PART TWO

Clinical Experiences
Differences in Peritoneal Equilibration Test Results in Patients Aged Above or Below 60˚Years

Alicja E. Grzegorzewska, Magdalena Leander, Irena Mariak

Peritoneal permeability, evaluated using the peritoneal equilibration test (PET), indicates that, in an adult population not selected for age, an increase in the transport rate of small solutes usually occurs in the course of peritoneal dialysis (PD) treatment.

We evaluated the dialysate-to-plasma ratio of urea (D/P urea), the D/P creatinine, the ratio of dialysate glucose at a designated dwell time to dialysate glucose at 0 ’dwell time (D/D0 glucose), and the mass transfer-area coefficients (KBDs) of those solutes in PETs performed in patients aged above or below 60˚years who were matched for sex, PD duration, and outcome. The single-center, retrospective study was carried out in a peritoneal dialysis unit in a university hospital.

Two groups of PD patients were chosen. Mean age of patients in group ’I (n = 21; 9 women, 12 men) was 67.7˚± 4.5˚years; PD duration was 20.1˚± 12.1˚months. In group ’II, the patients (n = 21; 9 women, 12 men) had a mean age of 42.8˚± 9.1˚years, and had been treated with PD for 20.7˚± 12.1˚months.

A standard PET was performed according to Twardowski et al every 3˚months from PD start to PD end. The first results, the mean results representing the entire PD course, and the last results were compared between groups. In addition, the first and the last results were compared within each group.

No significant differences were seen between the groups in peritoneal transport in the first PET. In the last PET, the curves for D/P urea and D/P creatinine, and the KBDs for urea, were significantly lower in the older patients than the curves obtained at PD start. In consequence, a tendency toward lower D/P ratios or KBDs for urea and creatinine in the last and mean PETs was observed in group ’I as compared with group ’II. No significant changes were seen in the peritoneal transfer of glucose in the course of PD or between groups.

Older patients may show a reduction in peritoneal permeability from the vascular to the mesothelial side of the membrane in the course of PD treatment; peritoneal transport in the opposite direction remains unchanged during approximately 20’months from the start of PD treatment. The patients under 60˚years of age maintain stable bi-directional permeability under a comparable PD duration.

Key words
Peritoneal equilibration test, D/P, KBD, small solutes

Introduction
The peritoneal equilibration test (PET) is used to assess the permeability of the peritoneal membrane. In Japanese patients treated with peritoneal dialysis (PD), elderly people were shown to have higher peritoneal permeability than middle-aged and young people, resulting in lower serum albumin levels in the elderly patients (1). Other studies did not show age-related differences in the peritoneal permeability in adult patients (2).

Garred et al (3) demonstrated relatively constant mass transfer-area coefficients (KBDs) of urea and creatinine during up to 3.5’years of peritoneal dialysis. Passlick—Deetjer et al (4) reported that PET values for creatinine changed significantly in adults after 24’months of PD, and values for urea and glucose changed significantly after 36’months. Other studies also indicated increments in peritoneal permeability during the course of PD, usually after several years of PD treatment (5—8). Increments in peritoneal transport rate were also shown in a rat model of peritoneal dialysis (9). In contrast to those results, Struijk et al
reported decreases in $K_{BD}$ for urea, creatinine, glucose, and lactate during the first 7 months of PD.

The aim of our study was to assess peritoneal membrane permeability in standard PETs performed in patients aged above or below the age of 60 years, who were matched for sex, PD duration, and outcome. Peritoneal permeability was evaluated using dialysate-to-plasma ratio of urea ($D/P_{urea}$), $D/P$ creatinine, ratio of dialysate glucose concentration at a designated dwell time to dialysate glucose concentration at 0 dwell time ($D/D_0$ glucose), and $K_{BD}$ of those same small molecular weight solutes.

**Patients and methods**

Between 14 October 1992 and 2 October 2000, 117 uremic patients were treated with ambulatory peritoneal dialysis in our PD unit by the same team of physicians and nurses, using the same protocols. At PD start, 90 patients were under 60 years of age, and 27 patients (23.1% of all patients) were over 60 years of age.

Among the 27 patients over 60 years of age, 21 patients whose PD duration exceeded 6 months were included in the study (group I). At the start of PD, the mean age of the group I patients (9 women, 12 men) was 67.7 ± 4.5 years (range: 60.4 ± 77.2 years). Those patients had been treated with PD for 20.1 ± 12.1 months. Ten patients from group I are still on PD, 4 patients were transferred to hemodialysis, and 5 patients died. In 2 cases described in the literature (11), improvement of renal function was sufficient to disrupt PD treatment.

To group I, we matched 21 patients from among the patients under 60 years of age. Matched parameters included sex, PD duration, and outcome. The mean age of the group II patients (9 women, 12 men) was 42.0 ± 9.1 years (range: 24.7—57.4 years), and they had been treated with PD for 20.7 ± 12.1 months. Ten patients from group II are still on PD, 4 were transferred to hemodialysis, and 5 died. In 2 cases, PD was stopped owing to successful renal transplantation.

Causes of end-stage renal disease in group I included chronic glomerulonephritis (3 cases), chronic pyelonephritis (7 cases), diabetic nephropathy (4 cases), hypertensive nephrosclerosis (2 cases), polycystic kidney disease (2 cases), and unknown disease (1 case). In group II, uremia developed owing to chronic glomerulonephritis (10 cases), chronic pyelonephritis (3 cases), diabetic nephropathy (4 cases), hypertensive nephrosclerosis (3 cases), and Henoch—Schönlein syndrome (1 case).

In each group, 14 patients were on continuous ambulatory peritoneal dialysis (CAPD) and 7 patients were treated with automated PD. All patients were using standard dialysis solutions exclusively (Baxter Healthcare S.A., Castlebar, Ireland, or Fresenius Medical Care, Bad Homburg, Germany). In the course of PD, 29 episodes of peritonitis occurred in each group.

In all patients, standard PETs were performed according to Twardowski et al (12) with the use of 2.27% glucose dialysis solution. The first PET was performed after 1.3 ± 0.9 months of PD treatment in group I and after 1.2 ± 0.7 months of PD treatment in group II. Early PETs (earlier than 0.5 month from PD start) were done in 5 patients of group I and in 4 patients of group II. Subsequent PETs were carried out every 3 months from PD start to PD end, excluding periods of clinically diagnosed infection and the first two months after treatment for infection ended. The last PET was performed after 20.0 ± 12.0 months of PD treatment in group I and after 20.2 ± 11.9 months in group II.

