Determinants of outcome dialysis
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Citation for published version (APA):

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Chapter 4

Nutritional status

Jager KJ, Merkus MP, Huisman RM, Boeschoten EW, Dekker FW, Korevaar JC, Tijsen JGP, Krediet RT, for the NECOSAD Study Group: Nutritional status over time in hemodialysis and peritoneal dialysis (submitted for publication)
Abstract

Background and Purpose. Malnutrition is a risk factor for mortality in the dialysis population. So far, prospective studies comparing the time course of nutritional status (NuS) in new hemodialysis (HD) and peritoneal dialysis (PD) patients have not been published. The aims of this study were to compare the time course of NuS in patients starting HD or PD and to identify the baseline determinants of that time course.

Methods. In this prospective multicenter cohort study, data were collected from 3 (baseline) to 24 months after the start of dialysis. Repeated measures analysis of variance was used to establish the time course of NuS. Differences were adjusted for baseline characteristics.

Results. Two hundred and fifty consecutive new patients were included, 132 started on HD and 118 on PD. Univariate analysis demonstrated a decrease in serum albumin (SA) in HD and an increase in PD. Body fat increased, lean body mass did not change. The protein equivalent of nitrogen appearance (PNA) normalized to ideal weight decreased in PD after one year. In multivariate analysis, SA at 2 years was 2.0 g/l (95% CI, 0.3 to 3.8) higher in start-on-PD patients. The increase in body fat was 3.2 kg (95% CI, 1.6 to 4.9) higher in PD females than in others. Diabetics gained 2.3 kg (95% CI, 0.6 to 4.1) more fat than nondiabetics. Kt/V_urea did not affect the time course of NuS, but a higher Kt_urea was associated with a higher SA at 24 months.

Conclusions. NuS at the start of dialysis, sex and diabetic status might be considered in making the choice for dialysis modality. Furthermore, providing a higher Kt_urea may improve protein metabolism.
Introduction

Malnutrition is a risk factor for morbidity and mortality. Many studies have shown that its prevalence in the dialysis population is high, up to 50 to 60%. A number of prospective studies have investigated the evolution of nutritional parameters over time in either hemodialysis (HD) or peritoneal dialysis (PD) patients. Only one prospective study compared the time course of nutritional status between HD and PD patients, but these were prevalent patients, already on dialysis for almost three years. Prospective studies comparing the evolution in nutritional status over time in new HD and PD patients have not been published. Therefore, our aims were (1) to compare the time course of nutritional parameters in patients starting HD or PD and (2) to identify the baseline determinants of that time course.

Patients and methods

Patients and follow-up period

ESRD patients older than 18 years, who started chronic dialysis as their first renal replacement therapy and survived the first 3 months on dialysis, were eligible for the study. From 13 Dutch dialysis centers we included consecutive patients who started dialysis between October 1, 1993 and April 1, 1995. Informed consent was obtained from all of them. The measurements at three months after initiation of dialysis were taken as baseline. During follow-up nutritional status was assessed at 6, 12, 18 and 24 months after the start of dialysis.

Data collection

In addition to demographic data we collected the following baseline information.

Renal disease and comorbid conditions. Primary renal disease was classified according to the codes of the European Renal Association-European Dialysis and Transplant Association (ERA-EDTA) Registry. Comorbidity present at the start of dialysis was scored. The number of comorbid conditions was expressed as Davies risk score: grade I: no comorbid conditions; grade II: 1 or 2 comorbid conditions; and grade III: > 2 comorbid conditions.

Laboratory investigations. Laboratory blood investigations included hemoglobin, serum albumin, plasma phosphate and plasma bicarbonate. In HD, the blood samples were taken prior to a dialysis session.

