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*Original article*

# Effect of Initial PET Status on Clinical Course in Peritoneal Dialysis Patients

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**Abstract**

**Introduction.** To investigate the effect on mortality of initial peritoneal equilibration test (PET) in PD patients (pts).
**Methods.** We included patients who initiated therapy between 2001-2014. Patients underwent initial PET in the first three months. They were divided into four groups according to the initial PET (high, high-average, low-average, low transport). Sociodemographic data, clinical courses and infectious complications between groups were compared, and the reasons for PD withdrawal were obtained. Technique survival analyses of patients were done.
**Results.** In a total of 367 pts were PD was started, 104 pts were excluded. Data of the remaining 263 patients were evaluated. Thirty-seven pts (23F, mean age 44.6±16.5 years, mean follow-up 30.5±20.8 months) had high transport, 90 pts (49F, mean age 41.5±16 years, mean follow-up 42.6±27.7 months) had high-average transport, 91 pts (55F, mean age 44.5±14.9 years, mean follow-up 50±29.2 months) had low-average transport and 45 pts (17F, mean age 43.5±14 years, mean follow-up (63.4±34.5 months) had low transport. There was no difference between groups in terms of age, gender, body mass index, initial daily urine and ultrafiltration volume, initial albumin levels, presence of diabetes mellitus ($p>0.05$). Peritonitis and catheter exit-site/tunnel infection attacks were higher in patients with high transport ($p=0.01$ and 0.008, respectively). There was a difference between groups with respect to the last status of patients ($p< 0.009$). The major causes of deaths were peritonitis and/or sepsis and cardiovascular causes in all patients. The mortality and technique survival rate was found higher in patients with high transport (log rank: 0.004 and 0.027, respectively). Age (OR:1.045, $p<0.001$), initial albumin (OR: 0.482, $p= 0.007$), daily urine volume (OR: 1.045, $p<0.001$) and presence of catheter exit-site/tunnel infection (OR: 0.249, $p<0.001$) were found to predict patient survival. Only presence of catheter exit-site/tunnel infection (OR: 0.452, $p=0.013$) were found to predict patient survival.
**Conclusions.** Initial PET has effects on PD patient survival; patients with high transport have the worst survival and frequent infectious complications.

**Key words:** peritoneal dialysis, PET, mortality

## Introduction

Patients with end-stage renal disease (ESRD), including those who are on peritoneal dialysis (PD), are at a much higher risk for premature death than the general population. Well-accepted risk factors for early mortality that have been identified in the PD population include age, diabetes, preexisting cardiovascular disease, and malnutrition/hypoalbuminemia [1-6].
The relationship between peritoneal membrane transport characteristics and the outcomes of patients receiving peritoneal dialysis [5,7-17] has been the subject of several studies. It was found that, in the CANUSA study population, ANZDATA registry and several other studies, high transport status was associated with mortality risk [5,7-13]. However, other studies such as ADEMEX and EAPOS, have found peritoneal membrane properties are not associated with patient survival [14-17].
Peritoneal equilibration test (PET) developed by Twardowski [18] characterizes the transport nature of the patient's peritoneal membrane. The transport character not only helps to decide the dwell time, but also plays a crucial role in determining the morbidity and mortality of patients on PD.
The aim of this study was to evaluate whether initial PET status had an effect on patients' and technique survival or not and to show presence of any other factors other than PET status in patients performing peritoneal dialysis in our Center.

