# Peritoneal Total Protein Transport Assessed from Peritoneal Equilibration Tests Using Different Dialysate Glucose Concentrations

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**Abstract**

Background. The peritoneal equilibration test (PET) permits assessment of peritoneal protein transport, but this potential marker of outcome in peritoneal dialysis (PD) patients lacks adequate standardization.

Objectives. To assess various approaches for estimation of peritoneal protein transport in PD patients during 2.27% and 3.86% glucose-based PETs, and to uncover the demographic, clinical, and biochemical correlates of this phenomenon.

Patients and Methods. We studied 90 PD patients who underwent 2.27% and 3.86% PETs in random order, and we used multivariate analysis to compare assessments of peritoneal protein transport in both tests, searching for correlations between $D_{240'} - D_{0'}$ protein concentration (PETΔPConc), total peritoneal protein excretion (PET-PPE), or total protein clearance (PET-PC) on the one hand (the main study variables), and PET-derived markers of peritoneal function and selected demographic, clinical, and biochemical variables on the other.

Results. The PETΔPConc was higher during the 2.27% PET (mean: 45.2 mg/dL vs 37.0 mg/dL for the 3.86% test; p = 0.003); the PET-PPE and PET-PC were comparable (1121.8 mg vs 1168.9 mg, p = 0.52, and 17.1 mL vs 17.8 mL, p = 0.66, respectively). All three variables sustained a significant, yet moderate correlation (all $r^2$ values < 0.30) with the 24-hour PPE rate. Multivariate analysis identified dialysate-to-plasma ratio ($D/P_{240'}$) of creatinine, end-to-initial dialysate ratio ($D_{240'}/D_{0'}$) of glucose, current daily peritoneal glucose load, ultrafiltration during PET, systolic blood pressure, and previous cardiovascular events (3.86% test only) as independent predictors of protein transport during PET.

Conclusions. Either PET-PPE or PET-PC seems preferable to PETΔPConc for characterization of peritoneal protein transport. Small-solute transport characteristics, ultrafiltration, and current peritoneal glucose load sustain independent correlations with peritoneal protein transport. The latter variable shows also a moderate association with markers of cardiovascular disease in PD patients.

**Key words**: Peritoneal equilibration test; protein transport; ultrafiltration; cardiovascular disease.

Peritoneal protein excretion (PPE) is an unwanted side effect of peritoneal dialysis (PD). It may contribute to malnutrition in PD patients, to an extent that is still a matter of controversy (1). Moreover, continued protein depletion may contribute to a clinical state akin to the nephrotic syndrome in many PD patients, with potentially similar adverse consequences including dyslipidemia, hormonal disturbances, and a prothrombotic environment (2-6).

Information is limited on the factors that influence the magnitude of PD-related PPE in the clinical setting, aside from the correlation of PPE with the overall solute transport characteristics of the peritoneal membrane (7-10). Peritoneal transport of proteins occurs essentially through large intercellular pores, limited by size rather than by charge restriction (11-14). The functionality of these pores may be affected by endothelial disorders and inflammatory states (15,16). This situation raise the possibility that PPE may operate as a marker of large-pore dysfunction, the latter indicating endothelial disease, inflammation, and in the end, cardiovascular risk for PD patients (15).

The peritoneal equilibration test (PET) is the standard procedure for categorizing peritoneal transport characteristics in clinical practice (17). As such, it is focused on creatinine and glucose, but it has also been modified to analyze the transport characteristics of other solutes (9). The classic PET is performed with 2.27% glucose-based dialysate, but support is growing for use of a 3.86% solution, because the latter concentration has been claimed to permit a more accurate assessment of capacity for ultrafiltration (UF) and for free-water transport (9,18). The PETs based on 1.36%, 2.27%, and 3.86% glucose-based dialysate all appear to yield similar results for creatinine, with some expected differences for other small solutes including glucose and sodium (19,20). Previous studies have provided reference values for the peritoneal transport of various proteins during PD (9,11,17,21), but few have assessed the same question using the PET in clinical practice. The PET has the potential to permit an assessment of PPE under standardized and reproducible conditions, which would increase the efficacy of the peritoneal total protein transport marker (over current estimations based on a 24-hour PPE) to predict peritoneal large-pore endothelial dysfunction and its correlates in clinical practice. However, this application of the PET demands an analysis of the factors that may potentially influence the results. We performed a study to compare, in the clinical setting, the patterns of peritoneal total protein transport in 90 PD patients who underwent PETs using 2.27% and 3.86% glucose-based lactate-buffered dialysate, and also to uncover any demographic, clinical, and biochemical correlates.

## PATIENTS AND METHODS

### GENERAL DESIGN

In a prospective design, 90 PD patients underwent, in random order, two modified PETs using 2.27% and 3.86% glucose-based lactate-buffered solutions. Of the 90 patients, 49 underwent the 2.27% test first, and 41 underwent the 3.86% test first. The median delay between the two tests was 4 months (range: 0 – 6). We compared the solute transport profiles from both tests, focusing on the behavior of dialysate total protein concentration. We analyzed the correlation between the observed protein transport profiles and selected clinical [age, sex, time on dialysis, diabetes, cardiovascular comorbidity, blood pressure (BP), ongoing drug therapies], prescription (PD modality, number of daily exchanges, total dialysate volume infused, peritoneal glucose load, use of icodextrin), laboratory [residual renal function (RRF), proteinuria, hemoglobin, plasma protein, C-reactive protein (CRP)], and peritoneal function variables (creatinine and glucose transport rates, UF, sodium sieving).

### POPULATION

We considered for the study all patients from our PD unit who fulfilled two conditions: stable clinical condition without peritonitis or any other significant event during the preceding 2 months, and informed consent to cooperate. Patients experiencing peritonitis, hemoperitoneum, peritoneal catheter malfunction, or catheter removal, or in general presenting any significant clinical event during the study period were excluded from analysis.

### STUDY PROTOCOL

All patients underwent estimation of PD adequacy (Kt/V) and RRF during the month preceding each PET. All the PET studies followed the general schedule for these tests, with small modifications. In brief, after an overnight dwell with 2.27% dialysate, 2 L of 2.27% or 3.86% dialysate was infused into the peritoneal cavity. Dialysate samples were collected according to standardized procedures after 0, 60, 90, 120, and 240 minutes of the dwell. At the end of the 4 hours, complete emptying of the abdominal cavity was allowed. We retrieved blood samples for analysis at 120 minutes of the PETs. All patients

used the same conventional PD solutions from the Baxter Healthcare (Deerfield, IL, U.S.A.) or Fresenius Medical Care (Heidelberg, Germany) laboratories before and during the tests.