Nutritional status. Nutritional status was assessed by the body mass index (BMI), body fat, lean body mass, serum albumin, and the protein equivalent of nitrogen appearance (PNA). All patients were advised by a dietitian, but there was no common diet prescription. Body fat and lean body mass were estimated by
anthropometry from the sum of thickness of the biceps, triceps, subscapular and iliac skinfolds\textsuperscript{17} by trained nurses. In HD patients these assessments were performed after a dialysis session. Subsequently, the observed lean body mass was divided by the predicted lean body mass, defined as the 50th percentile of persons of the same age and sex\textsuperscript{18} and expressed as percentage (LBM o/p (\%)). Serum albumin was determined by the method routinely used in the centers: bromcresol green (BCG) (N=5), bromcresol purple (BCP) (N=7) or an immunologic method (N=1). The mean lower limit of the reference values was 36 g/l for the BCG method, 34 g/l for the BCP and 39 g/l for the immunologic method. The following equations were used for the calculation of PNA: (1) PNA (g/24 hr) = 9.35 * urea generation rate (mg/min) + 0.294 * urea distribution volume (l) in HD\textsuperscript{19} and (2) PNA (g/24hr) = 19 + 7.62 * urea nitrogen appearance (g/24hr) in PD.\textsuperscript{20} PNA was normalized in three ways: to actual (nPNA), to standard (nPNA\textsubscript{S}) and to ideal\textsuperscript{18} (nPNA\textsubscript{I}) body weight.

The urea distribution volume (V) was determined by the formulae of Watson et al. for total body water.\textsuperscript{21} Underweight was defined as a BMI less than 20 kg/m\textsuperscript{2}, overweight as a BMI between 25 and 30 kg/m\textsuperscript{2} and obesity as a BMI higher than 30 kg/m\textsuperscript{2}. Loss of appetite during the past three weeks was scored on a 5-point Likert scale\textsuperscript{22}, graded 0 (not at all) to 4 (very severe). Nutritional status assessments at follow-up included serum albumin, BMI, body fat, lean body mass and nPNA\textsubscript{I}.

**Blood pressure.** Blood pressure was measured before and after each hemodialysis session over a period of two weeks preceding baseline. These pressures were averaged. Blood pressure in PD was measured at a routine visit in the outpatient clinic. Also during follow-up blood pressure values were recorded to study the potential interference of changes in hydration status over time with the measurement of anthropometric parameters.

**Renal function.** Urine was collected during the interdialytic interval in HD and during 24 hours in PD. From this we calculated residual GFR (rGFR), renal Kt/V\textsubscript{urea}, renal Kt\textsubscript{urea}, urinary urea appearance and renal urea and creatinine clearance at baseline. Residual GFR was defined as the mean of the urea and creatinine clearances and expressed in ml/min/1.73m\textsuperscript{2}.

**Therapy characteristics.** HD Kt/V\textsubscript{urea} at baseline was estimated using a second-generation Daugirdas formula.\textsuperscript{23} Peritoneal Kt/V\textsubscript{urea} was calculated from a 24-hour dialysate collection. Total clearance of waste products (renal function plus dialysis) was expressed as total weekly Kt/V\textsubscript{urea}, total weekly Kt\textsubscript{urea} and as total weekly urea appearance. All HD membranes were synthetic or cellulose derivatives.

**Analytical methods**

Patients were classified according to dialysis modality at baseline: start-on-HD and start-on-PD. Differences in baseline characteristics among these groups were analyzed with one way analysis of variance for continuous variables and with chi-square tests for categorical variables. A two sided P-value < 0.05 was considered
statistically significant. Results are presented as means (SD), unless stated otherwise.

The time course of nutritional status was assessed in an intention to treat analysis. During follow-up the patients remained in the start-on-HD or the start-on-PD group, irrespective of modality switches, deaths or transplants. Repeated-measures analysis of variance was used to assess changes in nutritional status over time (time effect), differences in nutritional status among groups (group effect) and interactions between changes in nutritional status by time and group (time by group effect). To study the effect of treatment modality, we adjusted for the baseline values of nutritional parameters, to address the possibility that differences in nutritional status may have influenced modality choice. In addition to this, we identified other potential confounders by including them as covariates in the analysis of variance. Factors that were univariately associated at a P-value ≤ 0.20 were considered for multivariate adjustment. Based on these findings and data from the literature, we decided to include age, sex, diabetic status and residual GFR in a uniform model to apply to all nutritional parameters, in addition to their baseline value. With this multivariate model, we calculated mean effects with their 95% confidence intervals (95% CI). To search for violations of the assumptions made in multiple regression, we produced normal plots of the residuals. These showed a normal distribution for all models.

