A Longitudinal Change of Peritoneal Equilibration Test Results in Peritoneal Dialysis Patients Aged 60 Years and above: A 4-year Observation Study in Comparison with A Younger Group

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Background: The number of elderly people with end-stage renal disease has grown in developed countries and medical teams now face the choice of dialysis therapy in elderly patients. In the present study, we retrospectively analyzed two peritoneal dialysis (PD) patients, of different ages, who were treated at the same unit by the same PD team of doctors and nurses. Our purpose was to study peritoneal membrane changes in elderly and younger PD patients.

Methods: 108 patients above 60 years of age or younger at the start of dialysis, were separated into two cohorts. Diabetic patients were excluded. Peritoneal equilibration test (PET) results taken over 4 continuous years were compared between the two groups.

Results: No significant differences were seen between the two groups in peritoneal transport (D/P Cr, D/D_0 glucose) during the 4-year observation. Total Kt/V and renal creatinine clearance (Ccr) values in the 4-year period were not significantly different between the two groups. Renal Ccr values showed a longitudinal decline in the two groups but the values of total Kt/V revealed a consistency over the 4-year period.

Conclusion: Elderly PD patients demonstrated a similar peritoneal permeability to younger PD patients based on a 4-year PET.
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Key words: peritoneal dialysis, peritoneal equilibration test

The number of elderly people of end-stage renal disease has grown in developed countries. When medical teams faced the choice of dialysis therapy in elderly patients, peritoneal dialysis (PD) was frequently considered because of a better preservation of residual renal function, avoidance of large volume and electrolyte shifts, better cardiovascular stability and unnecessary vascular access.[1] Similar survival and an equal or better quality of life in the elderly compared to their younger counterparts have been

shown.[2-5] The mortality and hospitalization rates were also similar. But most reports dealing with elderly patients were limited to peritonitis rates, survival rates and complications. Although the dialysis function of the peritoneal membrane is critical for long-term survival of PD therapy, few reports were available regarding peritoneal membrane changes. Vecchi et al observed stable urea D/P 4 hr levels and a non-significant decline in Kt/V levels in non-diabetic patients above 70 years of age for a 3-year period.[2] Alicja E et al observed mean aged 67 year-old peritoneal dialysis patients for 20 months, and found declined D/P Cr (4 hr) and stable D/D_0 glucose (4 hr) levels.[6] In the present study, we retrospectively analyzed two different ages of PD patients treated at the same unit by the same PD team of doctors and nurses. Our purpose was to study peritoneal membrane changes in elderly and younger PD patients. We hypothesized that a physiologically aged peritoneum may influence the solute transport characteristics of chronic PD patients.

METHODS

From Jan 1992-June 2006, we had 405 continuous ambulatory peritoneal dialysis (CAPD) patients (161 male, 244 female) in our PD unit. We enrolled patients who commenced PD therapy at an age of ≥ 60 years old and < 60 years old. The exclusion criteria were diabetic patients and patients who had had a peritonitis episode two months prior to a peritoneal equilibrium test (PET). Finally, a total of 108 PD patients were included for study. The ≥ 60-year-old group, was composed of 14 patients, 9 male, 5 female, the mean age of PD commence was 65 years old (range 60-75), and the mean PD duration was 69 months. The < 60- year- old group, consisted of 29 male, 65 female, the mean age of PD commence was 37 years old (range 20-49), and the mean PD duration 71 months. The causes of end-stage renal disease are shown in Table 1. All patients were dialyzed with commercially available dialysate (Dianeal PD solution, Baxter, Singapore) with a continuous ambulatory peritoneal dialysis (CAPD) regimen. Peritoneal transport was measured by standard PET (Table 2).[7] An initial PET was performed 2 months after patients had commenced CAPD, and then repeated once per year. When a peritonitis episode occurred, PET was followed up at least 2 months

Table 1. The Causes of End-stage Renal Disease

	Group 1, n = 14 (age ≥ 60)	Group 2, n = 94 (age < 60)
Chronic GN	9	78
Polycystic kidney disease	1	7
Lupus nephritis	1	7
Hypertension	3	4
Gouty nephropathy	–	1
IgA nephropathy	–	1
Interstitial nephritis	–	2

Abbreviation: GN: Glomerulonephritis

Table 2. Standard PET Procedure

(1) After an overnight exchange of an 8- to 12-h dwell, 2L of a 2.5% glucose concentration solution is instilled and allowed to dwell for 4 h.

