Peritoneal Transport Kinetics Correlate With Serum Albumin But Not With the Overall Nutritional Status in CAPD Patients

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● **The present study evaluates the influence of the peritoneal transport rate (PTR) on the nutritional status of continuous ambulatory peritoneal dialysis (CAPD) patients. Additionally, protein intake, dialysis adequacy, and other clinical variables were analyzed.** [illegible] (D/P4) [illegible] SA [illegible] age, and diabetes mellitus.

PROTEIN calorie malnutrition is highly prevalent in continuous ambulatory peritoneal dialysis (CAPD) patients.[1,2] Hypoalbuminemia, [illegible] with morbidity and mortality.[illegible] On the other hand, it has been demonstrated that a high peritoneal permeability, as defined by the dialysate to plasma (D/P) creatinine ratio, is inversely correlated with serum albumin (SA)[8-10] and directly correlated with peritoneal protein losses,[10-12] which in turn could be implicated as a risk factor to malnutrition and poor prognosis.[10,13] The strength of the isolated SA level as a marker [illegible] tioned,[14] and [illegible] nutritional status may be [illegible] based on a clinical evaluation, a diet history, anthropometric measurements, and various biochemical and [illegible] methods.[15]

Factors associated with the nutritional status of CAPD patients may include dietary protein intake, dialysis dose, and the peritoneal transport rate (PTR). In stable CAPD patients, dietary recalls and protein catabolic rate (PCR) usually are used as indexes of protein intake.[16] It has been suggested that a higher dialysis dose has a positive effect on the protein intake of hemodialysis[17] and CAPD patients,[illegible] which subsequently could influence nutritional status. Peritoneal kinetics could influence the obtainable dialysis [illegible] though the latter is mainly dependent [illegible] factors.[illegible] Furthermore, peritoneal kin[illegible] losses,[8-12] [illegible]

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on the nutritional status (evaluated as a composite nutritional index) of CAPD patients. Additionally, we investigated the role of protein intake, dialysis adequacy parameters, and some clinical variables on the patient's nutritional status.

PATIENTS AND METHODS

From a cohort of CAPD patients, we selected those to whom a peritoneal equilibration test (PET) and a nutritional evaluation were performed within a 2-month period, provided there was absence of peritonitis or any major clinical event that could affect PTR or nutritional status.

The PETs were performed as described by Twardowski et al.[20] The peritoneal transport type was established for each [illegible] differ significantly from those reported by Twardowski et al.[illegible] Two days before the PET, the patients were instructed to perform a 24-hour collection of drained dialysate as well as of urine, and on the day of the PET, blood samples were obtained to calculate the following parameters: creatinine clearance (CrCl), normalized to 1.73 m^2 of body surface area (BSA) and expressed as weekly total CrCl (dialysate + urinary); Kt/V$_{urea}$, also expressed as weekly total (dialysate + urinary); residual renal function (RRF), estimated as the average of renal creatinine and urea clearances; and PCR, determined according to Randerson et al[illegible] and normalized to ideal body weight (NPCR).

The nutritional evaluation included a 24-hour dietary recall and a nutritional scoring system. The dietary recall information was processed by a computerized system that calculates the nutritional value of the consumed meals. This system was developed and validated in the Mexican population,[24] and allows us to know the total calorie, protein, carbohydrate, and lipid intake. Once the total intake was known, the percentage of consumed calories and proteins was calculated and compared with the usual recommendation for patients on CAPD (30 to 35 kcal/kg body weight and 1.2 to 1.5 g/kg body weight, respectively[illegible]). We did not include the glucose absorption from the dialysis fluid in the calorie intake calculations. The nutritional scoring system used (adapted from Bilbrey and Cohen[25]), which has been previously validated in dialysis patients, includes eight clinical, biochemical, and anthropometric parameters: weight/height ratio, triceps skinfold thickness, mid-arm circumference, mid-arm muscle area, SA, transferrin, total lymphocyte count, and a subjective clinical examination. Each of the eight parameters of this scoring system is given three points if normal; four points are given if the parameter is mildly decreased, five if moderately decreased, and six if severely decreased. The value obtained for each parameter is summed, resulting in a nutrition index (NI), which is defined as normal (≤ 25), mild (26 to 28), moderate (29 to 31), and severe (≥ 32) malnutrition. SA level was determined by the bromcresol green method. Anthropometric measurements were performed using standard techniques and reference values.[26] The mid-arm muscle area (MAMA) was derived from the mid-arm circumference (MAC) and triceps skinfold (TSF):