To identify groups with a different evolution of nutritional status, we performed subgroup analyses. In addition, we investigated the potential relationship with parameters of dialysis dose at baseline, i.e total and dialysate Kt/V\textsubscript{urea}, Kt\textsubscript{urea} and urea appearance. In these analyses the rGFR within the model was replaced by the complementary renal factor of the parameter studied; e.g. the effect of dialysate Kt\textsubscript{urea} was adjusted for renal Kt\textsubscript{urea}. The effects of urea removal at baseline were studied separately in the start-on-HD and start-on-PD groups.

To study the influence of selective drop-out (deaths and transplants) and modality switches, we repeated the repeated-measures analysis of variance on a stay-on-treatment basis, i.e. in patients who stayed on their initial dialysis modality for the entire period of 24 months.

All analyses were carried out with SAS for Windows 6.12 statistical software (SAS Institute Inc., Cary, NC, USA). The repeated measures analysis of variance was performed with the PROC mixed procedure. This procedure provides maximum likelihood estimates for missing values on the basis of previous values of the same patient and the time course of the parameter in other patients.

Results

Baseline characteristics

Two hundred and fifty patients participated in the study, 132 of them started on
HD and 118 on PD. During follow-up 72 stayed on HD, 40 on PD, 25 (4 HD and 21 PD) changed dialysis modality, 60 (26 HD, 34 PD) received a transplant, 2 recovered renal function (2 HD) and 51 (28 HD, 23 PD) died. In the entire cohort the mean baseline serum albumin level was 36.9 (5.4) g/l. A value below 35 g/l was present in 32% of the patients. The mean BMI was 23.9 (4.1) kg/m². Sixteen percent of the patients were underweight, 27% were overweight and 7% obese. Twenty six percent had an nPNAi less than 0.8 g/kg/24hr.

The baseline characteristics of the start-on-HD and start-on-PD groups are shown in Table 1. Patients who started on HD were older than those who started on PD and they had lower hemoglobin levels. Several parameters indicated that nutritional status was slightly better in HD patients and fewer of them complained of a moderate to severe loss of appetite. In addition, HD patients had lower bicarbonate levels, a higher systolic and a lower diastolic blood pressure and, as expected, their values representing total urea removal were higher.

**Nutritional status over time: univariate analysis**

Figure 1 shows the crude changes in nutritional status over time in the two groups. Serum albumin levels in the start-on-HD group showed a modest decrease during the second year (P < 0.05). PD patients had lower levels at baseline, which increased over time (P < 0.01). The BMI increased in both modalities, but in HD this was not statistically significant. There was a slight, statistically non significant rise in body fat in HD and a larger one in PD (P<0.01), but no change in lean body mass. In PD nPNAi showed a temporary increase followed by a decrease.

**Nutritional status over time in start-on-HD versus start-on-PD patients: multivariate analysis**

Figure 2 compares the time course of nutritional parameters in the start-on-HD and the start-on-PD groups, adjusted for their baseline value, age, sex, diabetic status and rGFR. At 24 months the serum albumin levels were 2.0 g/l (95% CI, 0.3 to 3.8) higher in patients who started on PD, compared to those who started on HD. With respect to the other nutritional parameters, the differences in time course between the treatment modalities were small and not statistically significant.

We then compared PD females to all other patients, as subgroup analyses suggested that their change in nutritional status was different from that of others (time by sex effect for body fat: P=0.10; due to a more pronounced increase in females in the start-on-PD group). PD females had a lower BMI at baseline than other patients (22.4 (4.4) vs. 24.1 (4.0) kg/m²; P<0.05). In addition, they had lower serum albumin levels (35.4 (6.7) vs. 37.3 (5.1) g/l; P<0.05). The mean increase of BMI and body fat over time was 1.5 kg/m² (95% CI, 0.7 to 2.3) and 3.2 kg (95% CI, 1.6 to 4.9) higher in PD females than in the other patients. These increases were higher over the entire BMI range, from underweight to obese PD females. The time course of serum albumin was not different from that of others.
Table 1. Baseline characteristics of patients according to initial dialysis modality (mean (SD) or %).