Before every PET, drainage of dialysate from the overnight exchange was individually prolonged to empty the peritoneal cavity as much as possible. (The drain bag was weighed on an electronic scale during dialysate outflow and drainage was stopped when three consecutive weight readings, taken 5 minutes apart, yielded identical values.) Real outflow time was 18 ± 7 minutes in group I and 16 ± 4 minutes in group II. Residual dialysate volume was calculated for the first and the last PET, according to the formula of Twardowski et al (12), as the mean of residual volumes by urea and creatinine.

During each PET, dialysate samples (5 mL each) were collected at 0, 2, and 4 hours equilibration time after infusion, and blood samples were drawn at 2 hours after dialysate infusion. At the end of a 4-hour dwell, dialysate was collected and dialysate volume was measured.

The $D/P$ urea and $D/P$ creatinine were calculated at 0, 2, and 4 hours of each PET; $D/D_0$ glucose was calculated at 2 and 4 hours of each PET. The $K_{BD}$s for urea, creatinine, and glucose were calculated using data obtained in the first and in the last PET. For calculations of $K_{BD}$, the Waniewski model (13) was used.
The \( K_{BD} \)s of urea and creatinine were calculated according to the equation

\[
K_{BD} \ (\text{mL/min}) = \frac{(V_D/t)}{\ln \left[ \frac{V_0^{1-F} (C_B - C_D)}{V_1^{1-F} (C_B - C_D)} \right]}
\]

and the \( K_{BD} \) of glucose was calculated using the equation

\[
K_{BD} \ (\text{mL/min}) = \frac{(V_D/t)}{\ln \left[ \frac{V_0^{1-F} (C_{DO} - C_B)}{V_1^{1-F} (C_{DO} - C_B)} \right]}
\]

where \( C_B \) is the plasma water solute level at the midpoint of the 4-hour dwell (mg/dL); \( C_{DO} \) is the solute level in dialysate at the beginning of the dwell (mg/dL); \( C_B \) is the solute level in dialysate at the end of the dwell (mg/dL); \( F \) is a correction factor for convective transport (a value of 0.5 was applied); \( V_D \) is the interpolated dialysate volume at the midpoint of the dwell (mL); \( V_0 \) is the dialysate volume at the beginning of the dwell (mL); \( V_1 \) is the dialysate volume the end of the dwell (mL); and \( t \) is the dwell period in minutes.

For calculations of \( K_{BD} \), assumptions were made that, during the entire 4-hour dwell, the blood solute level is stable and that linear increments in dialysate volume occur up to 2 hours of dwell. Instilled volume of dialysis solution (2 L at 0 time) and measured dialysate volume plus 15 mL (3 = 5 mL removed for estimations) after the 4-hour dwell were used for interpolation. Inflow and outflow times were not used in calculations; \( K_{BD} \) values represent peritoneal transfer during the dwell (not during the entire exchange).

Plasma water (PW) solute concentrations were used in estimating \( K_{BD} \) (14,15). Solute concentrations in PW were calculated using whole-plasma (P) solute concentrations according to the formula (14)

\[
PW = \mu^\ast \omega \ast P^\ast
\]

where \( \mu^\ast = 1/\ (1 - V_{lip} \ast - 0.00071 \cdot C_{prot} \ast) \). The denominator in that equation is derived from the classic formula given by Eiseman et al (16), \( V_{lip} \ast \) is the fractional volume of plasma lipids (14,17), and \( C_{prot} \ast \) is the plasma concentration of total protein obtained at the midpoint of the 4-hour dwell.

Values of \( K_{BD} \) were calculated for three PET dwell periods as previously described (18): period I, between 0 time and the first 2 hours of dwell; period II, between 2 hours and 4 hours of dwell; and period III, between 0 time and 4 hours of dwell.

Urea, creatinine, and glucose were estimated using reagents from Cormay Reagents, Lublin, Poland. Measured creatinine concentration in dialysate was corrected using the glucose concentration in the examined samples, because glucose interferes in the creatinine assay based on the alkaline picrate reaction (Jaff method) (12,14,19,20).

The D/P creatinine and D/D\( _0 \) glucose obtained at 4 hours of the PET were used to evaluate the peritoneal membrane permeability (12). The D/P creatinine was used to evaluate the peritoneal permeability from the vascular to the mesothelial side of the peritoneal membrane (V M\( \bullet \) M); the D/D\( _0 \) glucose was applied to evaluate the peritoneal permeability in the opposite direction (M V\( \bullet \) V). Owing to the small number of cases being studied, the patients were divided only into high and low transporters. High V\( \bullet \) M transporters had D/P creatinine above 0.65; high M\( \bullet \) V transporters had D/D\( _0 \) glucose below 0.38. Low V\( \bullet \) M transporters had D/P creatinine ≤ 0.65; high M\( \bullet \) V transporters had D/D\( _0 \) glucose ≥ 0.38.

Results are expressed as mean ± standard deviation (SD). The first and last PET values, the \( K_{BD} \)s, and the PET results obtained as the arithmetical mean of all of a patient’s PET values in the course of PD treatment were used for statistical analysis. The Wilcoxon test for paired data or the Mann—Whitney test for unpaired data were used to compare differences to determine significance. The corrected chi-square test was applied for comparison of percentile differences in the peritoneal permeability between examined groups. Statistical significance was defined as a \( P^\ast \) value below 0.05.

Results

Residual dialysate volumes before PET in group I were 480 ± 299 mL (first PET) and 421 ± 233 mL (last PET). The respective data in group II were 471 ± 270 mL and 425 ± 264 mL. Dialysate volumes obtained after a 4-hour dwell were 2334 ± 213 mL (first PET) and 2312 ± 195 mL (last PET) in group I, and 2344 ± 271 mL (first PET) and 2298 ± 237 mL (last PET) in group II. The respective differences in residual or 4-hour dialysate volumes were not statistically significant.
No significant differences were seen between groups with regard to D/P urea, creatinine, or glucose (Table I) or K_{BD} (Table II) of those molecules in the first PET. In the last PET and in the mean PET, a tendency was observed in group I for D/P urea or D/P creatinine to be lower as compared with group II (Table I), but those results did not reach significance. Significantly lower K_{BD} urea values were seen in hours 2—4 of the last PET in group I as compared with the respective values in group II (Table II).

The older patients showed lower PET curves of D/P urea (Figure 1), K_{BD} urea (Figure 2), and D/P creatinine (Figure 3) at PD end as compared with PD start. Such significant differences were shown neither in the younger group nor for D/D_{0} glucose.