## CLINICAL DEFINITIONS

Cardiovascular comorbidity was categorized from the number of accumulated events at initiation of the study. We grouped five event types: coronary disease (unstable angina, myocardial infarction, need for revascularization), stroke (including transient ischemic attacks), peripheral arterial disease (amputation, need for revascularization), major arrhythmia (requiring drug therapy or invasive procedures), and other heart diseases (including clinically significant valvular disease and idiopathic dilated or hypertrophic myocardiopathies). We used the clinical records of the patients to compute mean levels of systolic and diastolic BP during the month preceding each PET.

## SAMPLE PROCESSING AND SECONDARY CALCULATIONS

A standard autoanalyzer (Advia 2400: Bayer Health-Care AG, Leverkusen, Germany) was used to quantify plasma and dialysate levels of glucose, creatinine, and total protein. Dialysate creatinine was corrected for simultaneous glucose level. Plasma and dialysate sodium concentrations were estimated using an indirect ion-selective electrode method. The mean of urea and creatinine clearances was used to compute RRF. Plasma CRP was estimated using an immunoturbidimetric assay (Roche Diagnostics, Mannheim, Germany).

A modified colorimetric assay (pyrogallol red) was used for estimation of dialysate total protein. We checked potential interferences from high glucose concentrations by testing samples of spent dialysate before and after adding glucose to the solution to a mean increase in concentration of 3015 mg/dL [927 mg/dL at baseline (range: 103 – 2304 mg/dL) vs 3942 mg/dL (range: 2920 – 4473 mg/dL) after addition of glucose]. Estimations of total protein concentration were highly consistent and marginally lower after addition of glucose to dialysate [mean: 47.5 mg/dL (range: 13.0 – 126.0 mg/dL) at baseline vs 47.1 mg/dL (range: 13.0 – 124.0) after addition of glucose,$p = 0.18$]. Incubation of the samples for 24 hours at 4°C or 37°C did not modify the results.

Peritoneal protein transport over time was estimated primarily by subtracting the protein concentration at baseline from the concentrations at various points during each PET ($D_{X'} - D_{0'}$). The dialysate-to-plasma ratio (D/P) of creatinine was calculated as the ratio between the dialysate creatinine concentration at any point and the plasma creatinine concentration at the midpoint of each test. Glucose transport was computed as the quotient $D_{X'}/D_{0'}$, and sodium dip as the difference $D_{60'} - D_{0'}$. During the test, UF was estimated as the difference between the weight of the dialysate bag before infusion and the weight after final drainage.

The main dependent variables of the study were $D_{240'} - D_{0'}$ protein concentration (PETΔPConc), total PPE during the PET (PET-PPE), and peritoneal total protein clearance during the 4-hour test (PET-PC, calculated as PPE divided by serum total protein). We compared the performance of these variables in the 2.27% and 3.86% PETs, searching also for correlations with the demographic, clinical, biochemical, prescription, adequacy, and PET-related variables being scrutinized. The 24-hour PPE was scrutinized as a secondary dependent variable and was assessed by simple mass balance of a full 24-hour dialysate collection (drained volume × protein concentration).

Daily UF is routinely recorded per dwell by our continuous ambulatory PD patients, who weigh the drained bags and then discount the weight of the plastic systems plus 100 g (estimated mean overfill). In the case of automated PD patients, we accept the estimations provided by the cycler.

## STATISTICS

Numerical variables are presented as means or medians and range, as appropriate. Distribution was checked according to the Kolmogorov–Smirnov–Lilliefors test. Direct comparisons between variables used the Student t-test, ANOVA, and the Mann–Whitney and Wilcoxon tests (numerical variables), and the chi-square distribution (categorical variables). Correlations between numerical variables were calculated using the Spearman correlation coefficient. Stepwise and forward multiple regression were applied for multivariate analysis.

## RESULTS

### OVERVIEW

Nine patients started, but did not complete, the protocol because of peritonitis (n = 3), hemoperitoneum (n = 1), clinical event unrelated to PD (n = 1), death (n = 1), renal transplant (n = 2), and voluntary withdrawal (n = 1).

Table 1 presents the main characteristics of the final study population. Total daily infused dialysate volume was 6.8 ± 2.2 L at the time of the 2.27% PET and 7.0 ± 2.4 L at the time of the 3.86% PET [p value nonsignificant (NS)]. The daily peritoneal glucose loads were 87.2 ± 47.0 g and 90.4 ± 45.9 g respectively (NS). No patient on automated PD had a dry day, although in 9 cases, daytime volume was less than 1000 mL. The delivered Kt/V was 2.41 ± 0.65 (2.27%) and 2.36 ± 0.59 (3.86%, NS). Estimated 24-hour PPE rates were 5.53 ± 2.21 g [2.27% (range: 2.1 – 17.2 g; 24-hour PC: 82.7 ± 33.0 mL)] and 5.54 ± 1.84 g [3.86% (range: 2.5 – 14.0 g; 24-hour PC: 83.8 ± 29.4 mL; NS)]. With regard to PET results, the observed values of $D/P_{240'}$ creatinine were 0.64 ± 0.14 (2.27%) and 0.63 ± 0.14 (3.86%, NS), slightly below classically reported values (17). Mean UF rates during PET were 131.4 mL [2.27% (–400 mL to 600 mL)] and 542 mL [3.86% (range: –150 mL to 1300 mL)].

As expected, PETΔPConc, PET-PPE, and PET-PC were tightly correlated ($r > 0.90$). On the other hand, we observed moderate yet significant correlations between any of PETΔPConc [2.27%: $r = 0.46$; 3.86%: $r = 0.38$; $p < 0.0005$), PET-PPE (Figure 1), and PET-PC (2.27%: $r = 0.53$; 3.86%: $r = 0.39$; $p < 0.0005$) on the one hand and 24-hour PPE on the other.