<table>
<thead>
<tr>
<th></th>
<th>Start-on-HD (N = 132)</th>
<th>Start-on-PD (N = 118)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Demography</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, years</td>
<td>59 (16)</td>
<td>54 (14)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Male, %</td>
<td>53</td>
<td>64</td>
<td>ns</td>
</tr>
<tr>
<td>Caucasian, %</td>
<td>93</td>
<td>92</td>
<td>ns</td>
</tr>
<tr>
<td><strong>Renal disease and comorbidity</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primary renal disease, %</td>
<td></td>
<td></td>
<td>ns</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>14</td>
<td>16</td>
<td></td>
</tr>
<tr>
<td>Glomerulonephritis</td>
<td>9</td>
<td>16</td>
<td></td>
</tr>
<tr>
<td>Vascular</td>
<td>23</td>
<td>23</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>54</td>
<td>45</td>
<td></td>
</tr>
<tr>
<td>Diabetes mellitus, %</td>
<td>17</td>
<td>20</td>
<td>ns</td>
</tr>
<tr>
<td>Comorbidity, grade II/III %</td>
<td>54</td>
<td>47</td>
<td>ns</td>
</tr>
<tr>
<td><strong>Nutritional status, blood pressure and adequacy</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hemoglobin, g/dl</td>
<td>10.2 (1.4)</td>
<td>11.4 (1.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Serum albumin, g/l</td>
<td>37.8 (4.6)</td>
<td>36.0 (6.0)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Plasma phosphate, mmol/l</td>
<td>1.9 (0.5)</td>
<td>1.7 (0.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Body weight, kg</td>
<td>69.1 (14.8)</td>
<td>68.5 (13.0)</td>
<td>ns</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>24.5 (4.4)</td>
<td>23.1 (3.5)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Underweight, %</td>
<td>14</td>
<td>19</td>
<td>ns</td>
</tr>
<tr>
<td>Body fat, kg</td>
<td>18.9 (7.9)</td>
<td>15.9 (6.7)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Lean body mass o/p, %</td>
<td>101.2 (12.8)</td>
<td>100.3 (11.4)</td>
<td>ns</td>
</tr>
<tr>
<td>PNA, g/24hr</td>
<td>69 (23)</td>
<td>71 (20)</td>
<td>ns</td>
</tr>
<tr>
<td>nPNA, g/kg/24hr</td>
<td>0.99 (0.26)</td>
<td>1.07 (0.28)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>nPNAi, g/kg/24hr</td>
<td>0.96 (0.29)</td>
<td>0.99 (0.25)</td>
<td>ns</td>
</tr>
<tr>
<td>nPNAs, g/kg/24hr</td>
<td>1.11 (0.28)</td>
<td>1.15 (0.30)</td>
<td>ns</td>
</tr>
<tr>
<td>Moderate/severe loss of appetite, %</td>
<td>5</td>
<td>12</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Plasma bicarbonate, mmol/l</td>
<td>20.6 (3.5)</td>
<td>26.0 (3.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Metabolic acidosis, %</td>
<td>85</td>
<td>15</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Systolic blood pressure, mm Hg</td>
<td>148 (16)</td>
<td>143 (22)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Diastolic blood pressure, mm Hg</td>
<td>81 (9)</td>
<td>85 (11)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>rGFR, ml/min/1.73m²</td>
<td>2.9 (2.5)</td>
<td>3.0 (2.2)</td>
<td>ns</td>
</tr>
<tr>
<td>Urea appearance, mmol/wk/1.73m²</td>
<td>urinary (391 (343)</td>
<td>445 (380)</td>
<td>ns</td>
</tr>
<tr>
<td></td>
<td>total (2109 (600))</td>
<td>1671 (578)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Kt, I/wk</td>
<td>22 (19)</td>
<td>22 (18)</td>
<td>ns</td>
</tr>
<tr>
<td></td>
<td>total (122 (34))</td>
<td>75 (19)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Kt/Vurea, /wk</td>
<td>0.6 (0.5)</td>
<td>0.6 (0.5)</td>
<td>ns</td>
</tr>
<tr>
<td></td>
<td>total (3.4 (1.0))</td>
<td>2.1 (0.5)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