At the start of PD therapy, the percentage of low V^*•M and low M^*•V transporters was lower as compared with group II (Table I), but those results did not reach significance. The percentile profile between the groups.

**TABLE I** Dialysate-to-plasma (D/P), D/P creatinine, and dialysate-to-dialysate (D/D_{0}) glucose at 0, 2, and 4 hours of the peritoneal equilibration tests (PETs) of patients in groups I and II

<table>
<thead>
<tr>
<th>Examined parameter</th>
<th>Group</th>
<th>0</th>
<th>2</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>First PET</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>D/P urea</td>
<td>I</td>
<td>0.14±0.09</td>
<td>0.57±0.18</td>
<td>0.82±0.11</td>
</tr>
<tr>
<td></td>
<td>II</td>
<td>0.09±0.08</td>
<td>0.56±0.19</td>
<td>0.74±0.19</td>
</tr>
<tr>
<td>D/P creatinine</td>
<td>I</td>
<td>0.07±0.06</td>
<td>0.39±0.15</td>
<td>0.62±0.13</td>
</tr>
<tr>
<td></td>
<td>II</td>
<td>0.09±0.08</td>
<td>0.40±0.16</td>
<td>0.60±0.17</td>
</tr>
<tr>
<td>D/D_{0} glucose</td>
<td>I</td>
<td>0.64±0.17</td>
<td>0.47±0.13</td>
<td>0.44±0.15</td>
</tr>
<tr>
<td></td>
<td>II</td>
<td>0.65±0.15</td>
<td>0.44±0.15</td>
<td>0.43±0.15</td>
</tr>
<tr>
<td><strong>Last PET</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>D/P urea</td>
<td>I</td>
<td>0.09±0.06</td>
<td>0.50±0.18</td>
<td>0.68±0.16</td>
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<tr>
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<td>II</td>
<td>0.15±0.08</td>
<td>0.49±0.20</td>
<td>0.73±0.19</td>
</tr>
<tr>
<td>D/P creatinine</td>
<td>I</td>
<td>0.05±0.05</td>
<td>0.36±0.13</td>
<td>0.54±0.17</td>
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<tr>
<td></td>
<td>II</td>
<td>0.09±0.07</td>
<td>0.35±0.17</td>
<td>0.55±0.18</td>
</tr>
<tr>
<td>D/D_{0} glucose</td>
<td>I</td>
<td>0.69±0.16</td>
<td>0.46±0.20</td>
<td>0.41±0.16</td>
</tr>
<tr>
<td></td>
<td>II</td>
<td>0.61±0.16</td>
<td>0.40±0.16</td>
<td>0.40±0.16</td>
</tr>
<tr>
<td><strong>Mean PET</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>D/P urea</td>
<td>I</td>
<td>0.11±0.04</td>
<td>0.48±0.10</td>
<td>0.69±0.11</td>
</tr>
<tr>
<td></td>
<td>II</td>
<td>0.13±0.04</td>
<td>0.50±0.11</td>
<td>0.74±0.25</td>
</tr>
<tr>
<td>D/P creatinine</td>
<td>I</td>
<td>0.05±0.03</td>
<td>0.34±0.10</td>
<td>0.57±0.12</td>
</tr>
<tr>
<td></td>
<td>II</td>
<td>0.08±0.05</td>
<td>0.38±0.13</td>
<td>0.58±0.16</td>
</tr>
<tr>
<td>D/D_{0} glucose</td>
<td>I</td>
<td>0.60±0.11</td>
<td>0.42±0.09</td>
<td>0.41±0.09</td>
</tr>
<tr>
<td></td>
<td>II</td>
<td>0.61±0.11</td>
<td>0.41±0.08</td>
<td>0.41±0.08</td>
</tr>
</tbody>
</table>

*P< 0.05 compared with respective results in group I (Mann—Whitney test).

**TABLE II** Diffusive mass transfer-area coefficients (K_{BD}, mL/min) of urea, creatinine, and glucose during the peritoneal equilibration test (PET) in patients of group I and II

<table>
<thead>
<tr>
<th>Examined parameter</th>
<th>Group</th>
<th>0—2</th>
<th>2—4</th>
<th>0—4</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>First PET</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>K_{BD} urea</td>
<td>I</td>
<td>11.9±6.9</td>
<td>17.5±8.1</td>
<td>15.1±6.0</td>
</tr>
<tr>
<td></td>
<td>II</td>
<td>11.9±8.1</td>
<td>13.5±11.0</td>
<td>12.9±8.6</td>
</tr>
<tr>
<td>K_{BD} creatinine</td>
<td>I</td>
<td>6.4±4.1</td>
<td>11.4±6.8</td>
<td>9.1±4.3</td>
</tr>
<tr>
<td></td>
<td>II</td>
<td>7.0±5.3</td>
<td>10.4±8.5</td>
<td>8.9±6.2</td>
</tr>
<tr>
<td>K_{BD} glucose</td>
<td>I</td>
<td>8.8±5.6</td>
<td>7.5±4.1</td>
<td>8.2±2.5</td>
</tr>
<tr>
<td></td>
<td>II</td>
<td>7.8±5.3</td>
<td>11.7±10.8</td>
<td>10.0±6.6</td>
</tr>
<tr>
<td><strong>Last PET</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>K_{BD} urea</td>
<td>I</td>
<td>10.5±6.4</td>
<td>9.4±8.0</td>
<td>10.3±5.5</td>
</tr>
<tr>
<td></td>
<td>II</td>
<td>9.5±8.3</td>
<td>15.9±10.7a</td>
<td>13.0±8.6</td>
</tr>
<tr>
<td>K_{BD} creatinine</td>
<td>I</td>
<td>6.4±3.7</td>
<td>8.1±5.7</td>
<td>7.4±4.5</td>
</tr>
<tr>
<td></td>
<td>II</td>
<td>5.9±4.4</td>
<td>8.7±6.0</td>
<td>7.4±4.5</td>
</tr>
<tr>
<td>K_{BD} glucose</td>
<td>I</td>
<td>7.0±4.5</td>
<td>9.3±5.4</td>
<td>8.7±4.4</td>
</tr>
<tr>
<td></td>
<td>II</td>
<td>9.9±5.5</td>
<td>11.0±7.6</td>
<td>10.8±5.6</td>
</tr>
</tbody>
</table>

*P< 0.05 compared with respective results in group I (Mann—Whitney test).

![FIGURE 1](image)

In Japanese PD patients, elderly people were shown to have higher peritoneal permeability than ability was not statistically different as compared with the first PET. No statistical differences were seen in the percentile profiles between the groups.

