The determinants of peritoneal transport status in incident peritoneal dialysis (PD) patients are not well defined. Comorbidity, inflammation status, race, age, and mesothelial cell mass are some factors correlated with the baseline dialysate-to-plasma ratio of creatinine. Our aim was to define factors in the pre-dialysis period that possibly correlate with baseline peritoneal transport characteristics.

Our study included patients starting PD at our center over the last 7 years. These patients should have been followed in our department for at least 1 year before PD start. Demographic and laboratory data were collected at 12 and 6 months before PD start. Protein intake was calculated from 24-hour urine collections. The Davies comorbidity index was scored for the pre-dialytic period. A baseline standard peritoneal permeability analysis was performed within the 6 first months of PD therapy. The mass transfer area coefficients (MTACs) for creatinine and urea were calculated.

Of 94 consecutive PD patients, 47 patients (age: 50.7 ± 15.2 years) met the inclusion criteria. Mean monthly pre-dialytic decline in the glomerular filtration rate (GFR) was 0.27 ± 0.17 mL/min per 1.73 m² body surface area, and daily protein intake was 0.77 ± 0.19 g/kg. Baseline MTACs of creatinine and urea were 12 ± 3.6 mL/min and 19.6 ± 5.3 mL/min respectively. No correlation was found between MTAC and any of age, Davies index, protein intake, lipid levels, C-reactive protein, or monthly GFR decline.

In our population, we observed no pre-dialytic factor interfering with baseline peritoneal status.

**Key words**
Protein intake, ESRD, Davies index

**Introduction**
The vascular surface area of the peritoneum, both anatomic and effective, varies widely among peritoneal dialysis (PD) patients. Based on solute transport rates, patients can be divided into fast, average, and slow transporters. Associations have been described between peritoneal transport status and several patient characteristics, including age, race, sex, body size, comorbidity, inflammation, mesothelial cell mass area, and serum albumin (1–5).

Recently, a study from Japan (6) focused on the pre-dialytic diet as a determinant of baseline membrane transport status. The authors claimed that, compared with patients eating a higher protein diet, patients eating a very low-protein diet during the pre-dialytic period had lower dialysate-to-plasma (D/P) ratios of creatinine. The aim of our study was to define pre-dialytic factors that correlate with baseline membrane status.

**Patients and methods**
Our study included 47 of 94 consecutive adult patients who started PD at our hospital during the last 7 years. Patients with a history of transplantation (n = 8), hemodialysis (n = 6), or a peritonitis episode (n = 1) were excluded. Another 32 patients were excluded because of insufficient data.

At our center, all chronic kidney disease patients with a glomerular filtration rate (GFR) below 20 mL/min are advised to follow a low-protein diet (0.7 g/kg daily), following international guidelines. Demographic and laboratory data are collected at 12 and 6 months before PD start and at PD initiation. A baseline standard peritoneal permeability analysis (SPA) is performed within the first 6 months of PD therapy.
Biochemical measurements
Creatinine was determined by an enzymatic method using an auto analyzer (Hitachi H911: Boehringer Mannheim, Mannheim, Germany). Glucose concentration was determined by the glucose oxidase–peroxidase assay (SMA II: Technicon, Terrytown, NJ, U.S.A.). Urea in plasma and effluent was determined by an enzymatic method using an auto analyzer (Hitachi H747: Boehringer Mannheim). Serum and urine protein and albumin were measured by a nephelometry spectrophotometry method (BN 100: Behring, Marburg, Germany). Serum C-reactive protein (CRP) was assessed by an immunoturbidimetric assay.

Cancer antigen 125 (CA125), a marker of mesothelial cell mass, was measured in the 4-hour effluent of the SPA by microparticle enzyme immunoassay using a monoclonal antibody against CA125 (IMx: Abbott Laboratories, Abbott Park, IL, U.S.A.). Protein intake was calculated from 24-hour urine collections using the Maroni formula (7). Residual GFR was calculated as the mean of urea and creatinine clearances from 24-hour urine collections.

Comorbidity
The Davies comorbidity index was scored for the 1-year pre-dialytic period (8). The index is scored on the presence of 7 comorbid conditions, classifying patients into 3 risk groups: low, medium, and high risk. The low-risk group had no comorbidities; the high-risk group had 3 or more comorbidities.