(2) Several times during the dwell, the patient is requested to roll from side to side.

(3) Dialysate urea, glucose, sodium, and creatinine are measured at 0, 2 and 4 h.

(4) A blood sample is taken after 2 h.

(5) The drain bag is measured to assess both drain and net UF volume.

(6) Dialysate-to-plasma ratios (D/P) are calculated for creatinine, urea, and sodium at 0,2 and 4 h.

(7) The ratio of glucose at drain time to the dialysate glucose concentration at time zero (Dt/D0) is measured.

Adapted from Twardowski et al, 1987.[7]

after the peritonitis episode had subsided. The PET used 2 L of 2.27% glucose concentration 2-L volume exchange. Samples were drawn at 0, 2, 4 hours and the blood sample was drawn at 2 hours. The subgroups were categorized by dialysate to plasma creatinine (D/P Cr) levels at 4 hours to high (H) > 0.81, high-average (HA) 0.65 to 0.81, low-average (LA) 0.5 to 0.65, low (L) < 0.5. Residual renal function (Renal Ccr) was calculated from the 24-hour urinary clearance by direct measurement of creatinine in the urine. Total weekly Kt/V (total Kt/V) was the sum of dialysate and renal urea clearance by measurement of urea from a 24-hour urinary collection and dialysate

exchange. The volume of distribution for urea was calculated from the Watson formula. The parameters of PET for four continuous years were analyzed in the two groups. The comparable variables were D/P Cr levels at 0, 2, 4 hours, the ratio between the glucose level in the dialysate effluent and that in the infused dialysate at 2, 4 hour (D/D$_0$ glucose), total Kt/V and renal Ccr. Data of biochemistry, hemogram, and peritoneal glucose exposure in daily PD regimen in the first and fourth year were also compared. Peritoneal glucose exposure was obtained by calculating the number of Dianeal PD solution exchanges multiplied by their concentration as Davies proposed.[8] Biochemistry data were measured with commercial kits with an autoanalyzer (Hitachi 7600.210, Hitachi, Ltd., Tokyo, Japan). Albumin was measured with the bromocresol green method. Creatinine levels were corrected for glucose interference with a factor established at the central laboratory. Intact parathyroid hormone (i-PTH) was measured with an immunoradiometric assay (Nichols Institute Diagnostics, California U.S.A.). Body surface area was determined by a monogram based on body weight and height.[9] Data management was performed by SPSS® (Version 10.0.7, Chicago, IL, U.S.A.). Parametric data are presented as mean values ± standard deviation. ANOVA or the Students t test was used to compare parameters between groups. Sequential data among the same group of patients were analyzed using one-way repeated-measures ANOVA. A modified Bonferroni procedure was used for each pairwise comparison. A value of $p < 0.05$ was considered statistically significant.

RESULTS

Initial peritoneal membrane transport categories were H 1/14, HA 7/14, LA 5/14, L 1/14 in elder patients, and H 4/94, HA 32/94, LA 52/94, L 6/94 in younger patients. In elderly patients, D/P Cr at 2 hours showed a significant decline in the 4th year, but D/P Cr at 4 hours did not show significant change when the levels were compared between the 1st and 4th years. In contrast, both D/P Cr at 2 and 4 hours in younger patients revealed a significant decline in the 4th year as compared to the 1st year (Fig. 1).

The D/D0 glucose levels at 2 and 4 hours in both groups were similar when PD therapy commenced. The levels increased in the second year and

remained stable in the subsequent 2 years in both groups (Fig. 2).

The residual renal function showed a significant decline in both groups in the 4-year period (Fig. 3). The adequacy index, Kt/V was maintained in the study period in both groups (Fig. 4).