**Discussion**

In our study, dialysate residual volumes before PET yielded higher values as compared with those demonstrated by Twardowski et al. (12), but they were similar in both groups and during the course of PD. Thus, we assume that the influence of residual volume on the results did not reach significance. No statistical differences were seen between the groups.
middle-aged and young people, with the higher permeability being a reason for a lower serum albumin level in the elderly patients (1). Our results confirm those data, which showed no age-related differences in peritoneal permeability in adult patients at baseline (2). The older Polish patients in our study also did not show significant differences in peritoneal permeability as compared with Argentinean patients above 60 years of age (21). However, in our study, the D/P ratios for urea and creatinine indicated a decrease of peritoneal permeability from the vascular to the mesothelial side of the membrane in older patients during the course of PD treatment. Because our patients were treated with PD for approximately 20 months, the D/P ratios and K\ BD\ s of small solutes should be unchanged. That assumption is based on results indicating no changes in peritoneal membrane permeability in PD patients followed for (on average) 15 months (22) or 18 months (23), and on data showing stable transport rates for more than 2 years (3,4).

It is interesting to speculate on the reasons for decreasing peritoneal permeability in the course of PD in older patients, but not in younger ones. Earlier data excluded an increase in hematocrit as a reason for the decrease in effective peritoneal surface area and peritoneal transport (10,24). As in other studies (25,26), the peritonitis rate in our study was not different in the examined older and younger patients. Additionally, the long-term effects of a definite bacterial peritonitis episode showed an increase in small solute transport (27). It has been shown that D/P creatinine, D/D\gold\ glucose, K\ BD\ creatinine, and K\ BD\ glucose obtained by the standard PET during the first 2 weeks of PD are more likely to change upon subsequent testing than the same data obtained after at least 4 weeks of PD (6). In our study, a similar number of early PETs
occurred in both groups. However, changes from the initial transport also indicate an increase, not a decrease, in the peritoneal permeability (6).

A possibility exists that, in older patients, peritoneal capillary blood volume and perfusion of capillaries are smaller than in younger patients. Several experimental studies have demonstrated the importance of effective peritoneal blood flow on peritoneal solute clearances (28—31). On the other hand, effective peritoneal blood flow, evaluated using a Kbd for CO₂ gas, was not significantly age-dependent and was not related to duration of PD at least to first 12 months of intermittent PD (32).

Our study indicates a decrease in the V♦M permeability of the peritoneum for low molecular weight solutes in the course of PD in older patients. Those changes did not occur in M♦V peritoneal membrane permeability. In the studies of Passlick—Deetjen et al (4), the PET values for glucose changed later than those for creatinine, indicating that M♦V transport is more resistant to time-dependent influences. However, the decrease in V♦M permeability did not change the general classification into low and high V♦M peritoneal transporters evaluated according to D/P creatinine at 4 hours of a PET dwell.

Our results suggest that older patients may show a decrease in peritoneal permeability from the vascular to the mesothelial side of the membrane in the course of PD treatment. Peritoneal transport in the opposite direction remains unchanged during approximately 20 months from the start of PD treatment. Patients under 60 years of age maintain stable bi-directional permeability under a comparable PD duration.

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References


Corresponding author:
Alicja E. Grzegorzewska, MD, PhD, Chair and Department of Nephrology, Al. Przybyszewskiego 49, Poznan 60-355 Poland.
Antonios H. Tzamaloukas,1 Glen H. Murata,2 Karen S. Servilla,1 Richard M. Hoffman2

To investigate the relationship between obesity, small-solute clearances, and nutrition in continuous peritoneal dialysis (CPD), we compared clearances and nutrition indices between 270 obese and 502 normal-weight CPD patients. Degree of obesity was classified by the ratio of body weight (W) to desired weight (DW) at the first clearance study. The DWs were obtained from the tables of the Metropolitan Life Insurance Company, assuming a medium skeletal frame. The obese patients (group I) had W/DW > 1.2 (1.38 ± 0.17), and the normal-weight patients (group II) had 0.9 ≤ W/DW ≤ 1.2 (1.05 ± 0.08). Nutrition indices derived from urea nitrogen and creatinine excretion were normalized by both W and DW.

The following variables differed between group I (first value) and group II: sex (women: 48.2% vs. 33.9%), W (87.6 ± 14.4 kg vs. 68.2 ± 8.7 kg), body surface area (1.95 ± 0.22 m² vs. 1.77 ± 0.16 m²), body water by method of Watson (41.2 ± 7.7 L vs. 36.3 ± 5.5 L), body mass index (31.8 ± 3.9 vs 24.3 ± 2.0), protein nitrogen appearance (PNA: 62.9 ± 17.6 g/kg in 24 h vs. 57.7 ± 15.7 g/kg in 24 h), PNA normalized to DW (1.08 ± 0.29 g/kg in 24 h vs. 0.96 ± 0.26 g/kg in 24 h), creatinine excretion (CrEx: 1111 ± 396 mg in 24 h vs. 991 ± 348 mg in 24 h), CrEx/W (12.6 ± 3.7 g/kg in 24 h vs. 15.4 ± 4.5 g/kg in 24 h), CrEx/DW (17.3 ± 5.3 g/kg in 24 h vs. 15.1 ± 4.8 g/kg in 24 h), lean body mass (LBM: 49.3 ± 13.8 kg vs. 43.6 ± 11.9 kg), LBM/W (0.56 ± 0.12 vs. 0.64 ± 0.15), and LBM/DW (0.77 ± 0.18 vs. 0.67 ± 0.16), all at p ≤ 0.034. Marginal differences (0.10 > p > 0.05) were found in the diabetes prevalence (53.0% vs. 40.8%), height (165.9 ± 11.7 cm vs. 167.4 ± 9.8 cm), and serum albumin (3.64 ± 0.55 g/dL vs. 3.53 ± 0.62 g/dL). No differences were found in age, duration of CPD until the first clearance study, percent of subjects with anuria, Kt/V urea, creatinine clearance, blood urea nitrogen, serum creatinine, and PNA normalized to W.

Obese CPD patients tend to have better nutrition indices than do normal-weight CPD patients with similar small-solute clearances. In obese subjects, normalization by W creates inappropriately low values for nutrition indices derived from urea nitrogen and creatinine excretion. Normalization of those indices by DW appears preferable.