### COMPARISON OF PET PROTEIN TRANSPORT PROFILES

Figure 2 shows the dialysate protein concentration profiles during both PETs. The average correlation between estimations for PETΔPConc in both tests was relatively good (all r values > 0.50,$p < 0.0005$), but agreement analysis disclosed significantly higher values for the PETΔPConc during the 2.27% test (45.2 ± 26.6 mg/dL) than during the 3.86% test [37.0 ± 18.4 mg/dL,$p = 0.003$; Figure 3(a)]. This bias was not apparent when either PET-PPE [1121.8 ± 594.7 mg (2.27% test) vs 1168.9 ± 539.9 mg (3.86% test), NS, Figure 3(b)] or PET-PC [17.1 ± 8.7

mL (2.27% test) vs 17.8 ± 8.2 mL (3.86% test), NS, not illustrated] was considered.

## PET-RELATED CORRELATES OF PROTEIN TRANSPORT, UNIVARIATE ANALYSIS

Peritoneal protein transport during a PET showed a significant univariate correlation with small-solute transport characteristics during the same test (Table 2). Remarkably, the correlation was better for $D_{240'}/D_{0'}$ glucose than for $D/P_{240'}$ creatinine. On the other hand, UF during PET sustained a significant correlation with PETΔPConc, but not with PET-PPE or PET-PC (Table 2).

## OTHER UNIVARIATE CORRELATES OF PERITONEAL PROTEIN TRANSPORT

Univariate analysis disclosed a moderate yet consistent inverse correlation of the current peritoneal glucose load delivered to the patient with PET-PPE (2.27% PET: r = –0.22, p = 0.04; 3.86% PET: r = –0.24, p = 0.02), but not with 24-hour PPE [r = –0.17,p = 0.11 (Spearman)). We observed no other significant association or trend between protein transport (either PET-related or 24-hour PPE) on the one hand and PD prescription characteristics (PD modality, total daily infused volume, daily number of dwells, use of icodextrin, Kt/V), drug therapies, or any of the laboratory variables presented in Table 1 on the other.

We observed a significant univariate correlation between systolic BP and PET-PPE (2.27% PET: r = 0.37,p = 0.001; 3.86% PET: r = 0.23,p = 0.03) or 24-hour PPE (r = 0.19,p = 0.07). There was also a trend to higher protein transport rates in patients with a background of cardiovascular events. This tendency was not significant overall, but a univariate association of peripheral artery disease ($D_{240'} – D_{0'}$ protein concentration: 54.2 ± 17.8 if present vs 35.2 ± 19.1 mg/dL if absent; p = 0.006) and coronary disease (54.5 ± 17.4 mg/dL vs 35.0 ± 13.2 mg/dL,p = 0.03) with peritoneal protein transport rate was observed.

MULTIVARIATE ANALYSIS

Table 3 presents the main results of the multivariate analysis. The $D/P_{240'}$ creatinine and $D_{240'}/D_{0'}$ glucose were both consistent predictors of peritoneal protein transport. Because of co-linearity, only $D/P_{240'}$ creatinine was considered for the best model. Current peritoneal glucose load, systolic BP, and background cardiovascular comorbidity (3.86% PET) also sustained independent correlations with the study variables. We did not detect a correlation between 24-hour PPE and cardiovascular comorbidity, but a weak trend to an association with systolic BP [$^2$ = 0.03; 95% confidence interval (CI): –0.001 to 0.06; p = 0.08) was observed using the 2.27% PET data set.

Multivariate analysis disclosed a scenario opposite to that seen in the univariate analysis for the association between protein transport and UF during PET. The latter variable showed a direct independent association with PET-PPE and PET-PC (Table 3), whereas the observed univariate correlation between PETΔPConc and UF (Table 2) did not persist after controlling for $D/P_{240'}$ creatinine.

In either or both PETs, the only independent predictor of 24-hour PPE was PETΔPConc, PET-PPE, or PET-PC; $D/P_{240'}$ creatinine, UF capacity, PD modality, daily infused dialysate volume, daily number of PD exchanges, and plasma protein level showed no associations with PPE in the multivariate analysis.

## DISCUSSION

Protein and amino acid losses during PD therapy have been a recurrent subject of interest since the early 1980s, and yet their significance has not been fully clarified. For years, protein malnutrition was the most feared consequence of this unwanted effect of PD. The observed inverse correlation between PPE and plasma protein level (particularly albumin level) appeared to lend support to this concern. Currently, hypoalbuminemia is viewed as a manifestation of a complex interrelation between malnutrition, inflammation, endothelial dysfunction, peritoneal transport, volume overload, and cardiovascular disease (10,15,22-30). The PPE may have a contributory, yet undefined, role in the pathogenesis of protein malnutrition in PD patients, but more emphasis is now laid on the systemic

consequences of continued depletion of specific proteins, including dyslipidemia, coagulation disorders, and hormonal disturbances (2-6). With this background, the absence of a correlation between PPE and simultaneous plasma total protein or albumin level in our study was not totally unexpected. Previous studies have shown remarkably variable degrees of association between plasma and dialysate protein levels (8,10,15,21,22,31).

Protein transport during a PET sustained a significant, but moderate, correlation with 24-hour PPE. It is unclear which variable offers a more representative estimation of peritoneal protein transport. The PPE is easier to interpret on clinical grounds, but it may be affected by factors other than peritoneal protein transport (for example, PD schedule). Transport during a PET seemingly represents a better approach to standardizing PPE in clinical practice. Interestingly, we could not build a predictive model for 24-hour PPE because, after controlling for PETΔPConc, PET-PPE, or PET-PC, neither the $D/P_{240'}$ creatinine, the PD modality, the daily number of exchanges, nor the daily infused dialysate volume showed an association with that variable. Some previous studies have underlined this limitation (7,10); others have been able to demonstrate variable degrees of association between PD prescription and PPE. For instance, Westra et al. (32) found a direct correlation between PPE and the number of nighttime dwells in patients on automated PD, and also a significant contribution of the daytime exchange to the final amount of protein recovered from dialysate. By comparison, other groups did not find marked differences in 24-hour PPE between patients treated with either wet- or dry-day automated PD (7).