SPA
All SPAs were performed using a 4-hour dwell with Dianeal or Physioneal 3.86% glucose dialysate (Baxter Healthcare, Castlebar, Ireland), as previously described by our group (9). Dextran 70 (a volume marker) was used to calculate peritoneal fluid kinetics. The total dextran concentration in dialysate was measured by high-performance liquid chromatography. Immunoglobulin G and α₂-macroglobulin were measured by nephelometry (BN 100) using commercial antisera (Dakopatts AB, Glostrup, Denmark), and β₂-microglobulin was determined by microparticle enzyme immunoassay using an IMx system. Parameters of peritoneal solute and fluid transport were calculated as previously described (9). Mass transfer area coefficients of low molecular weight solutes were calculated according to the Waniiewski model. For measurement of the effective lymphatic absorption rate, the disappearance of dextran from the peritoneal cavity was used. Transcapillary ultrafiltration during the dwell was calculated by subtracting the initial in situ intraperitoneal volume from the theoretical intraperitoneal volume at any time point, with both effective lymphatic absorption and sampling neglected. Protein clearances were calculated to express the transport of macromolecules. The total fluid amount—that is, both the amount drained and the residual volume—was used.

Statistical analysis
The Kolmogorov–Smirnov test was applied to test for normal distribution. The data are expressed as mean ± standard deviation for normally distributed continuous variables and as median and range for non-normally distributed continuous variables.

The data were analyzed in two ways:
- First, mean values for lipids, serum albumin, protein intake, residual GFR decline, and CRP were calculated for the three examinations (12 and 6 months before PD start, and at PD start). When data met the assumptions for parametric tests, the Pearson correlation test was used to determine correlations between variables. Otherwise, the Spearman correlation test was performed.
- Second, the patients were divided in two groups (fast and non-fast transporters). The Student paired t-test was used to compare the two groups. A linear mixed-model procedure was used to analyze differences in the time course of protein intake and albumin in the two groups of patients. The covariance structure between the observations was determined using the Akaike information criterion on the best fit. Time was included in the model as a covariate. To study whether the time course of protein intake differed between the groups, the interaction term between time and group was added to the model. A significant interaction term indicated a different time course between the groups.

The SPSS software package (version 16.0: SPSS, Chicago, IL, U.S.A.) was used for all statistical analyses.

Results
Table I shows the main characteristics and the peritoneal membrane transport features of the patients.
Diabetic nephropathy was the main cause of chronic renal failure. Almost 25% of the patients had 3 or more comorbidities (high-risk group); half belonged to the medium-risk group.

Table II presents the mean values of the main biochemical characteristics of the patients during the 1-year pre-dialytic period. We divided our patients in fast and non-fast transporters based on MTAC creatinine quartiles (the cut-off value was 15.62 mL/min).

No correlation was found between either MTAC (creatinine or urea) and age, protein intake, lipid levels, CRP, or residual GFR decline. We found no correlation between the same pre-dialytic characteristics and peritoneal clearances of albumin, β2-microglobulin, or immunoglobulin G. We observed a correlation between MTAC and dialysate CA125 (correlation coefficient: 0.43; \( p = 0.03 \)) at baseline. Fast and non-fast transporters showed no statistically significant differences (Table III). Our linear mixed model tested for possible differences between the two groups in protein intake and serum albumin during the pre-dialytic period and found no statistically significant difference (Figure 1).

Discussion and conclusions

Registry data and small-scale studies have investigated factors that could define inherent peritoneal membrane characteristics. Interest has focused mainly on fast transporters because of their reported poorer survival outcomes—although not all data confirm that hypothesis (10). However, factors that characterize inherent peritoneal membrane status are equivocal. Older age, high body mass index, and race have all been correlated with faster peritoneal transport status (1–3). For example, it seems that, compared with Caucasian or African patients, Chinese patients have lower D/P ratios. In other studies, only comorbidity (for example, diabetes mellitus) and male sex seemed to be associated with a fast transport status (4,5).