Key words
Obesity, urea clearance, creatinine clearance, nutrition, continuous peritoneal dialysis

Introduction
Recent evidence suggests that dialysis alters the effect of obesity on morbidity and mortality. Obesity increases the risk of death in general populations (1,2). In contrast, survival of obese hemodialysis patients is prolonged (3,4). Studies involving relatively small numbers of subjects have reported that obesity either has no effect on survival (5,6), or predicts long survival (7) of patients on continuous peritoneal dialysis (CPD).

The survival advantages of obesity are seen despite the difficulties in achieving adequate normalized clearances in large CPD patients (8) and may be related to better nutrition. Nutrition indices, such as serum albumin, tend to be higher in large CPD patients (9,10). The purpose of the present study was to investigate the association between obesity, small-solute clearances, and nutrition in CPD patients. We addressed two questions: (A) Are small-solute clearances different between obese and normal-weight CPD patients at the first clearance study? And, (B) is nutrition different between obese and normal-weight patients on CPD?
Patients and methods
The patients in the present study started CPD in several North American dialysis centers located in Albuquerque, Pittsburgh, and Toronto between 1991 and 2000. We analyzed normalized small-solute clearances and nutrition indices in CPD patients who were characterized as obese (group 'I') or normal-weight (group 'II') at the first clearance study after CPD initiation. The degree of obesity was classified by the ratio of actual weight (W) to desired weight (DW). The DW was obtained from the tables of the Metropolitan Life Insurance Company (11,12). Obesity was characterized as obese (group 'I') or normal-weight (group 'II') at the first clearance study after CPD initiation. The degree of obesity was classified by the DW/W > 1.2, and normal weight was defined as W/DW > 1.2, and normal weight was defined as 0.9 ≤ W/DW ≤ 1.2 (13).

Small-solute clearances [Kt/V urea, creatinine clearance (CCr)], nutrition indices derived from urea nitrogen excretion [including protein nitrogen appearance (PNA) and PNA normalized to body water divided by 0.58 (nPNA), where body water was calculated from actual weight], and nutrition indices derived from creatinine excretion [including lean body mass (LBM) and LBM normalized to body weight (LBM/W)] were calculated by standard methods (14). Adequate small-solute clearances were set according to the Dialysis Outcomes Quality Initiative (K/DOQI) guidelines (15). Adequate weekly Kt/V urea was set at ≥ 2.0 (13). Adequate weekly CCr was set at ≥ 1.73 m² per 1.73 m² for all subjects, because peritoneal equilibration test (PET) data were missing for a substantial number of patients.

Continuous variables were expressed as mean ± standard deviation and were compared by the two-tailed unpaired Student t-test. Categorical variables were compared between groups 'I' and 'II' by chi-square test.

Results
Table I shows anthropometric and demographic variables that differed between groups 'I' and 'II'. The obese group contained a higher percentage of women and a marginally higher percentage of subjects with diabetes mellitus than did the normal-weight group. Most size indicators [W/DW, body mass index (BMI), body surface area (BSA), body water by method of Watson (V_Watson)] were larger in the obese group. Only height was marginally greater in the normal-weight group.

Age of the subjects (group 'I': 55.8 ± 12.7 years; group 'II': 55.8 ± 14.4 years) and duration of CPD until the first clearance study (group 'I': 6.8 ± 3.4 months; group 'II': 7.2 ± 3.1 months) did not differ between the groups.

Table II shows weekly clearances and nutrition indices. Total Kt/V urea, total CCr, and percentage of subjects with anuria (group 'I': 24.1%; group 'II': 27.9%) did not differ between the groups. The percentage of subjects with adequate Kt/V urea and adequate CCr did not differ between the groups. Urine volume was marginally greater in the normal-weight group.

Table I. Anthropometric and demographic variables that differed between obese and normal-weight continuous peritoneal dialysis patients

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group 'I'</th>
<th>Group 'II'</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients (n)</td>
<td>270</td>
<td>502</td>
<td></td>
</tr>
<tr>
<td>W/DW</td>
<td>1.38±0.17</td>
<td>1.05±0.08</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>31.8±3.9</td>
<td>24.3±2.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BSA (m²)</td>
<td>1.95±0.22</td>
<td>1.77±0.16</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>V_Watson (L)</td>
<td>41.2±7.7</td>
<td>36.3±5.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>87.6±14.4</td>
<td>68.2±8.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Sex (women)</td>
<td>130 (48.2%)</td>
<td>170 (33.9%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>165.9±11.7</td>
<td>167.4±9.8</td>
<td>0.076a</td>
</tr>
<tr>
<td>Diabetic subjects</td>
<td>143 (53.0%)</td>
<td>205 (40.8%)</td>
<td>0.097a</td>
</tr>
</tbody>
</table>

a Marginal difference.

W= actual weight; DW= desired weight; BMI= body mass index; BSA = body surface area; V_Watson = body water by method of Watson.

Table II. Weekly clearances and nutrition indices in obese and normal-weight continuous peritoneal dialysis patients

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group 'I'</th>
<th>Group 'II'</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kt/V urea</td>
<td>2.01±0.55</td>
<td>2.02±0.57</td>
<td>NS</td>
</tr>
<tr>
<td>Adequate Kt/V urea</td>
<td>113 (41.9%)</td>
<td>275 (54.8%)</td>
<td>NS</td>
</tr>
<tr>
<td>CCr (L/1.73 m²)</td>
<td>69.2±27.4</td>
<td>68.3±25.8</td>
<td>NS</td>
</tr>
<tr>
<td>Adequate CCr</td>
<td>120 (44.4%)</td>
<td>264 (52.6%)</td>
<td>NS</td>
</tr>
<tr>
<td>Serum albumin (g/dL)</td>
<td>3.64±0.55</td>
<td>3.53±0.62</td>
<td>0.092</td>
</tr>
<tr>
<td>UNEx (mg in 24h)</td>
<td>6325±2355</td>
<td>5623±2110</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PNA (g in 24h)</td>
<td>62.9±17.6</td>
<td>57.7±15.7</td>
<td>0.034</td>
</tr>
<tr>
<td>nPNA_W (g/kg in 24h)</td>
<td>0.90±0.23</td>
<td>0.93±0.24</td>
<td>NS</td>
</tr>
<tr>
<td>nPNA_DW (g/kg in 24h)</td>
<td>1.08±0.29</td>
<td>0.96±0.26</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CrEx (mg in 24h)</td>
<td>1111±396</td>
<td>991±348</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LBM (kg)</td>
<td>49.3±13.8</td>
<td>43.6±11.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LBM/W</td>
<td>0.56±0.12</td>
<td>0.64±0.15</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LBM/DW</td>
<td>0.77±0.18</td>
<td>0.67±0.16</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Kt/V urea = creatinine clearance; UNEx = urea nitrogen excretion; PNA = protein nitrogen appearance; nPNA = PNA normalized to actual weight; nPNA_W = PNA normalized to desired weight; CrEx = creatinine excretion; LBM = lean body mass; W = actual weight; DW = desired weight.
(group I: 0.51 ± 0.61 L in 24 h; group II: 0.40 ± 0.48 L in 24 h; \( p = 0.010 \)) and dialysate drain volume \( (V_d) \) group I: 10.3 ± 2.6 L in 24 h; group II: 9.5 ± 2.0 L in 24 h; \( p < 0.001 \) were both higher in the obese group. However the ratio between \( V_d \) and \( V_{Watson} \) \( (V_d/V) \) was lower in the obese group \( (0.254 ± 0.065 \text{ L/L in 24 h vs. } 0.268 ± 0.062 \text{ L/L in 24 h}, \ p = 0.004) \). Values of dialysate-to-plasma (D/P) urea and creatinine did not differ between the groups. Group I had lower weekly peritoneal Kt/V urea \( (1.57 ± 0.38 \text{ vs. } 1.63 ± 0.38, \ p = 0.031) \), but renal Kt/V urea and peritoneal and renal CCr did not differ between the groups.