There were no significant differences between both groups in terms of serum albumin, glucose, calcium, phosphate and hemoglobin levels in the first and fourth years. In younger PD patients, there were
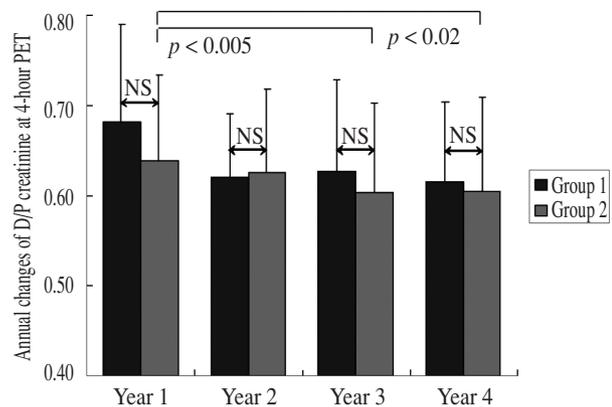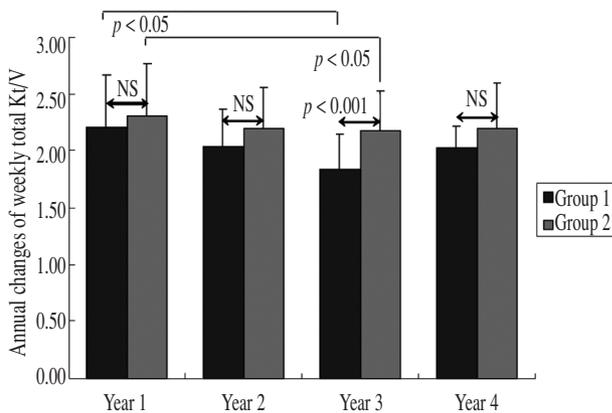

Fig. 1 Annual changes of D/P creatinine ratio at 4-h PET. Statistics: ANOVA between groups and One-Way Repeated-Measures ANOVA among sequential data at the same group of patients. A modified Bonferroni procedure was used for each pairwise comparison. Among group 1, $p = 0.162$; group 2, $p < 0.001$. Data represent the mean ± standard deviation.
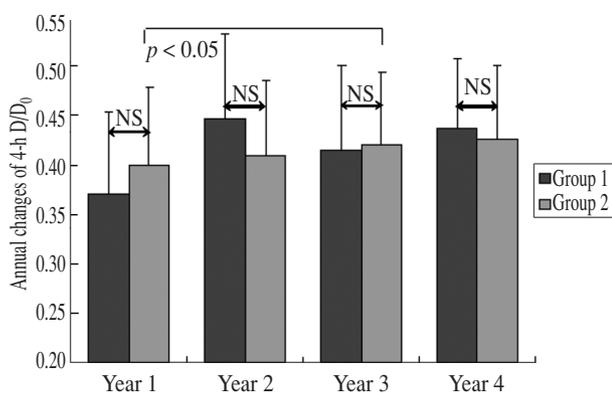
Fig. 2 Annual changes of PET 4-h D/D$_0$. Statistics: ANOVA between groups and One-Way Repeated-Measures ANOVA among sequential data at the same group of patients. A modified Bonferroni procedure was used for each pairwise comparison. Among group 1, $p = 0.944$; group 2, $p < 0.001$. Data represent the mean ± standard deviation.
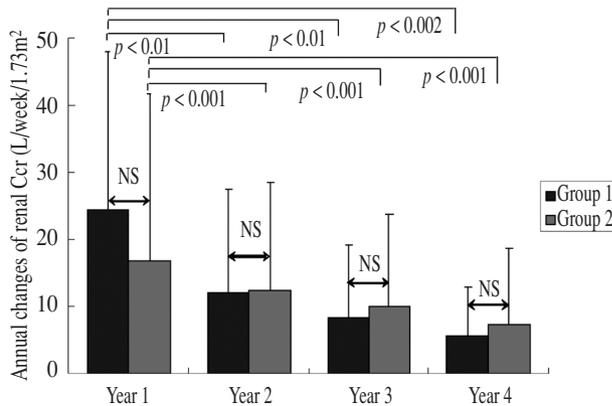
Fig. 3 Annual changes of renal Ccr. Statistics: ANOVA between groups and One-Way Repeated-Measures ANOVA among sequential data at the same group of patients. A modified Bonferroni procedure was used for each pairwise comparison. Among group 1, $p < 0.005$; group 2, $p < 0.001$. Data represent the mean $\pm$ standard deviation.