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## Material and methods

The records of 367 patients who underwent PD therapy due to ESRD in our PD unit between 2001 and 2014 were evaluated retrospectively. Patients younger than 18 years, with history of PD less than 90 days, unknown PET status within 3 months after initiation of PD, recovering renal function and no longer need for dialysis were excluded from the study. Remaining 263 patients' data were evaluated.
All patients had a PET within 3 months after initiation of PD as Twardovski *et al*. described [18]. They were divided into 4 groups according to the PET results including low, low-average, high-average, high transport.
Age, gender, educational level, sociodemographic characteristics such as presence of someone to administer PD [Self or Assisted PD (their children or other persons like health caregivers)], nature of the decision for PD (patient's own preference or compulsory choice), etiology of ESRD were investigated in-depth from patients' records. If present, duration of hemodialysis (HD) history before PD therapy was noted.
Systolic and diastolic blood pressure measurements, daily urine volumes, daily mean ultrafiltration (UF) amount, and cardiothoracic indices of all patients were recorded both at the beginning and at the end of the study.
Serum urea, creatinine, calcium, phosphorus, albumin, intact parathyroid hormone (iPTH), hemoglobin, and ferritin values were recorded at the beginning of PD treatment and during the last monitoring. Infectious complications such as peritonitis, exit site/tunnel infections were recorded and their incidences were calculated. All parameters were compared among groups.
The factors associated with mortality, patient and technique survival were examined for all of the patients. The effect of initial PET status on mortality was also investigated. Technique failure was defined as transfer to HD due to peritonitis, ultrafiltration failure, inadequate dialysis, exit-site and/or tunnel infection, and mechanical problems.
We performed statistical analyses with the Scientific Package for Social Science (version 17.0; SPSS Inc., Chicago, IL, USA). Kruskal-Wallis and Mann-Withney U tests were used for nonparametric variables. One Way ANOVA test was used for analyzing clinical and biochemical parameters among groups (post-hoc analysis, Tukey's test). The Kaplan–Meier method was used for patient and technique survival. A comparison of outcomes was done by the log rank test. Independent risk factors were also analyzed for patients' mortality and technique survival and hazard ratio (HR) was calculated by using backward logistic regression of the Cox proportional hazards method. Differences were considered statistically significant for the p values less than 0.05.

## Results

Out of 367 patients 104 were excluded from the study. The remaining 263 patients were divided into 4 groups according to PET results. Groups with low transport, low-average, high-average and high transport consisted of 45, 91, 90 and 37 patients, respectively. Sociodemographic, biochemical and clinical data of groups are given in Tables 1 and 2. Glomerulonephritis (23.9%) and

**Table 1.** Demographic and clinical data of patients

| PET Status | Low (n:45) | Low-average (n:91) | High-average (n:90) | High (n:37) | p |
|---|---|---|---|---|---|
| Mean age (years) | 43.5±14 | 44.5±14.9 | 41.5±16 | 44.6±16.5 | 0.59 |
| Gender (female) | 17 | 55 | 49 | 23 | 0.06 |
| Mean follow-up (months) | 63.4±34.5 | 50±29.2 | 42.6±27.6 | 30.5±20.8 | <0.001 |
| $Kt/V_{Urea}$ | 2.3±0.5 | 2.2±0.5 | 2.0±0.4 | 1.9±0.5 | <0.001 |
| Body mass index (kg/m²) | 23.2±4.2 | 23.3±4.3 | 21.9±4.8 | 23.3±5.4 | 0.15 |
| History of HD (presence, %) | 14.3 | 25.3 | 15.9 | 24.2 | 0.30 |
| Urine volume, initial (ml/day) | 475±454 | 365±462 | 407±461 | 280±256 | 0.54 |
| Urine volume, last visit (ml/day) | 106±251 | 89±229 | 159±315 | 132±333 | 0.43 |
| Ultrafiltration volume, initial (ml/day) | 1074±359 | 1064±483 | 1030±457 | 893±353 | 0.51 |
| Ultrafiltration volume, last visit (ml/day) | 1166±507 | 1227±602 | 1052±470 | 891±533 | 0.009 |
| Systolic blood pressure, initial (mmHg) | 120±27 | 117±28 | 112±23 | 120±24 | 0.20 |
| Systolic blood pressure, last visit (mmHg) | 125±36 | 121±27 | 111±27 | 106±26 | 0.009 |
| Diastolic blood pressure, initial (mmHg) | 79±16 | 74±16 | 71±14 | 69±14 | 0.04 |
| Diastolic blood pressure, last visit (mmHg) | 75±18 | 75±16 | 70±16 | 68±17 | 0.09 |
| Incidence of peritonitis (patient-months) | 37.7±31 | 33.8±26 | 28.1±21 | 20.7±19 | 0.01 |
| Incidence of catheter exit site/tunnel infection (patient-months) | 48.2±32 | 40.7±27 | 36±25 | 27.6±18.9 | 0.008 |

