{urea}}$ derived from the peritoneum was 0.55 ± 0.02, with 20 patients (64%) having $K_{\text{tr}}/V_{\text{urea}}$ values less than the minimum dialysis dosage value of 0.6. Thus the $K_{\text{tr}}/V_{\text{urea}}$ was highly dependent on the residual renal function, as 19% of the $K_{\text{tr}}/V_{\text{urea}}$ was contributed by the $K_{\text{r}}$-urea. Although Rottembourg et al. (36) and Lysaght et al. (37) have reported that residual renal function is better preserved in patients treated with CAPD than in those on hemodialysis, this residual function still becomes negligible after 4 to 5 yr of CAPD. In the past, the significance of the residual function may have been masked by the large numbers of patients who withdrew within 2 to 3 yr of CAPD therapy because of technique failure. With the improvements in technique, patients are now continuing with CAPD for longer periods, during which time residual renal function may decline significantly. Hence, a large proportion of CAPD patients will inevitably become underdialyzed unless dialysis adequacy is quantitatively and regularly reassessed. The results presented here suggest that loss of residual renal function is likely to be associated with increased morbidity in CAPD as currently practiced techniques of peritoneal dialysis are unlikely to deliver enough dialysis to prevent significant morbidity.

Preliminary studies have suggested that the dialytic dose determines the protein intake and, thus, nutritional adequacy in both CAPD and haemodialysis (14,27,38,39). The study presented here also demonstrates that a higher dialysis delivery, as indicated by a higher $K_{\text{tr}}/V_{\text{urea}}$, was associated with improved PCR. This study further shows that despite the fact that DPI is subject to daily variability, it is useful to assess CAPD patients' daily dietary compliance, and also shows a significant relationship with the long-term body protein stores, which in turn correlates with clinical outcome.

The results from this study show that the peritoneal membrane solute transport characteristics appear to be well maintained with time. Several studies have supported this view in the past and showed that the peritoneum is able to remove solute at a rate equivalent to that at the initiation of CAPD, even after up to 5 yr on dialysis (40). Despite the fact that women have a significantly lower D/P Cr ratio, there were no differences found in $K_{\text{tr}}/V_{\text{urea}}$ and total creatinine clearance rates. The PET is a simple procedure and can be used to measure peritoneal membrane performance; however, attempts to correlate the peritoneal transport characteristics with urea kinetic parameters, overall nutritional parameters, and clinical outcomes have failed. Perhaps the importance of the peritoneal membrane performance in determining dialysis adequacy is outweighed by the presence of residual renal function, without which the clearance study can never be completed. The PET is a useful tool in estimating the dialysis prescription in most CAPD patients; however, it should be supplemented with clearance studies and regular monitoring of residual function to ensure that adequate dialysis is delivered in the appropriate manner.

This study has thus demonstrated that urea kinetic parameters, serum albumin levels, and TBN measurement are good predictors of clinical outcome in CAPD patients. An integral relationship exists between dialysis delivery and nutritional status, which is best assessed by UKM. At present, $K_{\text{tr}}/V_{\text{urea}} = 0.6$ and NPCR = 1.0 g/kg per day appear to constitute the minimum standard of CAPD prescription, as patients receiving CAPD prescriptions of less than these values have been shown to suffer from higher morbidity. However, it is likely that increased dialysis delivery in this population may further improve clinical outcome. The PET used alone does not satisfactorily predict outcome and, if used, should be supplemented with tests of residual renal function to ensure that adequate solute clearances by CAPD are achieved.

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