$$\text{MAMA} = [\text{MAC} - \pi(\text{TSF})]^2/4\pi$$

$$(-6.5 \text{ for females or } -10 \text{ for males}).^{26}$$

The following clinical variables were also recorded and considered for analysis: age, sex, presence of DM, BSA (calculated by the Du Bois method[illegible]), time on dialysis, peritonitis rate, and hemoglobin.

Statistical Analysis

Data are presented as mean values ± SD or median (percentiles 25% to 75%). Pearson's correlation and simple linear regression were used to evaluate the univariate association between the NI or SA, with the studied variables. Kruskal-Wallis one-way analysis of variance (ANOVA) was used to compare the results of the nutritional evaluation of the different peritoneal transport types. Multiple linear regression and two-way ANOVA were used for the multivariate analysis of [illegible] between the NI and protein intake and dialysis dose. [illegible] statistical significance [illegible] patients were analyzed by the [illegible] method to clearly identify the differences [illegible] accepted as significant, although the exact [illegible] value is given [illegible] tially shown.

RESULTS

We studied 43 patients (28 women and 15 men), 18 of whom were diabetic (16 of 18 were non-insulin-dependent). None of our patients received recombinant human erythropoietin (rHuEPO). The mean age was 47.9 ± 18.3 years, the mean time on dialysis was 19.6 ± 20.9 months, and the peritonitis rate was 0.50 ± 0.87 episodes/patient/yr. Patients performed a mean of 3.9 ± 0.6 exchanges/d; 32 (77%) were on a standard CAPD regimen, ie, they received four 2-L exchanges/d. Six patients (14%) received three 2-L exchanges/d, three (7%) received five 2-L exchanges/d, and one (2%) received five 1-L exchanges/d. The mean BSA was 1.64 ± 0.21 m^2 and mean weight was 61.5 ± 11.6 kg. Serum creatinine was 9.19 ± 3.92 mg/dL, blood urea nitrogen (BUN) was 50.32 ± 16.45 mg/dL, weekly total CrCl was 78.4 ± 4.8 L/wk/1.73 m^2, and weekly total Kt/V$_{urea}$ was 2.05 ± 0.97. RRF was 3.19 ± 4.50 mL/min and NPCR was 0.88 ± 0.19 g/kg. The NI was normal in nine patients, whereas six, nine, and 18 patients had mild, moderate, and severe malnutrition, respectively. The nutritional evaluation results according to the PTR are shown in Table 1. PTR was distributed as follows: eight patients were high, 14 were high-average, 16 were low-average, and four were low transporters.

Table 1. Results of the Nutritional Evaluation According to the Peritoneal Transport Type

	Transporter Type				
Variable	High (n = a)	High-Average (n = 14)	Low-Average (n = 16)	Low (n = 4)	P Value
Percentage calorie intake*	69.2 (56-100)	70.6 (50-134)	67.4 (46-87)	59.7 (54-71)	0.90
Percentage protein intake*	79.3 (59-107)	74.2 (49-147)	83.9 (53-109)	69.9 (60-89)	0.99
Hemoglobin (g/dL)	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Serum albumin (g/dL)	[illegible]	[illegible]	[illegible]	[illegible] (3.5-4.0)	0.02†
Total lymphocyte count (x μL)	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Weight/height ratio	[illegible]	[illegible]	[illegible]	[illegible]	0.53
Midarm circumference (cm)	[illegible]	[illegible]	[illegible]	[illegible]	0.38
Midarm muscle area (cm²)	[illegible]	[illegible]	[illegible]	[illegible]	0.47
Tricipital skinfold thickness (mm)	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Transferrin (mg/dL)	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
NI	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]

NOTE. Data are mean values (percentiles 25% to 75%)
* From the usual recommendation.[6]
† Difference only between high and low transporters.