Fig. 4 Annual changes of weekly total Kt/V. Statistics: ANOVA between groups and One-Way Repeated-Measures ANOVA among sequential data at the same group of patients. A modified Bonferroni procedure was used for each pairwise comparison. Among group 1, $p = 0.698$; group 2, $p < 0.002$. Data represent the mean $\pm$ standard deviation.

higher serum glucose levels than elderly PD patients although not statistically significant. But two patients in the younger group developed diabetes in the study period. The i-PTH levels were higher in elderly PD patients than younger PD patients although this was only significant in the first year. Glucose exposure was higher in younger PD patients than elderly patients in the first year ($p = 0.021$), but this differ-

ence disappeared in the fourth year (Table 3).

The peritonitis rate was 1/112.0 patients-month in elderly patients, 1/60.2 patients-month in younger patients (Table 3).

DISCUSSION

Our PD patients were followed-up for four years, the small-molecular weight solute transport, indexed by D/P Cr at four hours, did not show a significant decline in elderly PD patients. This result was similar to what Vecchi et al reported in their 3-year observation in elderly PD patients.[2] But it was

Table 3. First and Fourth Year's Laboratory Data and Peritoneal Glucose Exposure

	Group 1 (n:14)	Group 2 (n:94)	p
Alb-1 (g/dl)	3.80 ± 0.46	3.71 ± 0.32	0.335
Glu-1 (mg/dl)	96.82 ± 14.39	107.73 ± 20.93	0.072
Ca-1 (mg/dl)	8.97 ± 0.88	9.13 ± 1.23	0.622
P-1 (mg/dl)	5.10 ± 1.69	4.70 ± 1.23	0.383
Hb-1 (g/dl)	8.82 ± 1.53	8.55 ± 1.67	0.550
Hct-1 (%)	26.61 ± 4.90	26.91 ± 5.67	0.836
iPTH-1 (pg/ml)	410.65 ± 340.30	203.27 ± 226.11	0.009
Glu-D-1 (mg/dl)	6.60 ± 1.05	7.35 ± 1.37	0.021
Alb-4 (g/dl)	3.71 ± 0.50	3.38 ± 0.61	0.032
Glu-4 (mg/dl)	91.88 ± 11.32	134.93 ± 81.84	0.061
Ca-4 (mg/dl)	9.52 ± 0.95	9.49 ± 0.79	0.864
P-4 (mg/dl)	5.81 ± 1.76	4.89 ± 0.98	0.009
Hb-4 (g/dl)	8.63 ± 1.54	8.73 ± 1.66	0.820
Hct-4 (%)	25.72 ± 4.84	24.94 ± 7.84	0.715
iPTH-4 (pg/ml)	407.29 ± 453.77	258.94 ± 338.77	0.236
Glu-D-4 (mg/dl)	7.18 ± 1.72	6.93 ± 1.43	0.598
BSA (m²)	1.53 ± 0.16	1.56 ± 0.14	0.515
Peritonitis episode (per patient-month)	1/112.0	1/60.2	0.001

Abbreviations: -1: first year; -4: fourth year; Alb: serum albumin; Glu: serum glucose; Glu-D: sum of peritoneal glucose exposure; BSA: body surface area.
Data shown mean $\pm$ SD.
Statistics: Student-t test.

contrary to Alicja et al who reported that solute transport declined in a 20-month observation in elderly PD patients.[6] The age of our patients was similar to the patients' age of the Alicja series, but the period of observation was longer in our series. In a previous 7-year study of peritonitis-free CAPD patients, D/P Cr at 4 hour PET had a natural declining trend.[10] Our observation duration was only 4 years and was limited to a small cohort of elderly PD patients. That might be a plausible reason for our different results.