**Table 2.** Laboratory data of patients

| PET Status | Low (n:45) | Low-average (n:91) | High-average (n:90) | High (n:37) | P |
|---|---|---|---|---|---|
| Urea level, initial (mg/dl) | 112±34 | 122±54 | 121±42 | 112±45 | 0.52 |
| Urea level, last visit (mg/dl) | 86±37 | 95±38 | 99±42 | 88±39 | 0.25 |
| Creatinine level, initial (mg/dl) | 8.5±2.9 | 8.9±3.0 | 9.5±3.1 | 8.8±2.6 | 0.24 |
| Creatinine level, last visit (mg/dl) | 8.5±2.3 | 8.8±2.7 | 9.7±2.6 | 8.4±2.2 | 0.03 |
| Albumin level, initial (g/dl) | 3.5±0.6 | 3.7±0.5 | 3.7±0.5 | 3.6±0.5 | 0.11 |
| Albumin level, last visit (g/dl) | 3.6±0.7 | 3.6±0.5 | 3.7±0.5 | 3.3±0.5 | 0.03 |
| Hemoglobin level, initial (gr/dl) | 10.6±1.8 | 10.7±1.7 | 10.5±1.8 | 11±1.9 | 0.62 |
| Hemoglobin level, last visit (gr/dl) | 11.3±2.3 | 11.3±2 | 11.3±1.9 | 11.6±1.9 | 0.89 |
| Ferritin, initial (ng/mL) | 335±259 | 482±436 | 363±274 | 376±418 | 0.08 |
| Ferritin, last visit (ng/mL) | 308±233 | 405±414 | 381±375 | 452±729 | 0.53 |
| Calcium level, initial (mg/dl) | 9.0±1.0 | 9.1±1.0 | 9.0±0.7 | 8.8±1.0 | 0.50 |
| Calcium level, last visit (mg/dl) | 9.2±0.9 | 9.2±0.9 | 9.2±0.8 | 9.0±0.8 | 0.93 |
| Phosphorus level, initial (mg/dl) | 4.9±1.5 | 4.9±1.8 | 5.2±1.7 | 5.3±2.0 | 0.50 |
| Phosphorus level, last visit (mg/dl) | 4.3±1.3 | 4.3±1.3 | 5.0±1.4 | 4.6±1.4 | 0.004 |
| Parathyroid hormone level, initial (pg/dl) | 303±355 | 326±321 | 387±555 | 248±203 | 0.39 |
| Parathyroid hormone level, last visit (pg/dl) | 393±395 | 437±528 | 483±529 | 397±308 | 0.75 |

diabetic nephropathy (21.9%) were the leading causes of ESRD in all patients. There was no difference in terms of etiology of kidney disease among groups (p=0.35). Most of the patients had completed primary school: 57.1% of low transport group, 51.7% of low-average transport group, 62.7% of high-average and of high transport groups. Education level was similar among groups (p=0.52).

PD was performed by patients themselves in 92.9% of low, 90.8% of low-average, 90% and 72.7% of high-average and of high transport groups, respectively. In other words, high transporters were performing assisted PD more frequently compared to other groups. (p=0.02).

PD therapy was done mandatory in 30% of high transporters (p=0.04) while it was 7.1% in low, 13.8% in low-average, 14.8% in high-average transport patients. History of hemodialysis was similar among groups (p=0.3).

Peritonitis and catheter exit site/tunnel infections were significantly frequent in high transport group patients (p=0.01 and 0.008, respectively).

A total of 201 patients were withdrawn from PD during the follow-up period. Eighty patients were transferred to HD, 73 patients had died, 42 patients had transplantation, and 6 patients were dropped out due to transfer to another PD unit. The remaining 62 patients were still performing PD.