Peritoneal protein transport occurs essentially through large intercellular pores. Size restriction appears to be the main barrier to diffusion; the significance of the glycocalyx and other charge-dependent barriers is a matter of debate (13,14,16). The final dialysate protein content after a single PD exchange may depend on other factors too, including transfer of proteins from the interstitial space to the peritoneal fluid [particularly during the first minutes of the dwell (33)], ultrafiltration, and lymphatic reabsorption in relation to the length of the dwell. The functionality of the large pores has been claimed to be sensitive to disorders compromising endothelial function, including inflammatory states (16). That

association has been demonstrated using the personal dialysis capacity test (34), but that test is more cumbersome than the PET. Other groups have suggested the possibility that 24-hour PPE could be used as a marker of large-pore dysfunction, endothelial disease, inflammation, and in the end, cardiovascular risk of PD patients (15,31,35). The results of our study are consistent with that hypothesis, showing a significant, yet moderate, correlation between PPE during PET and current cardiovascular comorbidity in PD patients. The direct association between systolic BP and protein transport during PET (Table 3) can be interpreted on that basis or, alternatively, as an hemodynamic effect of BP on transport through large pores. Conversely, 24-hour PPE showed a much lower discrimination capacity for that purpose.

Importantly, protein transport during a PET (and, more so, in a 24-hour PPE) correlated poorly with serum CRP. In general, CRP is not a consistent predictor of disorders of peritoneal transport (23), although some reports suggest a correlation with large-pore surface (34). Other markers of inflammation, including interleukin 6, have proved to be more sensitive than CRP (28), but those markers were not tested in the present study.

Our study disclosed a complex relationship between UF and protein transport. The PETΔPConc sustained a univariate inverse correlation with UF that did not persist when multiple regression analysis was applied. Conversely, a direct correlation between PET-PPE or PET-PC and UF was evident only on multivariate analysis. These apparent paradoxes can be explained by the interaction of several opposing factors. First, there is a natural trend to an inverse correlation between UF capacity and small-solute transport, meaning that higher UF rates tend to be associated with lower peritoneal transport rates. On the other hand, UF proceeds through ultrasmall and small pores, exerting a kind of sieving effect on dialysate protein concentrations (decrease of PETΔPConc). A high UF rate can boost transmembrane protein transport, both directly by convective transport through large and small pores, and indirectly by maintaining a favorable concentration gradient. This phenomenon may potentially increase final protein excretion (as estimated by PET-PPE) and compensate partially for the decline of PETΔPConc. The results of univariate analysis show the crude effects of those

interactions; multiple regression controls for the confounding effect of solute transport characteristics ($D/P_{240'}$ creatinine). To summarize, our results could be consistent with the notion that UF may slightly increase total protein transport during PET, but that the effect may be masked by "protein sieving" if PETΔPConc rather than PET-PPE is scrutinized. We must emphasize that the clinical significance of any putative increase in PPE driven by UF is questionable, as shown by the fact that PET-PPE and PET-PC were not significantly different during the 2.27% and the 3.86% PETs.

The differences observed in PETΔPConc patterns between the 2.27% and 3.86% PETs can be explained by the different UF profiles induced by those solutions. Alternatively, high concentrations of glucose could bias the estimations of dialysate total protein or albumin concentration—more so during the 3.86% PET than the 2.27% PET. The reported methods of estimation of dialysate protein concentration are heterogeneous (7-10,13,31,33,36-38), although the nephelometry and colorimetric methods are the most common. In general, glucose is not considered to interfere markedly in the estimation of plasma or dialysate protein level, but concentrations as high as those observed during a 3.86% PET may have not been routinely tested for most of the methods. This mechanism can be discarded in our study because the effect of a marked increase in the concentration of dialysate glucose on the estimations of protein concentration was negligible.

A remarkable finding of our study was the consistent inverse correlation between the daily peritoneal glucose load delivered to patients and the main study variable, PETΔPConc (Table 3). The significance of this finding is unclear, but PETΔPConc may be a marker for other unidentified factors, because patients requiring high daily peritoneal glucose loads may show specific yet heterogeneous characteristics, including large body size, low or absent RRF, automated PD as the treatment modality, or UF failure. It could also be argued that a higher peritoneal glucose load could be a negative surrogate for the use of icodextrin, the latter representing a marker of high peritoneal transport. However, the effect of the peritoneal glucose load on PPE persisted after controlling for co-variables such as the use of icodextrin or the UF capacity of the patient (as

estimated from UF during PET). To our knowledge, no evidence so far links peritoneal glucose toxicity to decreased large-pore density or activity in PD patients.

## SUMMARY

The PETΔPConc, PET-PPE, and PET-PC all permit a standardized approach to the characterization of peritoneal protein transport and use as a marker of large-pore dysfunction and, eventually, systemic endothelial disease. All those markers are tightly correlated, but PET-PPE and PET-PC may be more appropriate, because they cover the effect of UF during the PET and permit direct comparisons between 2.27% and 3.86% tests. Ultrafiltration, small-solute transport characteristics ($D/P_{240'}$ creatinine), and daily peritoneal glucose load are independently correlated with peritoneal protein transport. Daily peritoneal glucose load also shows a moderate, significant association with markers of cardiovascular disease.

## DISCLOSURES

MPF is a member of the European PD Advisory Board of Baxter Corporation. MPF and ARC have performed as consultants for Baxter and for Gambro Corporation. The remaining authors declare no financial conflict of interest.

## REFERENCES


1. Pollock C.A., Cooper B.A., Ibels L.S., Kantzow E. Nutritional aspects of peritoneal dialysis. In: Gokal R., Khanna R., Krediet R.T., Nolph K.D., eds. The Textbook of Peritoneal Dialysis. Dordrecht: Kluwer Academic Publishers; 2000: 515–43.
2. Robey C., Shreedhar K., Batuman V. Effects of chronic peritoneal dialysis on thyroid function tests. Am J Kidney Dis 1989; 13: 99–103.
3. Culleton B.F., Wilson P.W. Thrombogenic risk factors for cardiovascular disease in dialysis patients. Semin Dial 1999; 12: 117–25.