At baseline, the BMI of diabetics was higher than that of non-diabetics: 25.3 (4.3) vs. 23.6 (4.0) kg/m² (P<0.05). Their serum albumin level was 35.0 (5.1) g/l compared to 37.4 (5.3) g/l in nondiabetics (P<0.01). The mean increase of body fat over time was 2.3 kg (95% CI, 0.6 to 4.1) higher in diabetics, compared to non-
Figure 1. Change over time in serum albumin (g/L), BMI (kg/m²), body fat (kg) and nPNAi (g/kg/24hr) in univariate analysis, according to dialysis modality at baseline: (○) start-on-HD and (■) start-on-PD patients (means, 95% CI).

Figure 2. Change over time in serum albumin (g/L), BMI (kg/m²), body fat (kg) and nPNAi (g/kg/24hr) after adjustment for the baseline value of the nutritional parameter, age, sex, diabetes mellitus and residual GFR: (○)start-on-HD and (■)start-on-PD patients (means,95%CI).
After multivariate adjustment, there was no effect of baseline total or dialysate Kt/V on the time course of nutritional status in any of the dialysis modalities. However, start-on-HD patients with a total Kt/V higher than 124 liter/week had 3.4 g/l (95% CI, 1.1 to 5.6) higher serum albumin levels at the end of follow-up than patients with a lower Kt/V (upper panel Figure 3). Dialysate Kt/V was a determinant of the time course of serum albumin. Total urea appearance was also associated with the evolution of serum albumin in the start-on-HD group, but less strong than total Kt/V. A similar association with respect to Kt/V was found in the start-on-PD group: patients with a total Kt/V higher than the median of 75 liter/week had 2.7 g/l (95% CI, 0.3 to 5.1) higher serum albumin levels than those with lower total Kt/V levels (lower panel Figure 3). In these patients we did not find an independent effect of dialysate Kt/V. The time course of BMI, body fat or lean body mass was not affected by urea removal in either dialysis modality.

There was no difference in the time course of total body weight between start-on-HD patients using synthetic membranes (N=62) or cellulose derivatives (N=70). Nor was there an association of bicarbonate levels at baseline with the subsequent time course of serum albumin levels, BMI or lean body mass in HD or PD.

**Discussion**

In the only other prospective study in new HD patients so far, Parker et al. have shown that body weight increased in patients using a bio-compatible synthetic dialysis membrane, whereas it remained stable in patients on cellulose membranes. Our data did not show a difference between patients using synthetic membranes and cellulose derivatives. They also showed a rise in serum albumin in the first 18 months after the start of dialysis, irrespective of the membrane used. In our HD patients serum albumin remained constant up to 12 months, followed by a gradual decrease. Parker et al. did not report Kt/V values, but in the light of our findings the increase of serum albumin might have been due to a higher Kt/V.
Nutritional status over time peritoneal dialysis

The improvement of nutritional status over the first two years of dialysis in our stay-on-PD patients confirmed the data from previous prospective studies in new PD patients.\textsuperscript{7,10,12-14}