Twenty patients were transferred to HD, 15 patients had died, 5 had transplantation, 1 patients dropped out in low transport group. Sixteen patients were transferred to HD, 28 died, 14 were transplanted, and 2 were dropped out in the low-average transporters. In the high-average transporters, 31 were transferred to HD, 16 diede, 14 had transplantation while 2 were dropped out from the study. Thirteen patients were transferred to HD, 14 patients died, 9 patients had transplantation and only 1 patient was dropped out in high transport group. Low transporters had the lowest rate of transplantation and the highest rate of transfer to HD while death rate was higher in high transport patients. There was a statistically significant difference in terms of the last status of patients among groups (p=0.009).

The most frequent causes of death in all patients were peritonitis/sepsis (42.1%) and cardiac reasons (35.8%). Causes for transfer to HD were mostly due to peritonitis/sepsis (62.4%) and inadequate dialysis (28.2%). PET

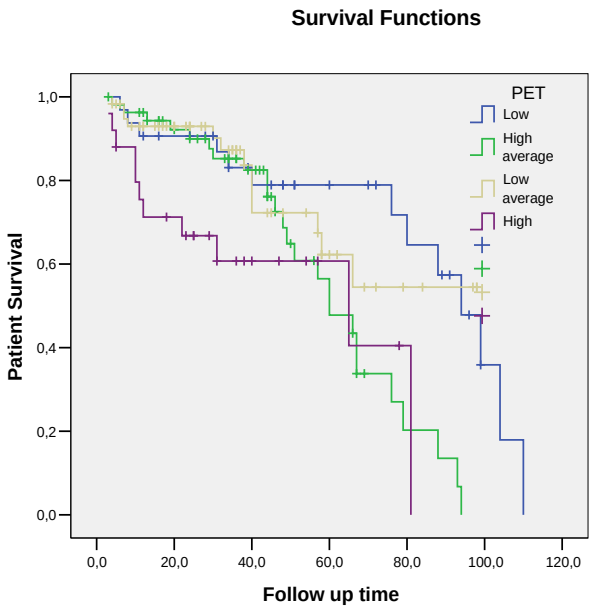


**Fig. 1.** Patient survival according to PET characteristics

groups were similar when causes of death and transfer to HD were compared among groups.

Mean survival time was 81.6±6.6 months in Kaplan-Meier analysis and survival rate was 90.6%, 83.1%, and 71.7% at 1, 3, and 5 years, respectively in patients with low transport status. Mean survival time was 72.4±5.6 months and survival rate was 92.9%, 87.3%, and 54.5% at 1, 3, and 5 years, respectively in low-average transport group. In high-average transport group, mean survival time was 60.1±4.1 months and survival rate was 96.3%, 82.5%, and 47.8% at 1, 3, and 5 years, respectively. Mean survival time was 51.0±7.3 months and survival rate was 71.2%, 60.7%, and 40.5% at 1, 3, and 5 years, respectively in patients with high transport status. Patients' survival was the worst in high transport group (log rank: 0.004) (Figure 1). The factors affecting patients' survival by Cox proportional hazard model backward stepwise LR (Likelihood Ratio) analysis method was found to be advanced age (OR:1.045, 95%[CI]:1.019-1.071, p<0.001), daily urine volume OR:1.045, 95%[CI]: 1.019-1.071, p<0.001), initial serum albumin level (OR:0.482, 95%[CI]:0.284-0.817, p=0.007), and number of catheter exit site/tunnel infection episodes (OR:0.249, 95%[CI]: 0.119-0.524, p<0.001).

Mean technique survival duration was found to be 72.8±6.4 months and survival rate was 96.6%, 75.4%, and 51.6% at 1, 3, and 5 years, respectively in low transport group. Mean technique survival duration was found to be 43.7±3.9 months and survival rate was 91.2%, 48.5%, and 25.1% at 1, 3, and 5 years, respectively in patients with low-average transport status. In high-average transport group, mean technique survival duration was found to be 54.4±4.5 months and survival rate was 92.6%, 66.2%, and 38.4% at 1, 3, and 5 years, respectively. Mean technique survival duration was found to be 43.2±5.3 months and technique survival rate was 95.7%, 53.3%, and 20% at 1, 3, and 5 years, respectively in high transport group. Comparison of technique survival among groups yielded a statistically different significance (log rank: 0.027) (Figure 2). The only factor effective on technique survival was found to be number of catheter exit site/ tunnel infection episodes (OR:0.452, 95%[CI]:0.241-0.847, p= 0.013) by means of Cox proportional hazard model backward stepwise LR (Likelihood Ratio) analysis method.