4. Kim S.B., Yang W.S., Park J.S. Role of hypoalbuminemia in the genesis of cardiovascular disease in dialysis patients. Perit Dial Int 1999; 19(Suppl 2): 144–9.
5. Burkart J. Metabolic consequences of peritoneal dialysis. Semin Dial 2004; 17: 498–504.
6. Liu J., Rosner M.H. Lipid abnormalities associated with end stage renal disease. Semin Dial 2006; 19: 32–40.
7. Kathuria P., Moore H.L., Khanna R., Twardowski Z.J., Goel S., Nolph K.D. Effect of dialysis modality and membrane transport characteristics on dialysate protein losses of patients on peritoneal dialysis. Perit Dial Int 1997; 17:449–54.
8. Cooper S., Iliescu E.A., Morton A.R. The relationship between dialysate protein loss and membrane transport status in peritoneal dialysis patients. Adv Perit Dial 2001; 17: 244–7.
9. Smit W., van Dijk P., Langedijk M.J., Schouten N., van den Berg N., Struijk D.G.et al. Peritoneal function and assessment of reference values using a 3.86% glucose solution. Perit Dial Int 2003; 23: 440–9.
10. Clerbaux G., Francart J., Wallemacq P., Robert A., Goffin E. Evaluation of peritoneal transport properties at onset of peritoneal dialysis and longitudinal follow-up. Nephrol Dial Transplant 2006; 21: 1032–9.
11. Heimbürger O., Waniewski J., Werynski A., Lindholm B. A quantitative description of solute and fluid transport during peritoneal dialysis. Kidney Int 1992; 41: 1320–32.
12. Rippe B. A three-pore model of peritoneal transport. Perit Dial Int 1993; 13(Suppl 2): 35–8.
13. Buis B., Koomen G.C.M., Imholz A.L.T., Struijk D.G., Reddingius R.E., Arisz L.et al. Effect of electric charge on the transperitoneal transport of plasma proteins during CPD. Nephrol Dial Transplant 1996; 11: 1113–20.
14. Devuyst O., Goffin E. Water and solute transport in peritoneal dialysis: models and clinical applications. Nephrol Dial Transplant 2008; 23: 2120–3.
15. Heaf J.G., Sarac S., Afzal S. A high peritoneal large pore fluid flux causes hypoalbuminemia and is a risk factor for death in peritoneal dialysis patients. Nephrol Dial Transplant 2005; 20: 2194–201.
16. Rippe B., Venturoli D., Simonsen O., de Arteaga J. Fluid and electrolyte transport across the peritoneal membrane during CAPD according to the three-pore model. Perit Dial Int 2004; 24: 10–27.

17. Twardowski Z.J., Nolph K.D., Khanna R., Prowant B.F., Ryan L.P., Moore H.L.et al. Peritoneal equilibration test. Perit Dial Bull 1987; 7: 138–47.
18. La Milia V., Pozzoni P., Virga G., Crepaldi M., Del Vecchio L., Locatelli F. Peritoneal transport assessment by peritoneal equilibration test with 3.86% glucose: a long-term prospective evaluation. Kidney Int 2006; 69: 927–33.
19. Smit W., Langedijk M., Schouten N., van der Berg N., Struijk D., Krediet R. A comparison between 1.36% and 3.86% dextrose dialysis solution for the assessment of peritoneal membrane function. Perit Dial Int 2000; 20: 734–41.
20. Pride E., Gustafson J., Graham A., Spainhour L., Mauck V., Brown P.et al. Comparison of a 2.5% and a 4.25% dextrose peritoneal equilibration test. Perit Dial Int 2002; 22: 365–70.
21. Kagan A., Bar-Khayim Y., Schafer Z., Fainaru M. Kinetics of peritoneal protein loss during CAPD: I. Different characteristics for low and high molecular weight proteins. Kidney Int 1990; 37: 971–9.
22. Blake P.G., Flowerdew G., Blake R.M., Oreopoulos D.G. Serum albumin in patients on CAPD—predictions and correlations with outcomes. J Am Soc Nephrol 1993; 3: 1501–7.
23. Wang T., Heimbürger O., Cheng H.H., Bergström J., Lindholm B. Does a high peritoneal transport rate reflect a state of chronic inflammation? Perit Dial Int 1999; 19: 18–22.
24. Kang D.H., Yoon K.I., Choi K.B., Lee R., Lee H.Y., Han D.S.et al. Relationship of peritoneal membrane transport characteristics to the nutritional status in CAPD patients. Nephrol Dial Transplant 1999; 14: 1715–22.
25. Chung S.H., Chu W.S., Lee H.A., Kim Y.H., Lee I.S., Lindholm B.et al. Peritoneal transport characteristics, comorbid diseases and survival in CAPD patients. Perit Dial Int 2000; 20: 541–7.
26. Margetts P.J., McMullin J.P., Rabbat C.G., Churchill D.N. Peritoneal membrane transport and hypoalbuminemia: cause or effect? Perit Dial Int 2000; 20: 14–18.
27. Cueto–Manzano A.M., Correa–Rotter R. Is high peritoneal transport rate an independent risk factor for CAPD mortality? Kidney Int 2000; 57: 314–20.
28. Pecoits–Filho R., Stenvinkel P., Wang A.Y., Heimbürger O., Lindholm B. Chronic inflammation in peritoneal dialysis: the search for the holy grail? Perit Dial Int 2004; 24: 327–39.

29. Fernandez Reyes M.J., Bajo M.A., Hevia C., del Peso G., Ros S., de Miguel A.G.et al. Inherent high peritoneal transport and ultrafiltration deficiency: their mid-term clinical relevance. Nephrol Dial Transplant 2007; 22: 218–23.
30. Oh K.H., Moon J.Y., Oh J., Kim S.G., Hwang Y.H., Kim S.et al. Baseline peritoneal solute transport rate is not associated with markers of systemic inflammation or comorbidity in incident Korean peritoneal dialysis patients. Nephrol Dial Transplant 2008; 23: 2356–64.
31. Sanchez Villanueva R., Bajo A., del Peso G., Fernández Reyes M.J., González E., Romero S.et al. Higher daily peritoneal protein clearance when initiating peritoneal dialysis is independently associated with peripheral artery disease: a possible new marker of systemic endothelial dysfunction? Nephrol Dial Transplant 2009; 24: 1009–14.
32. Westra W.M., Kopple J.D., Krediet R.T., Appell M., Mehrotra R. Dietary protein requirements and dialysate protein losses in chronic pe rito neal dialysis patients. Perit Dial Int 2007; 27: 192–5.
33. Waniewski J., Wang T., Heimbürger O., Werynski A., Lindholm B. Discriminative impact of ultrafiltration on peritoneal protein transport. Perit Dial Int 2000; 20: 39–46.
34. van Biesen W., van der Tol A., Veys N., Dequidt C., Vijt D., Lameire N.et al. The personal dialysis capacity test is superior to the peritoneal equilibration test to discriminate inflammation as the cause of fast transport status in peritoneal dialysis patients. Clin J Am Soc Nephrol 2006; 1: 269–74.
35. Perl J., Huckvale K., Chellar M., John B., Davies S.J. Peritoneal protein clearance and not peritoneal membrane transport status predicts survival in a cotemporary cohort of peritoneal dialysis patients. Clin J Am Soc Nephrol 2009; 4: 1201–6.
36. Kabanda A., Goffin E., Bernard A., Lauwerys R., van Ypersele de Strihou C. Factors influencing serum levels and peritoneal clearances of low molecular weight proteins in continuous ambulatory peritoneal dialysis. Kidney Int 1995; 48: 1946–52.
37. Arbeiter K., Stemberger R., Greenbaum L., Mueller T., Konstantin A., Herkner K.et al. Peritoneal transport kinetics of proteins in children on chronic peritoneal dialysis. Perit Dial Int 2003; 22: 162–8.
38. Rojas–Campos E., Cortés–Sanabria L., Martínez–Ramírez H.R., González L., Martín del Campo F., González Ortíz M.et al. Effect of oral administration of