[illegible] with [illegible] D/P4 Cr [illegible] nutrition [illegible] vival vari- [illegible] PTR (Fig 1) [illegible] re severe the [illegible] a significant [illegible]

[illegible] For correlation [illegible] D/P [illegible] tion was found between NI and the weekly total CrCl (r = -0.28, r^2 = 0.057), but no correlation was found with calorie or protein intake (either total or percentage from recommendation) or any other clinical, biochemical, or anthropometric variable. NPCR was directly correlated with the [illegible]

[illegible] RRF (r = 0.37, P = 0.01) [illegible] rate at 4 hours of the standard [illegible] as expression of PTR, and the [illegible] NI value were selected as [illegible] ables. The NI did not correlate with [illegible] (recall the higher the index, the mo malnutrition); however, it showed [illegible] NI as a dependent variable, and PTR, [illegible] and dialysis adequacy as independent variable. Dialysis adequacy was measured as weekly total CrCl or Kt/V_{urea}; consequently, two models wer constructed using each dialysis adequacy vari able at one time. The NI was not influenced b PTR, NPCR, or dialysis adequacy using eithe CrCl or Kt/V_{urea} (Table 2). To further explore th possible role of dialysis adequacy on the NI, w performed a two-way ANOVA using PTR an

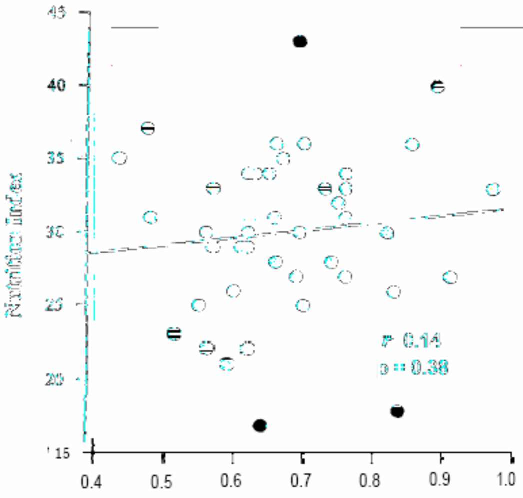

Fig 1. Correlation between the D/P4 Cr rate and the NI showing the lack of association between these variables (note that the NI is higher as the malnutrition becomes more severe).

Table 2. Multiple Regression Models to Predict NI Using Kt/V or CrCl Independently as Dialysis Adequacy Variables

	KW (R = 0.18, R^2 = 0.03, P = 0.73)		CrCl (R = 0.35, R^2 = 0.12, P = 0.17	
Variable	Coefficient	P Value	Coefficient	P Valu
D/P4 Cr	5.129	0.504	8.927	0.231
KW	-0.812	0.421		
CrCl			-0.042	0.03
NPCR	3.224	0.531	0.674	0.88

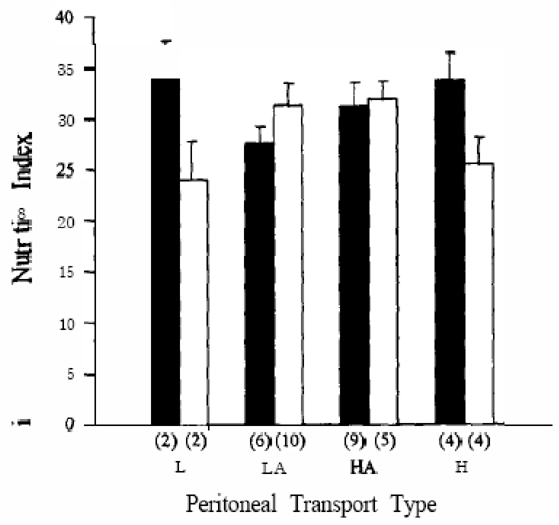

Fig 2. Two-way ANOVA results of the NI (mean ± SE) according to the different peritoneal transport types and the total weekly KW. The solid bars represent patients with total weekly KW < 1.8 and the open bars represent patients with total weekly KW ≥ 1.8. The numbers in parentheses indicate the number of patients in each group. There were no significant differences according to transport type [$r = 0.48$; $P = 0.70$] or KW [$r = 3.38$; $P = 0.07$].

dialysis adequacy indicators as independent factors. In this analysis, the NI was used again as the dependent variable, and PTR (classified as type of transport: high, high-average, low-average, or low) and dialysis dose (classified as low [Kt/V < 1.8 or CrCl < 60 L/wk/1.73 m^2] and high [Kt/V ≥ 1.8 or CrCl ≥ 60 L/wk/1.73 m^2]) were used as the independent variables. We decided to used the median value of both Kt/V (1.8) and CrCl (60 L/wk/1.73 m^2) as the cut-off point between high and low dialysis dose, as the most balanced patient distribution was observed at these levels.