**Nutritional status over time baseline determinants in start-on-HD and start-on-PD patients**

**Dialysis modality.** Adjusted for other covariates, there was a difference in the time course of serum albumin levels in favor of the start-on-PD patients and a larger gain in body fat in PD females. Pollock et al. studied the evolution of nutritional status in both dialysis modalities with an initial cross-sectional assessment after almost 4 years on dialysis in HD patients and after less than 2 years on dialysis in PD patients.\textsuperscript{15} In their population, anthropometric and total body nitrogen measurements suggested that nutritional status was better on PD, whereas serum albumin levels were lower, compared to HD patients. Total body nitrogen tended to fall over time in HD, but it increased in PD patients. All other studies comparing HD and PD patients lack follow-up.\textsuperscript{6,24-26} Some authors concluded that there were no modality differences in nutritional status.\textsuperscript{6} Others found that PD patients had lower serum albumin values,\textsuperscript{24,25} a higher body weight,\textsuperscript{24} more body fat,\textsuperscript{25} a lower BMI,\textsuperscript{26} a higher protein intake,\textsuperscript{24} and that they were more often malnourished.\textsuperscript{24,25} All these studies could not distinguish whether these differences should be attributed to differences in case-mix, therapy history or to a modality difference.

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**Figure 3.**

*Upper panel.* Change over time in serum albumin (g/l) of the start-on-HD patients with a total Kt/v (○) < 124 liter/week and (●) ≥ 124 liter/week after adjustment for the baseline value of serum albumin, age, sex and diabetes mellitus (means, 95% CI).

*Lower panel.* Change over time in serum albumin (g/l) of the start-on-PD patients with a total Kt/v (○) < 75 liter/week and (●) ≥ 75 liter/week after adjustment for the baseline value of serum albumin, age, sex and diabetes mellitus (means, 95% CI).
Sex. In line with our findings, other studies reported a larger impact of PD on the nutritional status of females compared to males.\textsuperscript{10,12} This finding may be explained by the peritoneal glucose absorption, which may have a more pronounced effect in women, whose caloric demand is generally lower than that of males. Tzamaloukas et al. have shown that fluid retention in PD patients is often accompanied by increased blood pressure values.\textsuperscript{27} Therefore, we analyzed blood pressure values during follow-up to gain support for our assumption that we had measured a difference in the gain of body fat and not in hydration status. In PD females, the mean increase in systolic pressure over time was 15 mm Hg (95% CI, 11 to 24) and that in diastolic pressure 5 mm Hg (95% CI, 0.3 to 9), whereas in other patients blood pressure remained stable. Therefore, a part of the observed gain in body fat was probably not fat, but water and due to a larger fluid retention. However, no studies are available suggesting a sex difference in peritoneal ultrafiltration.

Diabetes mellitus. The prevalence of malnutrition in diabetics depends upon the type of diabetes within the population studied as well as on the definition used for malnutrition. Studies comparing the time course of nutritional status in diabetics and nondiabetics are lacking. Cross-sectional studies have demonstrated a higher prevalence of malnutrition in diabetics,\textsuperscript{24} especially in insulin dependent diabetics.\textsuperscript{28} Our diabetic patients, approximately 55% of whom had type II diabetes mellitus, had lower serum albumin levels but a higher BMI than nondiabetics, which increased further during follow-up. An analysis of the blood pressure values showed non significant differences in time course: a mean increase of 7 mm Hg (95% CI, -2 to 16) in systolic pressure and a mean decrease of 2 mm Hg (95% CI, -3 to 6) in diastolic pressure in diabetics compared to nondiabetics. This makes a large component of overhydration in the observed weight gain less likely.

Dialysis dose. The CANUSA study showed a relationship between changes in dialysis adequacy (defined as total Kt/V\textsubscript{urea} and creatinine clearance) and changes in nutritional status of PD patients.\textsuperscript{7} However, Flanigan et al. found little evidence that the efficiency of peritoneal dialysis had a major influence on nutritional status.\textsuperscript{29} A cross-sectional analysis by Frankenfield et al. showed that a low urea reduction ratio was associated with a high BMI and a low serum albumin level in HD. They concluded that a prospective study was required to determine, whether an increase in delivered dialysis dose would affect serum albumin concentration.\textsuperscript{30} In such a prospective study in HD patients with negligible residual renal function, randomized for dialysis dose, Kloppenburg et al. showed that a relationship between dialysis Kt/V\textsubscript{urea} and nutritional status was absent.\textsuperscript{31} However, correction for the urea distribution volume can flaw the relationship between Kt\textsubscript{urea} and clinical outcome.\textsuperscript{32} This would explain why an effect of Kt\textsubscript{urea} on the time course of serum albumin could be demonstrated in our relatively small study, whereas no effect of Kt/V\textsubscript{urea} was detected, potentially due to a lack of statistical power.
Metabolic acidosis. Others have demonstrated beneficial effects of the correction of metabolic acidosis on body weight, midarm circumference\textsuperscript{13} and on protein turnover\textsuperscript{33} in CAPD patients. Also in HD protein turnover was reduced by a correction of metabolic acidosis.\textsuperscript{34} However, in keeping with the findings of Graham et al. we did not detect an association between acid-base status and a change in BMI\textsuperscript{14} or lean body mass.\textsuperscript{33,34}