losartan, prazosin and verapamil on peritoneal solute transport in CAPD patients. Perit Dial Int 2005; 25: 576–82.

**Table 1** Study Population

| Characteristic | Value |
|---|---|
| Age (years) | 57.4±14.2 (20,84) |
| Sex (male/female) | 48/42 (53.3/46.7) |
| With diabetes | 33 (36.7) |
| Previous CV events | |
| Ischemic heart disease | 21 (23.3) |
| Stroke | 10 (11.1) |
| Peripheral arterial disease | 11 (12.2) |
| Major arrhythmia | 6 (6.6) |
| Other heart diseases | 7 (7.8) |
| Patients with at least one event | 37 (41.1) |
| Systolic BP (mm Hg) | |
| 2.27% test | 133.5±18.0 (90,180) |
| 3.86% test | 134.4±18.6 (85,185) |
| Diastolic BP (mm Hg) | |
| 2.27% test | 78.2±10.6 (60,105) |
| 3.86% test | 78.2±11.1 (50,105) |
| Modality (CAPD/APD) | 68/22 (75.6/24.4) |
| Time on PD (months) | 6 (2,107) |
| Peritonitis since the start of PD (none/1/>1) | 61/15/14 (67.8/16.7/15.5) |
| Icodextrin for long dwell | 41 (45.6) |
| ACEI–ARA drugs | 44 (48.9) |
| Calcium antagonists | 45 (50.0) |
| Furosemide | 47 (52.2) |
| Glomerular filtration rate (mL/min) | 6.1±4.2 (0,16.0) |
| Daily diuresis (mL) | 1117±651 (0,2500) |
| Proteinuria (g/day) | 0.98±1.18 (0,5.4) |
| Plasma total protein (g/dL) | |
| 2.27% test | 6.66±0.58 (5.1,8.1) |
| 3.86% test | 6.60±0.62 (4.8,7.8) |
| Plasma albumin (g/dL) | |
| 2.27% test | 3.74±0.36 (2.3,4.6) |
| 3.86% test | 3.72±0.37 (2.1,4.5) |
| Hemoglobin (g/dL) | |

**Table 1** Study Population

| Characteristic | Value |
|---|---|
| 2.27% test | 12.1±1.7 (7.7,16.7) |
| 3.86% test | 12.0±1.6 (7.0,16.3) |
| C-reactive protein (mg/L) | 2.6 (1,117) |

[a] Values were recorded at study initiation unless otherwise specified and are presented as number (percentage), or mean ± standard deviation (range), except for time on dialysis and C-reactive protein, which are presented as median (range).

CV = cardiovascular; BP = blood pressure; CAPD = continuous ambulatory peritoneal dialysis; APD = automated peritoneal dialysis; PD = peritoneal dialysis; ACEI = angiotensin converting–enzyme inhibitor; ARA = angiotensin II receptor agonist.

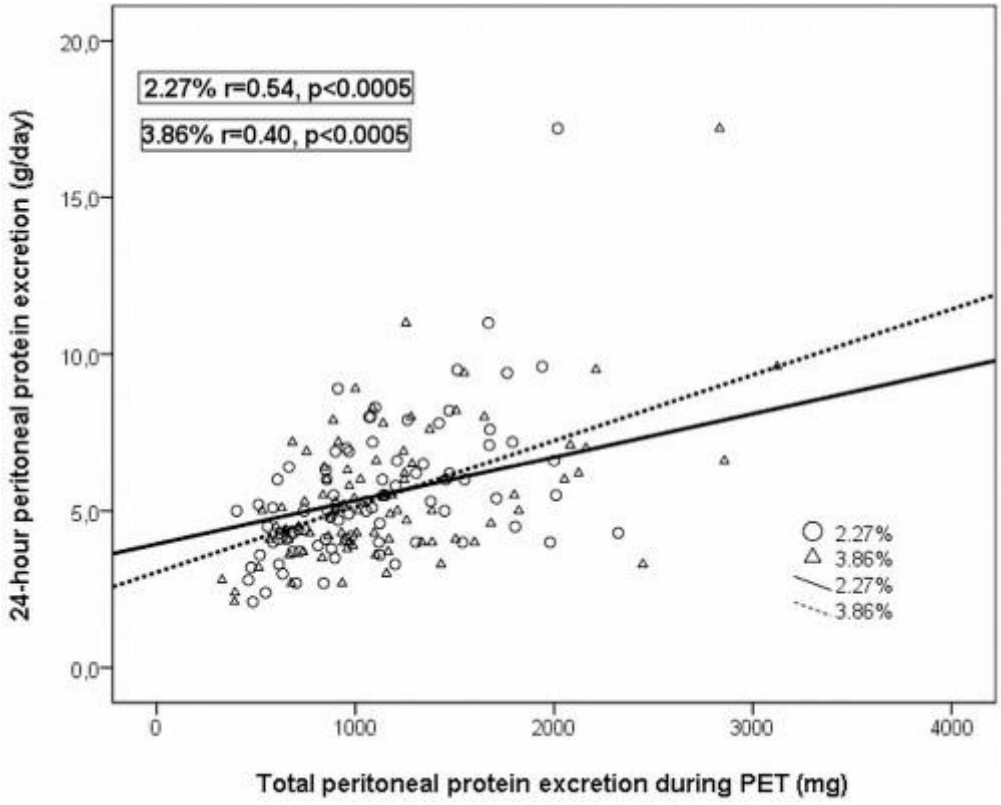


**Figure 1** Spearman correlation between peritoneal protein excretion during peritoneal equilibration tests (PETs) using 2.27% or 3.86% glucose-based dialysate and in a 24-hour dialysate collection.