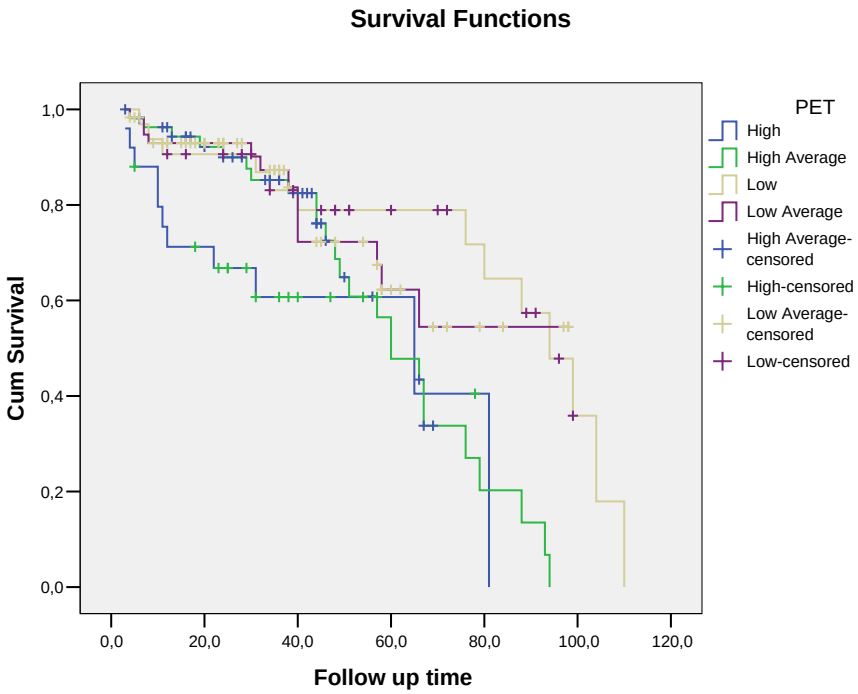


**Fig. 2.** Technique survival according to PET characteristics

## Discussion

The results of this study demonstrated that patients with high transport status had increased mortality rates, worse technique survival rate and frequent infectious complications than the other groups. Older age, number of catheter exit size/tunnel infection attacks, hypoalbuminemia, and low daily urine volume at the beginning of PD were predictors of mortality. Only number of catheter exit size/ tunnel infection attacks was found to predict technique survival.

Many conflicting results have been reported on the relationship between high peritoneal transport and mortality in PD patients [5,7-17]. Some studies have found that high transporters have increased mortality [7-13] while other studies such as ADEMEX and EAPOS, have found peritoneal membrane properties were not associated with patient survival [14-17]. Analysis from the ANZDATA registry has confirmed the association of high transport rates with increased mortality and technique failure [19]. An analysis of the CANUSA data,

Churchill [5] *et al*. demonstrated that the relative risk of technique failure or death was increased by 19% for each 0.1 increase in D: P Cr 4 hour. Two-year survival probabilities of high, high-average, low-average and low transporters were 70.5, 72.4, 80.4 and 90.9%, respectively. The two-year probabilities of both patients and technique survival were increased in high transporters. Another study demonstrated that patient survival for years 1, 3, and 5 were 85%, 64%, and 35%, respectively for high transporters [20]. However, other studies such as ADEMEX and EAPOS, have found that peritoneal membrane properties were not associated with poor patient survival [14,16]. The ADAMEX trial assessed peritoneal transport status by the dialysis adequacy and transport test which may have given different results compared with PET test [16]. In addition, EAPOS study has included patients without residual urine volume and performing only automated peritoneal dialysis (APD). The number of deaths was a few in this study [14]. These factors might lead to differences in study population. We found patient survival rate to be 71.2%, 60.7%, and 40.5% at 1, 3, and 5 years, respectively. They were lower than in the other PET transport groups.