Other factors. In recent years malnutrition has been linked to inflammation.\textsuperscript{35} Proinflammatory cytokines may cause muscle wasting and hypoalbuminemia and increase serum concentrations of C-reactive protein (CRP). The latter was shown to be an even better predictor of death than serum albumin.\textsuperscript{36} We did not measure markers of inflammation in our patients. Hence, we were not able to correct for potential baseline differences in inflammatory state.

**Nutritional status over time: stay-on-HD and stay-on-PD patients**

In the intention to treat analysis we found a difference in the time course of serum albumin in favor of patients starting on PD. However, in the stay-on-HD versus stay-on-PD analysis, comparing patients staying on their initial dialysis modality during follow-up there was no modality difference. There are two potential explanations: an effect of selective drop-out in the stay-on-HD versus stay-on-PD analysis, or an effect of the different laboratory methods used to measure serum albumin.

To study the effects of selective drop-out on these results, we analyzed the distribution of the initial dialysis modalities within the groups of deceased patients, dialysis switchers and transplant recipients. More patients starting on PD were present in the groups of modality switchers and transplant recipients. As serum albumin levels tended to increase in these two groups, the exclusion of these groups from the stay on treatment analysis resulted in a lower increase in the stay-on-PD group.

It is unlikely that a difference in laboratory methodology has influenced the stay-on-PD versus stay-on-HD analysis, as the time course of serum albumin was corrected for baseline levels. However, in the intention to treat analysis the drop out might have been different for the various laboratory methods. The percentage of the use of BCG remained constant in start-on-PD patients, but increased from 42 to 57\% in the start-on-HD group. As the BCG method provides higher serum albumin levels than BCP,\textsuperscript{37,38} this indicates that the difference in the intention to treat analysis was even higher than reported.

Our data indicate that starting-on-PD would result in higher serum albumin levels at two years. However, they have to be interpreted with caution. This was an observational study without randomization for dialysis modality. Unmeasured case-mix differences at baseline may have had an impact on outcome, e.g. on the way serum albumin levels reacted to the improvement of uremia. Secondly, differences in
outcome may be due to a difference in dialysis adequacy instead of to a modality difference.

**Conclusion**

This prospective study presents data on the time course of nutritional status of patients in the first two years on dialysis. At the start of dialysis, the energy stores of these patients seemed less affected than their protein metabolism. In general, there was a slight further improvement in energy stores over time. Serum albumin levels increased in patients who started on PD. Diabetics and PD females gained more body fat than other patients, although increased blood pressure values in the latter group suggested that a part of the weight gain was due to fluid retention. Dialysis dose, defined as $Kt/V_{urea}$, did not affect the time course of serum albumin, but a higher $Kt_{urea}$ at baseline was associated with a higher serum albumin at two years after the start of dialysis. There were no relationships between dialysis dose and an increase in energy stores.

Mostly, dialysis modality choice is made on the basis of patient preference and medical criteria. The results of this study implicate that the nutritional status at the start of dialysis, together with the patient's sex and diabetic status, are among the factors to consider when a choice for one of the dialysis modalities is made. Patients whose energy stores are low may benefit to a larger extent from PD, whereas this treatment may have undesirable effects in overweight or obese females and diabetics. Furthermore, the results of this study indicate that $Kt_{urea}$ may be a better measure of dialysis dose than $Kt/V_{urea}$ and that the patient's protein metabolism may be improved by providing a higher $Kt_{urea}$.

**References**