Serum albumin was marginally higher in the obese group (Table II). Serum urea nitrogen (group I: 55.1 ± 17.9 mg/dL; group II: 55.1 ± 17.0 mg/dL) and serum creatinine (group I: 9.9 ± 3.4 mg/dL; group II: 9.9 ± 3.7 mg/dL) did not differ between the groups. Urea nitrogen excretion and PNA were higher in the obese group. The nPNA\(_W\) did not differ between the groups, but the nPNA\(_PW\) was higher in the obese group. Creatinine excretion and LBM were higher in the obese group. Creatinine excretion normalized to actual weight \( (\text{group I: } 12.6 ± 3.7 \text{ mg/kg in 24 h; group II: } 15.4 ± 4.5 \text{ mg/kg in 24 h; } p < 0.001) \) and LBM normalized to actual weight were higher in the normal-weight group. Creatinine excretion normalized to desired weight \( \text{(group I: } 17.3 ± 5.3 \text{ mg/kg in 24 h; group II: } 15.7 ± 4.8 \text{ mg/kg in 24 h; } p < 0.001) \) and LBM normalized to desired weight were higher in the obese group.

**Discussion and conclusions**

A recent analysis of nutrition indices in a sample of CPD patients representative of the U.S. peritoneal dialysis population showed disparate results, particularly between serum albumin and other nutrition indices (16). Mean BMI in that analysis was 27.0 kg/m², which corresponds to a W/DW of 1.18 in women and 1.22 in men (17). Those values are close to the cut-off values for obesity \( (W/DW' = 1.20) \) used in the present study. Therefore, approximately 50% of American patients who are currently on CPD are obese. Analysis of the delivered dose of CPD and of nutrition in that large segment of CPD patients is therefore important.

The present study found similar normalized clearance values between obese and normal-weight CPD patients at the first clearance study. Renal normalized clearances were also similar. An attempt to compensate for the large size of the obese patients was made by prescribing larger daily fill volumes, which resulted in larger daily drain volumes \( \text{(Table II). However, that attempt was incomplete. To completely compensate for large body size, the ratio } V_d/V \text{ must stay the same throughout the range of body sizes (18). In the present study, the ratio } V_d/V \text{ was lower in the obese group and resulted in a lower value for peritoneal Kt/V urea. The higher } V_d \text{ delivered to the obese group was sufficient to offset the higher BSA in that group, and to produce similar peritoneal CCr values in the obese and the normal-weight groups, because the increase in BSA as obesity develops is relatively less than the corresponding increase in } V \text{ (19). Therefore, obesity causes high } V/BSA \text{ ratios and relatively greater difficulty in achieving adequate Kt/V than adequate CCr, especially in anuric subjects (8,19).}

The main finding of the present study was that, although small-solute clearances were similar between obese and normal-weight CPD patients, the obese subjects had consistently higher values for their nutrition indices than did the subjects with normal body weight. One important finding was that nutrition indices derived by normalizing urea nitrogen and creatinine excretion to actual weight tended to be unrealistically low in obese patients. Harty et al indicated that normalization of nutrition indices by actual weight tends to cause low values in large subjects, and that those low values are at odds with other nutrition indices (20). In the present report, normalization of the same indices by desired weight produced values consistent with the other nutrition indices.

We conclude that nutrition is uniformly better in obese patients than in normal-weight patients receiving a comparable dose of CPD. Desired weight appears to be more suitable than actual weight as the size indicator used to normalize nutrition indices derived from urea nitrogen and creatinine excretion in both obese and underweight (21) CPD subjects.

**Acknowledgment**

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**References**


2. Calle EE, Thun MJ, Petrelli JM, Rodriguez C, Heath


Corresponding author:
Antonios H. Tzamaloukas, Renal Section (111C), New Mexico VA Health Care System, 1501 San Pedro SE, Albuquerque, New Mexico 87108 U.S.A.
The optimal time to start renal replacement therapy remains controversial. Residual renal function (RRF) and nutrition status being important prognostic factors, the present study evaluates the impact of timely start of peritoneal dialysis (PD) on their evolution.

Our study used a prospective database on pre—end-stage renal disease patients at a tertiary care center. We included 18 patients who were planned to start PD at a GFR > 8 mL/min between 1 January and 31 December 1999.

At the start of PD (month 0), creatinine clearance (CCr) was 11.3 ± 3.9 mL/min, actual glomerular filtration rate (GFR) was 8.6 ± 3.3 mL/min, and Kt/V was 1.56 ± 0.65. The monthly declines of GFR and CCr before and after the start of PD were —0.47 ± 0.64 mL/min (GFR) and —0.59 ± 0.46 mL/min (CCr), and —0.06 ± 0.30 mL/min (GFR) and —0.05 ± 0.39 mL/min (CCr) respectively (p = 0.034 and 0.001, respectively). Before the start of PD, CCr was 21.9 ± 4.6 mL/min (month —12) and 18.1 ± 4.8 mL/min (month —6, p < 0.001). After the start of PD, CCr was 12.0 ± 4.3 mL/min (month 3), 12.5 ± 4.9 mL/min (month 6), and 13.1 ± 5.4 mL/min (month 12, p = 0.9). Serum albumin dropped until just before the start of PD: 3.89 ± 0.59 g/dL (month —6) and 3.78 ± 0.51 g/dL (month —3) versus 2.56 ± 1.60 g/dL (month 0, p = 0.04). Serum albumin then increased to 3.42 ± 0.95 mg/dL (month 3 after the start of PD) and 3.35 ± 0.86 mg/dL (month 6 after the start of PD, p = 0.04).