The peritoneal equilibration test characterizes the peritoneal membrane transport properties by determining the ratio of the creatinine concentration in the dialysate to that in the plasma after a 4-h dwell (D/Pc) and has been shown to vary considerably among individuals [18]. The relationship between reduced survival on PD and high transport status may relate to properties of the peritoneal membrane that predispose to the development of conditions associated with a poor prognosis. This is more common in high transporters [21], as rapid solute transport leads to early dissipation of the osmotic gradient for fluid removal [22] hence, reduced drain volumes [5], left ventricular hypertrophy and hypertension are more common in high transporters [23], and are both interrelated with intravascular volume overload [24,25]. We found that high transporters had lower amounts of daily urine volume and ultrafiltration volume even though there was no statistical significance. All of our patients admitted to out PD unit were under strict salt restriction. Acceptable blood pressure values even in high transport group may be the result of our strict salt restriction policy.

High transporters will have greater peritoneal losses of protein [26]. Other markers of a poor prognosis such as hypoalbuminemia [27] and elevated inflammatory markers [28] are also more common in higher transport groups. Factors like these may play a role in the higher rate of adverse outcomes observed in high transporters [26]. Our high transporters had similar serum albumin levels at initiation of PD compared to other groups. Albumin level decreased significantly afterwards. We could not measure amount of peritoneal protein loss so we cannot speculate its effect on hypoalbuminemia. It can be said that high transport patients with hypoalbuminemia at initiation of PD may face with further decreases in albumin levels to the level that it may affect their mortality.

The leading cause of death and transfer to HD was peritonitis/sepsis in our study. The rates of both conditions were similar in groups. However, high transporters had more often peritonitis and catheter exit site infections. Some factors were found to increase peritonitis risk. A meta-analysis found that non-modifiable peritonitis risk factors were ethnicity, female gender, chronic lung disease, coronary artery disease, congestive heart failure, cardiovascular disease, hypertension, antihepatitis C virus antibody positivity, diabetes mellitus, lupus nephritis or glomerulonephritis as underlying renal disease, no residual renal function while modifiable ones were malnutrition, overweight, smoking, immunosuppression, no use of oral active vitamin D, psychosocial factors, low socioeconomic status, PD against patient's choice, and hemodialysis as former modality [29]. We showed that in high transport group, presence of someone to perform PD was more likely and also percentage of patients performing PD due to vascular problems were more common than in the other transport groups. These factors may enlighten the increased peritonitis incidence in high transport group.

The single-center Stroke PD study [11,30] and the multicenter CANUSA study [5] found that high transport was associated with worse technique survival independent of other important risk factors, such as age, comorbidities, and residual renal function. A meta-analysis of 20 observational studies [31] also demonstrated that a higher peritoneal membrane solute transport rate was associated with a trend to higher technique failure. The 2-yr probabilities of technique survival were increased in high transporters [5]. Another study showed that cumulative combined technique survival at the end of 1, 3, and 5 yr were 76%, 57%, and 16% for high transport group, and 83%, 66%, and 30% for non-high group. There were no significant differences in the risk of either technique failure between patients in two transport groups [20]. This study revealed worse technique survival in high transport group and technique survival rate was 95.7%, 53.3%, and 20% at 1, 3, and 5 years, respectively.

The most significant limitation of this study is its retrospective design. In addition, changes in transport status of peritoneal membrane as the times passes can not be considered. Sum of renal and peritoneal clearances were given, unfortunately the summands were not known separately. Amount of protein loss from urine and peritoneal fluid could not be assessed and hence presence of any possible effect on serum albumin level could not be predicted.

## Conclusions

In conclusion, it was shown that high transporters had worse patient and technique survival. Infectious complications were also more frequent in this group. Mortality was higher in patients with advanced age, hypoalbumine-

mia at initiation of PD, decreased amount of daily urine volume, frequent catheter infections. Transfer to HD can be an option in high transport patients if they have hypoalbuminemia, frequent infectious complications and no urine output.

*Conflict of interest statement.* None declared.

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