Kt/V and PTR were unable to explain the NI (Fig 2); neither of these variables was associated with differences in the NI. Dividing each of the four peritoneal transport types according to the two levels of Kt/V, there were no intragroup or intergroup differences in NI. Patients with low and high transport rates and with low dialysis dose appeared to have a poorer, but not statistically significant NI. When CrCl was used as the adequacy dialysis variable, neither CrCl nor the PTR could significantly explain the NI (Fig 3).

Once we evaluated the influence of PTR, NPCR, and dialysis adequacy on the NI, we studied whether the SA level, which has been repeatedly used as a marker of malnutrition, was influenced by these variables. In the univariate analysis, a significant inverse correlation between SA and PTR was observed (Fig 4). Other significant associations were observed between SA and BSA ($r = 0.41$; $P = 0.007$), age ($r = -0.39$; $P = 0.01$), DM (0 = no DM and 1 = DM; $r = -0.35$; $P = 0.02$), and the drained volume at the end of the PET ($r = 0.33$; $P = 0.03$). No other studied variable was significantly associated with SA.

In the multiple regression analysis, the adequacy variables did not significantly predict SA. With this analysis, PTR strongly predicted the SA level, and the clinical variables BSA, age, and DM were also important predicting factors. As collinearity between age and DM was detected, we developed two models that most significantly predict SA: one that included D/P4 Cr, BSA, and age, and another one that includes D/P4 Cr, BSA, and DM (Table 3). The significance of the variables DM and age was nullified when

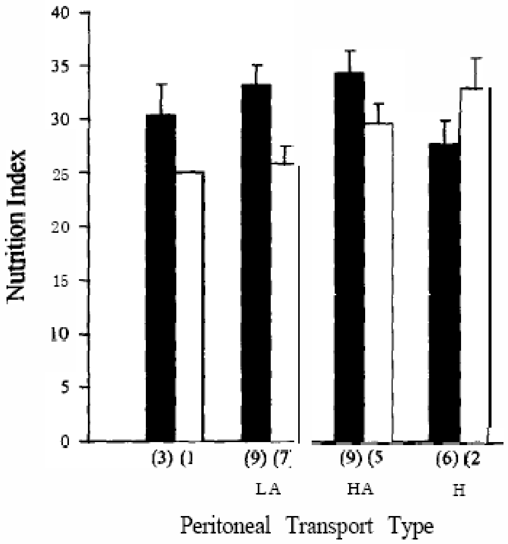

Fig 3. Two-way ANOVA results of the NI (mean ± SE) according to the different peritoneal transport types and the total weekly CrCl. The solid bars represent patients with total weekly CrCl < 80 L/wk/1.73 m^2 and the open bars represent patients with total weekly CrCl ≥ 60 L/wk/1.73 m^2. The numbers in parentheses indicate the number of patients in each group. There were no significant differences according to transport type [$r = 0.84$; $P = 0.43$] or CrCl [$r = 2.38$; $P = 0.13$).

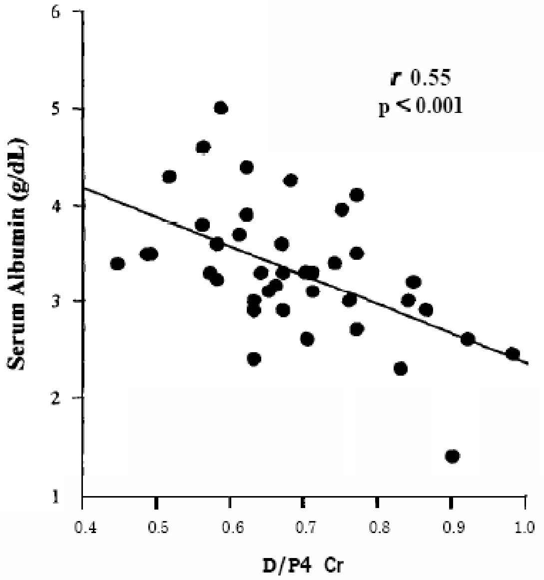

Fig 4. Inverse correlation between the D/P4 Cr rate and SA. The higher the PTR, the lower the SA.