In the previous studies, the influence of the peritonitis episode on solute transport was complex and heterogeneous.[11-13] In general, recurrences or clusters of infection caused an increase in D/P Cr, whereas a single peritonitis episode had no significant effect on D/P Cr. In our previous report, peritonitis episodes might have caused a decline in solute transport function.[12] In the present study, elderly patients did not have recurrent or cluster peritonitis episodes and they had longer peritonitis-free periods than younger patients. This seemed to contribute to the constant change of D/P Cr in the study period.

In the present study, the opposite direction of peritoneal transport, indexed by D/D_0 glucose at 4 hours, showed significant increase in the second year but the change remained stable in the subsequent years. Alicja et al reported that elderly patients could have a stable D/D_0 glucose at 4 hours in a 20-month duration.[6] From an observation of the natural change of PET, it also showed a stable D/D_0 glucose at 4 hours in a 7-year duration.[10] Our results were in agreement with the observations in the above cited studies.

From the observation of gender difference, men tended to have higher solute transport than women which was explained by their larger body size.[14] Body surface area was similar in our elderly and younger patients. We therefore thought body size was not an influencing factor on solute transport in our PD patients.

In the study by Johansson et al, elderly patients had a greater large-pore flow and lower ultrafiltration coefficient than younger patients when they commenced PD therapy, and the peritoneal membrane function remained stable during the 39-month PD therapy.[15] Our elderly patients had higher D/P Cr levels than younger patients when they began PD therapy. This trend remained in the 4-year period. In

contrast, the comparison of D/D_0 glucose levels had a heterogeneous distribution. Our result was different to the report from Vecchi et al, where they demonstrated similar peritoneal permeability between the two groups.[2] We thought a larger number of patients and a longer observation period were needed to further clarify this issue.

Davies demonstrated that early exposure to a higher intraperitoneal glucose concentration would result in a disproportional deterioration in ultrafiltration capacity.[8] Our elderly patients had lower residual renal function than younger patients in the beginning of PD therapy. This resulted in an increased peritoneal glucose exposure in elderly patients after a 4-year PD therapy. But even so, our patients did not develop ultrafiltration failure during the 4-year treatment. This result was comparable to the study from Johansson.[15] Our younger patients had a higher peritoneal glucose exposure than elderly patients when they commenced PD therapy, but the difference disappeared in the fourth year. Our two groups had a similar decline in their residual renal function. This result was similar to the report from Vecchi.[2] Age-related peritoneum change is still a concern in long-term PD therapy and warrants further investigation in the future.

In conclusion, the PET results demonstrated a centralization migration in both elderly and younger PD patients in a comparable period. Elderly PD patients can maintain a stable peritoneal solute transport in a 4-year period. The longer observation was warranted for further evaluation peritoneal membrane function in elderly PD patients.

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腹膜功能在 60 歲以上腹膜透析患者的變化：
與年輕族群比較，四年的觀察報告

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背　景： 在已開發國家，老年末期腎病患者的比例日益升高，因此醫療團體也面臨年老患者選擇腎臟替代療法所考量的問題，本文目的在研究老年及年輕腹膜透析患者，兩族群腹膜功能變化的差異。

方　法： 針對高雄長庚醫院在 1992 年 1 月至 2006 年 6 月期間，108 位非糖尿病的腹膜透析患者，分為 60 歲以上及 60 歲以下兩族群，觀察 4 年內一連串腹膜功能的變化。

結　果： 觀察 4 年發現，兩族群腹膜功能 (D/P Cr, D/D_0 glucose) 無顯著差異。兩族群的腎臟肌酸酐廓清率 (Ccr) 在 4 年內皆逐年下降，但同時兩族群腹膜的廓清力 (Kt/V) 及殘存腎功能 (Ccr)，在 4 年內亦無顯著差異。

結　論： 根據 4 年的腹膜功能試驗顯示，老年腹膜透析患者的腹膜通透性與年輕腹膜透析患者類似。

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關鍵詞： 腹膜透析，腹膜功能試驗