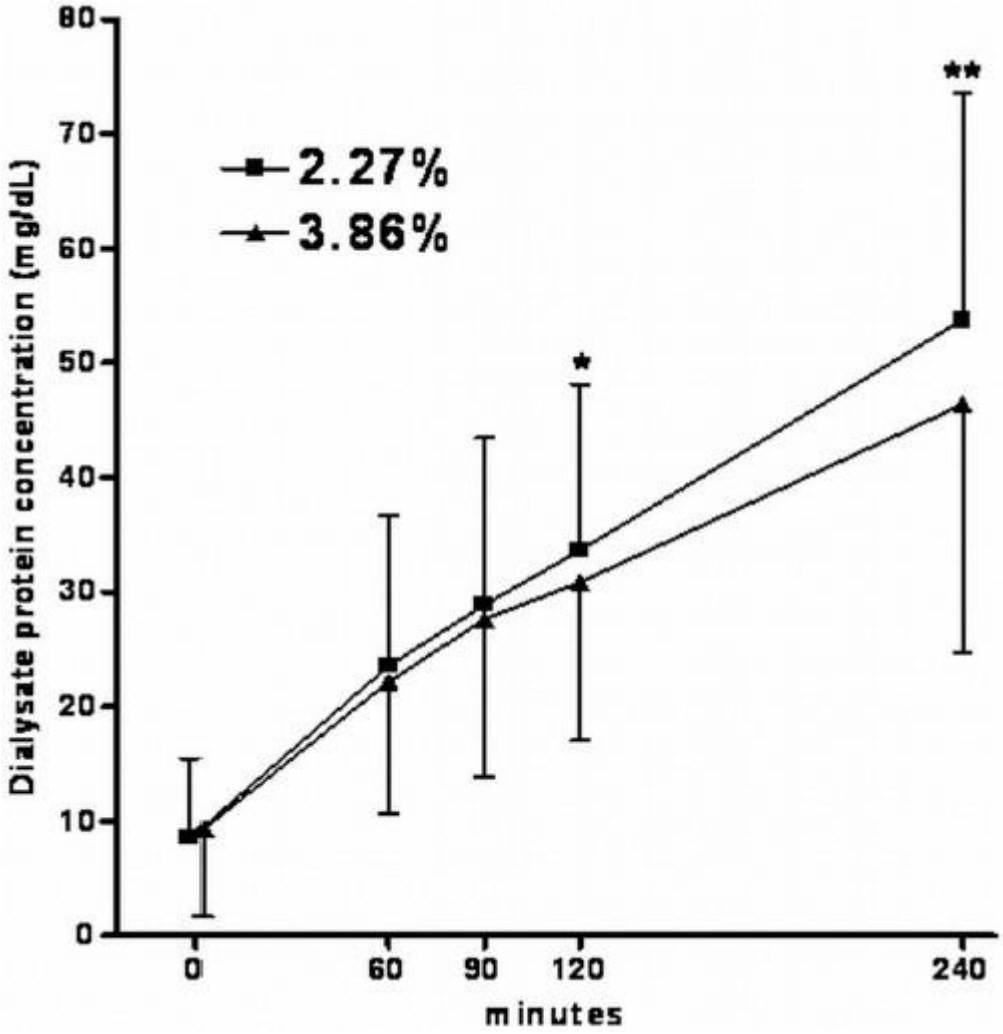


**Figure 2** Dialysate protein transport profiles during peritoneal equilibration tests (PETs) using 2.27% and 3.86% glucose-based dialysate. Values are presented as mean ± standard deviation. *p = 0.046; **p = 0.008 (Wilcoxon).

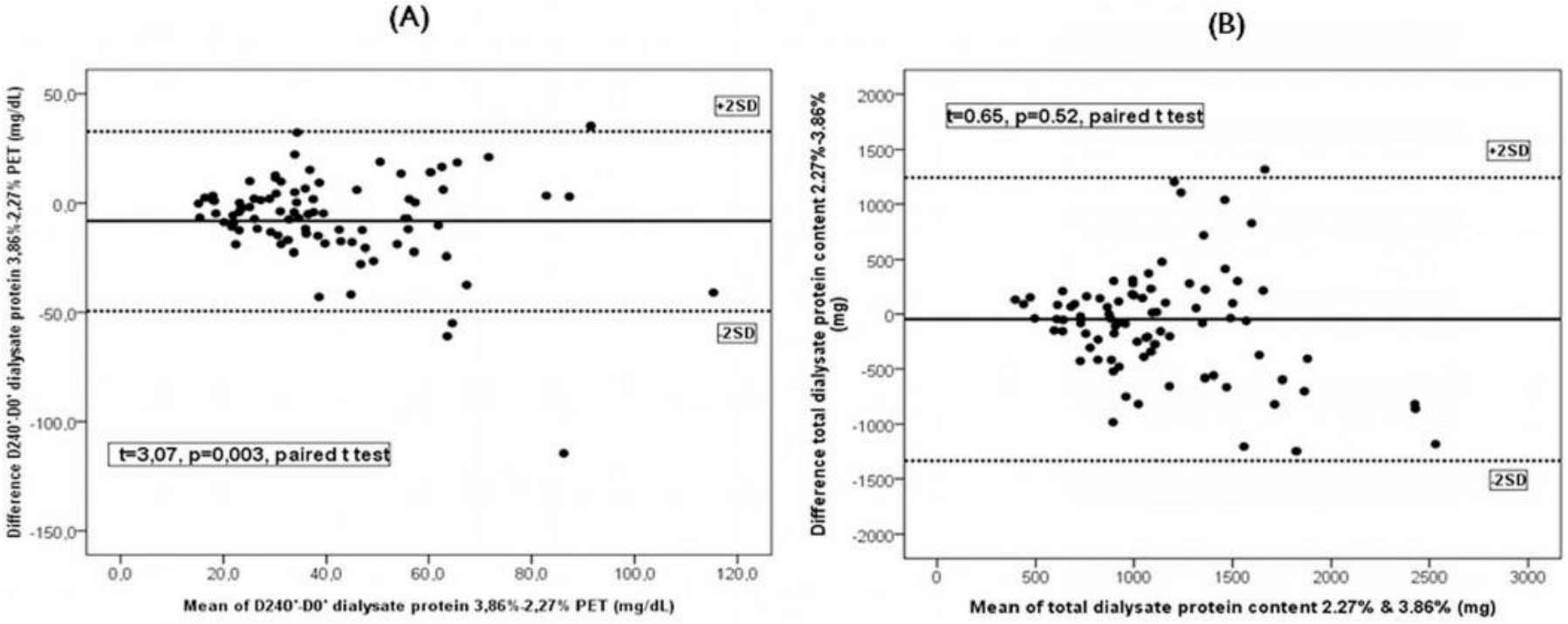


**Figure 3** Bland–Altman plot for agreement between estimations of peritoneal protein excretion during peritoneal equilibration tests (PETs) using 2.27% or 3.86% glucose-based dialysate. (A) End-to-initial dialysate ($D_{240'} – D_{0'}$) protein concentration. (B) Total protein excretion.