both were included in the same model due to collinearity. As D/P4 Cr was the most important predicting factor in these models, we performed two-way ANOVA, using SA as the dependent variable and the PTR and dialysis adequacy variables as the independent factors, similar to the NI analysis (Figs 5 and 6). Dividing each of the four peritoneal transport types according to two levels of dialysis dose, we did not observe any intragroup difference in the SA level. Nevertheless, we showed an intergroup trend to a decrease in the SA level the higher the transport type was, independent of a high or low dialysis dose. In

Table 3. Best Multiple Regression Models To Predict SA

	Model 1 (R = 0.72, R^2 = 0.48, $P <$ 0.0001)		Model 2 (R = 0.71, R^2 = 0.46, $P <$ 0.0001)	
Variable	Coefficient	*P* Value	Coefficient	*P* Value
Age	-0.011	0.015		
DM			-0.345	0.033
BSA	1.191	0.002	1.133	0.004
D/P4 Cr	-2.489	0.0004	-2.655	0.0002

NOTE. Age and DM were nullified when both were included in the same model, as they were collinear variables.

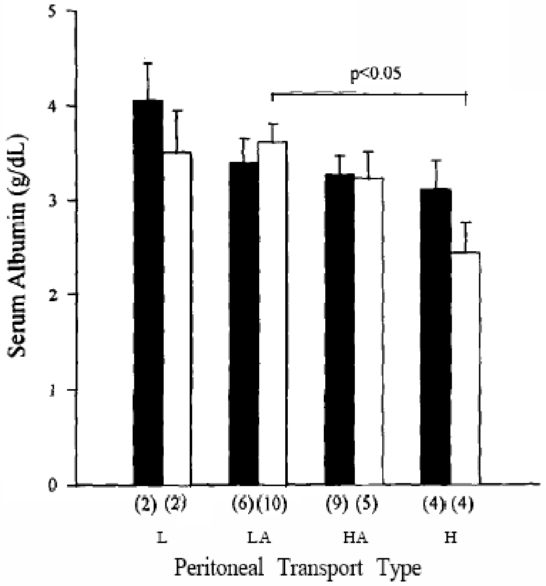

Fig 5. SA (mean ± SE) according to the different peritoneal transport types and the total weekly KW. The solid bars represent patients with total weekly Kt/V < 1.8 and the open bars represent patients with total weekly KW ≥ 1.8. The numbers in parentheses indicate the number of patients in each group.

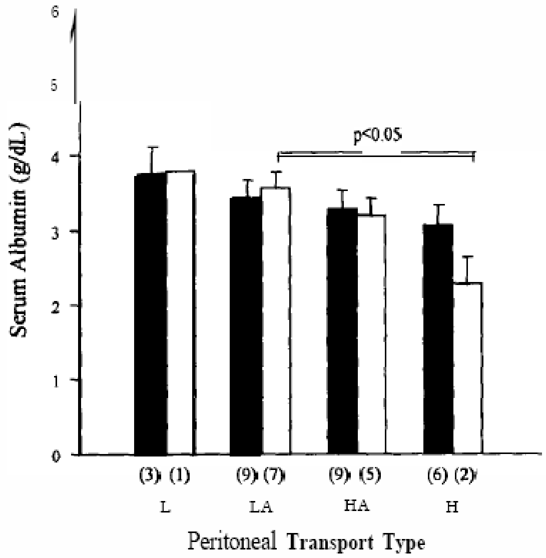

Fig 8. SA (mean ± SE) according to the different peritoneal transport types and the total weekly CrCl. The solid bars represent patients with CrCl < 60 L/wk/1.73 m^2 and the open bars represent patients with CrCl ≥ 80 L/wk/1.73 m^2. The numbers in parentheses indicate the number of patients in each group.

spite of the previous trend, the only significant difference in the SA level was observed between low-average and high transporters when both had a high dialysis dose, being higher in the former.