In the months preceding the start of PD, the normalized protein catabolic rate (nPCR) dropped from 1.41 ± 0.36 g/kg daily (month —6) and 1.3 ± 0.46 g/kg daily (month —3) to 1.12 ± 0.25 g/kg daily (month 0). It then stabilized at 1.17 ± 0.25 g/kg daily (month 3) and 1.18 ± 0.17 g/kg daily (months 6).

One patient died owing to a cerebrovascular accident after 18 months of PD, and one was transferred to hemodialysis because of ultrafiltration failure after 19 months of PD. During 264 patient-months, 14 peritonitis episodes occurred. Of the 14 episodes, 12 resolved without complication, and the catheter was replaced in 2 episodes.

After timely start of PD, the rate of RRF decline decreases. Already, at a GFR > 8 mL/min, uremia has a negative impact on nutrition parameters. Timely initiation of PD could reverse the negative evolution of albumin and stop the decline of nPCR. No severe complications related to PD were seen. In view of the important impact of RRF and nutrition on patient outcome, our data may favor an early start of PD.

Key words

Early start, residual renal function, uremic toxins

Introduction

The debate on the optimal timing for starting renal replacement therapy (RRT) is still ongoing. The ideal level of residual renal function (RRF) that warrants assistance of artificial RRT depends upon various factors.

First and most important, the desired medical benefits of starting RRT should outweigh the potential medical risks. That balance depends upon the degree of harm caused by a certain degree of renal impairment and the quality of the RRT. If the RRT is of high quality and has little negative effect, then the goal of no harm is easier to attain.

Second, if the medical benefits are established, the cost—benefit in financial and health care budgets should also be established. Because both RRT and the complications caused by renal failure involve highly specialized care in terms both of staffing and of materials and medications the cost—benefit ratio depends on the capacity of the RRT to reduce the cost of the complications of end-stage renal failure. If earlier initiation of RRT results in an improvement or stabilization of other comorbid conditions, then
the cost—efficiency and cost—benefit of early start could be acceptable, both on the level of the individual patient and on the macroeconomic societal level.

Peritoneal dialysis (PD) could be the modality of choice for early start dialysis, because it adduces a lower economic cost and a lower exposure to artificial extracorporeal materials (1). In addition, by using incremental dialysis, the PD treatment can be more easily tailored to declining RRF than can hemodialysis (HD). Because RRF and nutrition status are, among others, two important predictors of outcome and complications in end-stage renal disease patients (2), we evaluated the impact of early start PD on the evolution of these two parameters.

**Patients and methods**

The data used for the present analysis were retrieved from a database of patients attending the nephrology outpatient clinic of the University Hospital Gent. The database prospectively collects data for all patients attending the outpatient clinic. Patients for whom data on RRF were available for more than 18 months before the start of PD, and who were willing to perform PD, were eligible for the study if their glomerular filtration rate (GFR) was between 8 mL/min and 12 mL/min and if no uremic symptoms were present. Glomerular filtration rate was defined as the mean of creatinine and urea clearances. Eligible patients were informed by the attending physician and by the predialysis team about the potential advantages and disadvantages of an earlier initiation of RRT by PD. During the period 1 January 1999—31 December 1999, 18 early-referred patients were included in the study. All patients were started on continuous ambulatory peritoneal dialysis (CAPD) with four 2-L exchanges of 1.36% glucose solution.

Every 6 weeks, patients collected 24-hour urine and dialysate samples for calculation of RRF, PCR, and peritoneal clearance. Routine blood sampling was also done. Serum albumin was measured by a nephelometric method. For calculation of normalized protein catabolic rate (nPCR), the formula of Bergström et al was used (3).

Statistical analysis was carried out using SPSS 10.0 (SPSS Inc., Chicago, IL, U.S.A.). For serial data, repeated-measures ANOVA was used, with least significant difference testing for post-hoc differences between time points.

**Results**

During the inclusion period, 18 patients (9 men, 9 women) were added into the study. Underlying causes of renal failure were diabetes (diagnosed in 5 patients), polycystic kidney disease (2 patients), interstitial nephritis (2 patients), nephroangiosclerosis (5 patients), and chronic glomerulonephritis (4 patients). Mean age at the start of PD was 56.2 ± 6.8 years.

At the start of PD (month 0), creatinine clearance (CCr) was 11.3 ± 3.9 mL/min, actual GFR was 8.6 ± 3.3 mL/min, and Kt/V was 1.56 ± 0.65 per week. The monthly decline of GFR was —0.4 ± 0.64 mL/min before, and —0.06 ± 0.30 mL/min after the start of PD (p = 0.034). The monthly decline of CCr was —0.56 ± 0.46 mL/min before, and —0.0 ± 0.39 mL/min after the start of PD (p = 0.001). At months —12 and —6, CCr was 21.9 ± 4.6 mL/min and 18.1 ± 4.8 mL/min (ANOVA with CCr at month 0: p < 0.001). At months 3, 6, and 12, CCr was 12.0 ± 4.3 mL/min, 11.5 ± 4.9 mL/min, and 13.1 ± 5.4 mL/min (ANOVA with CCr at month 0: p = 0.9). Serum albumin dropped from 3.89 ± 0.59 g/dL at month —6 and 3.78 ± 0.51 g/dL at month —3 to 2.56 ± 1.60 g/dL just before the start of PD (month 0; ANOVA: p = 0.04). Serum albumin increased after the start of PD to 3.42 ± 0.95 g/dL and 3.35 ± 0.86 g/dL at months 3 and 6 respectively (ANOVA: p = 0.04). The nPCR decreased from 1.41 ± 0.36 g/kg daily and 1.34 ± 0.46 g/kg daily at months —6 and —3 to 1.12 ± 0.25 g/kg daily at month 0. After the start of PD, nPCR stabilized at 1.17 ± 0.25 g/kg daily at month 3 and 1.18 ± 0.17 g/kg/day at month 6.

One patient died after 18 months of PD (owing to a cerebrovascular accident), and one patient was transferred to HD after 19 months of PD (because of ultrafiltration failure). At 1 February 2002, 5 patients had been successfully transplanted, including the one that switched to HD. The other 12 patients are still on PD. During 264 patient—months, 14 episodes of peritonitis occurred. Of the 14 episodes, 12 resolved without complication. The catheter was successfully replaced in 2 episodes.