The recent Japanese study was the first attempt in the literature to correlate baseline membrane status with pre-dialytic factors (6). The authors retrospectively analyzed 37 incident PD patients with a very low-protein diet (0.39 g/kg daily) prescribed during the pre-dialysis period. Patients were divided in two groups according to daily protein intake. The authors reported that, compared with the group having a higher protein intake, the group with the lowest protein intake had a lower D/P ratio of creatinine as measured by a peritoneal equilibration test at the start of PD therapy. Furthermore, a positive correlation was found between the D/P creatinine ratio and protein intake. In contrast, our study found no correlation between baseline MTAC creatinine and protein intake. Furthermore, no correlation was observed between baseline MTAC creatinine and the rate of decline in residual renal function, the Davies index, or any other biochemical parameter. No differences were found in pre-dialytic parameters when we compared fast and non-fast transporters. We could not confirm any other relation between the pre-dialytic period and baseline membrane characteristics.

We doubt that the extremely low pre-dialytic protein intake in Japanese patients (0.5 g/kg vs. 0.77 g/kg daily) could possibly explain our different results. Mass transfer area coefficients and D/P ratios depend mainly on the vascular peritoneal surface area. Apparently, genetic factors such as race determine the anatomic surface area, and a variety of known and unknown
parameters can influence the effective surface area. Moreover, genetic factors such as interleukin 6 polymorphisms likely contribute (11), as do various substances locally produced in peritoneal tissue. From this viewpoint, the plausibility of a link between pre-dialytic characteristics and the vascular peritoneal surface area is highly unlikely.

Our study has its own obvious limitations: retrospective design, small sample size, and short pre-dialytic follow-up. Nevertheless, it would be exciting

### TABLE II  Biochemical characteristics during the 1-year pre-dialytic period

<table>
<thead>
<tr>
<th>Variable</th>
<th>Valuea</th>
</tr>
</thead>
<tbody>
<tr>
<td>Albumin (g/L)</td>
<td>39±3.61</td>
</tr>
<tr>
<td>Cholesterol (mmol/L)</td>
<td>4.16±3.7</td>
</tr>
<tr>
<td>Low-density lipoprotein (mmol/L)</td>
<td>2.22±1.82</td>
</tr>
<tr>
<td>Triglycerides (mmol/L)</td>
<td>1.67±0.85</td>
</tr>
<tr>
<td>High-density lipoprotein (mmol/L)</td>
<td>1.32±1.19</td>
</tr>
<tr>
<td>C-Reactive protein (mg/L)</td>
<td>3.40 (1.0–48.0)</td>
</tr>
<tr>
<td>Residual GFR decline (mL min⁻¹ mo⁻¹/1.73 m²)</td>
<td>0.27±0.17</td>
</tr>
<tr>
<td>Daily protein intake (g/kg)</td>
<td>0.77±0.19</td>
</tr>
</tbody>
</table>

a  Mean ± standard deviation, or median and range.
GFR = glomerular filtration rate.

### TABLE III  Comparison of pre-dialytic characteristics between the transport groups

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Transport groupa</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Fast</td>
</tr>
<tr>
<td>Patients (n)</td>
<td>9</td>
</tr>
<tr>
<td>High-risk (% comorbidity)</td>
<td>11.1</td>
</tr>
<tr>
<td>Age (years)</td>
<td>74.4±13</td>
</tr>
<tr>
<td>Residual GFR decline (mL min⁻¹ mo⁻¹/1.73 m²)</td>
<td>0.28±0.2</td>
</tr>
<tr>
<td>Daily protein intake (g/kg)</td>
<td>0.73±0.2</td>
</tr>
<tr>
<td>Albumin (g/L)</td>
<td>37.6±4</td>
</tr>
<tr>
<td>C-Reactive protein (mg/L)</td>
<td>3 (1.0–57.0)</td>
</tr>
</tbody>
</table>

a  No differences were significant.
GFR = glomerular filtration rate.

![FIGURE 1  Time course of protein intake (p = 0.3) and serum albumin (p = 0.55) during the pre-dialytic period.](image)
if factors that influence baseline membrane status could be defined. In that ideal case, strategies could be developed to protect or alter membrane characteristics before PD start. Well-designed prospective studies focused on specific pre-dialytic factors (sodium intake, Ca and P metabolism, or glucose control, for example) may be more appropriate for defining possible associations with baseline peritoneal membrane status.

References

Corresponding author:
Olga Balafa, MD, PhD, Department of Nephrology, Academic Medical Center, Meibergdreef 9, Amsterdam 1105 AZ Netherlands.
E-mail: O.Balafa@amc.uva.nl