**Table 2** Peritoneal Equilibration Test (PET)–Related Correlates of Peritoneal Protein Transport, Univariate Analysis

| Variable | $D_{240'} - D_{0'}$ protein | | Total protein excretion | | Total protein clearance | |
|---|---|---|---|---|---|---|
| | 2.27% PET | 3.86% PET | 2.27% PET | 3.86% PET | 2.27% PET | 3.86% PET |
| $D/P_{240'}$ creatinine | 0.55 (0.0005)[a] | 0.45 (0.0005)[a] | 0.49 (0.0005)[a] | 0.41 (0.0005)[a] | 0.45 (0.0005)[a] | 0.36 (0.0005)[a] |
| $D_{240'}/D_{0'}$ glucose | –0.71 (0.0005)[a] | –0.54 (0.0005)[a] | –0.62 (0.0005)[a] | –0.44 (0.0005)[a] | –0.59 (0.0005)[a] | –0.46 (0.0005)[a] |
| UF during PET (mL) | –0.30 (0.005)[a] | –0.32 (0.002)[a] | –0.08 (0.48)[a] | –0.08 (0.46)[a] | –0.06 (0.59)[a] | –0.04 (0.72)[a] |
| Sodium dip 60′ (mmol/L/L) | –0.30 (0.004)[a] | –0.29 (0.006)[a] | –0.24 (0.026)[a] | –0.19 (0.09)[a] | –0.27 (0.012)[a] | –0.15 (0.17)[a] |

[a] Spearman correlation coefficients (p value).

D = dialysate; P = plasma; UF = ultrafiltration

**Table 3** Clinical Correlates of Peritoneal Protein Transport During the Peritoneal Equilibration Test (PET), Multivariate Analysis[a]

| Dependent variable | Covariates | β | 95% CI of β | p Value |
|---|---|---|---|---|
| $D_{240'} - D_{0'}$ protein (mg/dL) | $D/P_{240'}$ creatinine | 108.0 | 75.3 to 140.6 | 0.0005 |
| 2.27% PET | Peritoneal glucose load (×g/day) | –0.14 | –0.24 to –0.04 | 0.005 |
| Model $r^2 = 0.40$ | Systolic BP (×10 mmHg) | 2.41 | –0.12 to 5.05 | 0.06 |
| $D_{240'} - D_{0'}$ protein (mg/dL) | $D/P_{240'}$ creatinine | 53.1 | 27.8 to 78.3 | 0.0005 |
| 3.86% PET | Peritoneal glucose load (×g/day) | –0.10 | –0.16 to –0.04 | 0.003 |
| Model $r^2 = 0.37$ | Systolic BP (10 mmHg) | 2.81 | 0.93 to 4.84 | 0.005 |
| | CV comorbidities (n) | 4.30 | 0.25 to 8.35 | 0.038 |
| Total dialysate protein excretion (mg) | $D/P_{240'}$ creatinine | 2349 | 1602 to 3096 | 0.0005 |
| 2.27% PET | Peritoneal glucose load (×g/day) | –3.3 | –5.5 to –1.1 | 0.004 |
| Model $r^2 = 0.36$ | Ultrafiltration during PET (×dL) | 6.22 | 1.43 to 11.02 | 0.012 |
| | Plasma total protein (×g/dL) | 158.2 | –10.8 to 327.3 | 0.07 |
| | Systolic BP (×10 mmHg) | 5.4 | 0.1 to 10.9 | 0.047 |
| Total dialysate protein excretion (mg) | $D/P_{240'}$ creatinine | 1298 | 618 to 1976 | 0.0005 |
| 3.86% PET | Peritoneal glucose load (×g/day) | –2.4 | –4.1 to –0.7 | 0.007 |
| Model $r^2 = 0.37$ | Ultrafiltration during PET (×dL) | 4.03 | 0.76 to 7.29 | 0.01 |
| | Systolic BP (×10 mmHg) | 7.1 | 1.9 to 12.2 | 0.008 |
| | CV comorbidities (n) | 97.1 | 9.6 to 203.8 | 0.033 |

**Table 3** Clinical Correlates of Peritoneal Protein Transport During the Peritoneal Equilibration Test (PET), Multivariate Analysis[a]

| Dependent variable | Covariates | β | 95% CI of β | p Value |
|---|---|---|---|---|
| Total protein clearance (mL) | $D/P_{240'}$ creatinine | 3.90 | 2.73 to 5.08 | 0.0005 |
| 2.27% PET | Peritoneal glucose load (×g/day) | –0.01 | –0.10 to –0.003 | 0.001 |
| Model $r^2 = 0.38$ | Ultrafiltration during PET (×dL) | 0.010 | 0.002 to 0.016 | 0.009 |
| | Systolic BP (×10 mmHg) | 0.009 | 0.002 to 0.022 | 0.045 |
| Total protein clearance (mL) | $D/P_{240'}$ creatinine | 2.31 | 1.07 to 3.54 | 0.0005 |
| 3.86% PET | Peritoneal glucose load (×g/day) | –0.011 | –0.018 to –0.002 | 0.002 |
| Model $r^2 = 0.34$ | UF during PET (×dL) | 0.006 | 0.000 to 0.010 | 0.039 |
| | Systolic BP (×10 mmHg) | 0.8 | –0.02 to 1.71 | 0.08 |
| | CV comorbidities (n) | 0.19 | –0.002 to 0.38 | 0.055 |

[a] Stepwise multiple regression analysis. Best models for each PET.

CI = confidence interval; D = dialysate; P = plasma; BP = blood pressure; CV = cardiovascular; UF = ultrafiltration.