**Discussion**

The optimal level of RRF at which to start RRT is still a topic of debate. Many different guidelines have been proposed, each with its own level of RRF that should urge start of RRT. Nevertheless, the underlying crite-
ria on which those guidelines are based are mostly comparable. They relate to the positive impact of RRF on outcome (4), the negative impact of malnutrition on outcome (2), and the increased risk for left ventricular hypertrophy (5) with its associated comorbidity.

Peritoneal dialysis has some advantages over HD as first RRT modality. Once the concept of early start is accepted, PD may be the optimal modality, because the costs and the exposure to potential hazards are lower in PD as compared with HD. Furthermore, incremental dialysis is easier to start with PD than with HD (6).

The present study indicates that, potentially, an earlier start of RRT with PD may positively influence the decline of RRF and of nPCR. Of course, our findings are preliminary, as no randomized control group was established, and the number of patients was small. The data thus need confirmation in a larger-scale study.

The evaluation of the impact of an earlier start of RRT on outcome is hampered by various problems. First, it is very difficult (if not impossible) to randomize patients between early and conventional treatment start. Indeed, the European Multicenter Study about Healthy Start (EMSAH) had to be interrupted owing to recruitment difficulties. After being informed, the convinced patients wanted to start early without randomization, and the unconvinced patients refused to be randomized because they did not want an early start (Dratwa M. Personal communication). The impossibility of launching a randomized study creates many problems of corrections for differences in the patient mix, for indications for starting dialysis in the various groups, and for differences in lead-time bias. Second, in view of the enormous potential impact of early start on health care resources and labor, a pharmacoeconomic evaluation of early-start RRT is also needed. Early-start RRT will likely only be accepted by health care policymakers when the benefits of early-start RRT are clearly demonstrated to reduce the costs of comorbidity caused by a delayed or normal start to such extent that they counterbalance the extra costs induced by the RRT treatment per se.

The CANUSA study (4) and many other studies since have demonstrated the impact of RRF on outcome. Those findings are not very surprising, because RRF has an important impact on total solute clearance (especially the clearance of middle molecules such as \( \beta_2 \)-microglobulin) and on volume control in many patients. Adequate RRF also favors the quality of life of the patient, because it allows some freedom in fluid and dietary intake, and it makes adapting the PD regimen to the social needs of the patient that much easier. The preservation of RRF by early-start PD is thus of utmost importance.

Ikizler et al (7) demonstrated the negative impact of declining RRF on dietary protein intake. Port (8) and Ismail et al (9) demonstrated that the mortality risk of patients increases if serum albumin at the start of RRT is below 3.5 g/dL, with an exponential increase in the risk if serum albumin falls below 3.0 g/dL. Signs of deterioration in nutrition status should urge the start of RRT. In our patients, despite a GFR > 8 mL/min, a tremendous decline in nPCR and serum albumin occurred in the months preceding the start of RRT, a trend that was interrupted and stabilized by the start of PD.

The prevalence of left ventricular hypertrophy increases as RRF declines (5). In PD patients, a clear correlation also exists between RRF and hypertension, and between RRF and left ventricular hypertrophy. As long as RRF is well preserved, blood pressure control in PD patients is adequate (10), and left ventricular hypertrophy is less pronounced than in HD patients. But, as RRF declines, the picture changes, and in long-term (anuric) PD patients, left ventricular hypertrophy is more pronounced than in long-term HD patients (11).

Our observation of preservation of RRF and nutrition status is therefore of importance, because it may indicate that early-start PD potentially reduces the comorbidity associated with end-stage renal disease. Whether the costs adduced by the need for PD at an earlier stage can be compensated by the reduced costs from improved outcome is a question that remains to be answered.

The explanation of why RRF is better preserved by starting early PD is speculative. First, it may be that, by performing PD, the hemodynamic status of the patient is improved. Rottembourg et al (12) demonstrated that PD patients tend to be slightly fluid overloaded. Also, case reports seem to indicate that PD has a positive inotropic cardiac effect. The increase of cardiac output can potentially improve renal perfusion, and thus GFR.

Another mechanism might be the removal of nephrotoxic uremic retention products. Evidence for this
hypothesis was first given by Niwa and Ise (13), who investigated the impact of indoxyl sulfate on progression of glomerulosclerosis and deterioration of RRF. In partially nephrectomized rats with biopsy-proven glomerulosclerosis, Motojima et al (14) removed indoxyl sulfate either by PD or by application of oral sorbents (AST-120). Treatment was initiated 8 weeks after partial nephrectomy. The rats were randomized into a treatment group and a placebo group in a fashion matched for degree of glomerular sclerosis at the start. The treatment group received either PD (8 cycles of 1 hour, 6 days weekly) or AST-120, an oral charcoal sorbent. Whole-kidney GFR was significantly higher in the rats on PD than in those on placebo (0.50 ± 0.08 mL/min vs. 0.3 ± 0.03 mL/min, p < 0.05). Light-microscopy studies revealed that rats treated with PD and AST-120 had equally attenuated progression of glomerular sclerosis as compared with placebo-treated animals. Another argument in favor of the hypothesis on the removal of glomerulotoxic uremic retention products is the better preservation of RRF by PD as compared with HD (15). Indeed, the so-called middle molecules are not, or only to a limited extent, removed by HD (16). In contrast, McKane et al (17) recently demonstrated that the progression of decline of RRF was equal in PD and in HD if high-flux membranes were used instead of classic low-flux membranes.

A third potential pathway might be the induction of vascular endothelial growth factor (VEGF) by the instillation of glucose-containing dialysates into the peritoneal cavity. Increased VEGF expression in the peritoneum has been demonstrated after the instillation of glucose-containing dialysate, in animals (18) and patients (19) alike. Kang et al (20) demonstrated that VEGF has protective effects in a rat remnant-kidney model. After 8 weeks, the rats treated with VEGF showed reduced fibrosis and better preservation of RRF, as demonstrated by a lower peritubular capillary rarefaction index, and less collagen type III deposition. As expected, increased glomerular endothelial cell proliferation was also seen.

Conclusion
Although still preliminary, the results of our analysis point to a beneficial effect of early-start PD on the preservation of RRF and on parameters of nutrition status. Confirmation of our results in larger-scale studies is warranted.

Corresponding author:
Wim Van Biesen, MD, Renal Division, University Hospital Gent, De Pintelaan 185, Gent 9000 Belgium.