DISCUSSION

Our CAPD population is younger than most others reported,[28] which could be partially influenced by the fact that we do not have a chronic hemodialysis program, so almost all our chronic dialysis patients are on CAPD. In our sample, calorie and protein intake were lower than recommended.[15] Similarly, the NPCR was lower than recommended.” As we have previously observed,’ there was a high frequency of malnutrition in our patients, which is similar to the highest reported in literature; yet, the frequency of severe and moderate malnutrition levels was higher than that reported by most others.[1,25,29]

We did not find any correlation between PTR and the NI. The observed association between the NI and BSA appears predictable, as the elements of BSA (weight and height) are also components of the NI (weight/height ratio). The inverse correlation between poor nutritional status and hemoglobin level could reflect better general status or nutrient intake in patients with a higher hemoglobin. The inverse correlation between malnutrition and RRF, as previously observed,’ could reflect a better clearance of uremic toxins and a better general status in patients with higher RRF.

In CAPD, as in most other clinical situations, there is no isolated variable that may explain the nutritional status of patients. Therefore, we used a multivariate analyses to study the influence of PTR, NPCR, and dialysis dose on the NI. We found no significant models that could explain the NI when either CrCl or Kt/V (as dialysis adequacy variables) was used. The use of BSA, hemoglobin, or RRF, which were significantly correlated in the univariate analysis, did not result in a significant multivariate model predicting the NI.

We found no correlation between the NI and nutrient intake, NPCR, and adequacy of dialysis; however, as this is a cross-sectional study, we cannot evaluate the modification of the protein intake or the dialysis dose over time, which subsequently could influence the NI.

On the other hand, an inverse correlation was found between the PTR and SA (the higher the PTR, the lower the SA) (Fig 4). As protein intake was not different between the transport groups and NPCR was not a significant factor predicting the SA level, lower protein intake does not appear to be related to the lower SA levels seen in the higher transport types. Other factors, such as increased peritoneal protein losses[10-12] or lower protein synthesis, could be implicated.

We found that SA can be predicted by two multiple regression models, including D/P4 Cr rate, BSA, and either age or DM. Blake et al,[8] using a multiple regression analysis, and Malhotra et al,[30] using a logistic model, also have found that the major predictors for a low SA are advanced age, diabetes, and PTR, whereas dialysis dose was not associated. However, none of these investigators described the DM type or reported whether they found collinearity between age and DM. We demonstrated collinearity between the variables age and DM (as most of our DM patients are non insulin-dependent and consequently elderly); nevertheless, we believe it is important to consider age and DM independently as aging is a factor of malnutrition in normal subjects.[31] Although there was a trend for the SA level to decline as the transport type became faster, with either high or low dialysis doses, the only significant difference was observed between high and low-average transporters, when both of them had the higher dialysis dose. We cannot exclude, however, that the small number of patients (when the original sample was broken down to small subgroups according to the different transport types and dialysis doses) precludes the demonstration of other real differences between the groups. The tendency in the high transporters to show a lower SA, and more notably with high dialysis dose, could reflect, besides the known higher peritoneal[11] albumin losses in this group, the further increase as the dialysate drainage increase.[32] Based on our results, we speculate that patients with a peritoneal transport type around the mean and who are receiving an appropriate dose of dialysis are those most likely to show higher SA levels on CAPD, whereas the high transporter patients receiving a high dose of dialysis could be the most likely to show lower SA levels.

Our results suggest that PTR, although inversely related with SA, is not related with a more comprehensively evaluated nutritional status (as measured by a NI). Harty et al[12] found no correlation between PTR, peritoneal protein losses, and direct measures of body composition, yet they suggested a possible link between peritoneal permeability, overhydration, and hypoalbuminemia. The low SA associated with poor prognosis in CAPD patients, and primarily associated with higher peritoneal transporters, could be associated with factors other than malnutrition. In this sense, hypoalbuminemia seems to be a marker rather than a direct cause.

We conclude that there is no correlation between PTR (as measured by PET) and the nutritional status (determined by a NI). In this study, dialysis adequacy or protein intake did not appear to significantly contribute to developing malnutrition in patients on CAPD. The most important correlation of the SA level was the inverse one observed with PTR. Age and DM, which could show interdependence, should be considered as clinically important predicting factors for the SA level.

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