CLINICAL OUTCOMES OF PERITONEAL DIALYSIS PATIENTS TRANSFERRED FROM HEMODIALYSIS: A MATCHED CASE-CONTROL STUDY

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♦ **Objective:** Our study aimed to evaluate clinical outcomes of patients transferred to peritoneal dialysis (PD) because of complications related to hemodialysis (HD).

♦ **Methods:** In a 1:2 matched case-control study, we compared patient and technique survival between patients initially treated with HD for at least 3 months and then transferred to PD (transfer group) and patients started on and continuing with PD (no-transfer group).

♦ **Results:** All baseline characteristics except for initial residual urinary output were comparable between the groups. Compared with patients in the transfer group, patients in the no-transfer group had a higher initial daily residual urinary output [850 mL (range: 600 – 1250 mL) vs 0 mL (range: 0 – 775 mL/d), $p = 0.000$]. The main reasons for transfer to PD were vascular access problems and cardiovascular disease. Patient survival and technique failure rates did not significantly differ between the groups ($p > 0.05$). The 1-, 3-, and 5-year patient survival rates were 80.0%, 53.7%, and 27.6% in the transfer group and 89.7%, 60.2%, and 43.1% in the no-transfer group. Age (per 10 years) and serum albumin were independent risk factors for long-term survival in PD patients. Relative risk of either death or technique failure was not significantly increased in patients transferred from HD.

♦ **Conclusions:** Patients who transferred to PD after failing HD had outcomes on PD similar to those for patients who started with and were maintained on PD. Age (per 10 years) and serum albumin were independent risk factors for long-term survival in PD patients.

KEY WORDS: Case-control study; hemodialysis; outcome; transfer.

Hemodialysis (HD) and peritoneal dialysis (PD) are different but valuable modalities of renal replacement therapy (RRT) for patients with end-stage renal disease (ESRD). Early reports on comparative mortality in HD and PD were inconsistent (1,2). More recent evidence has indicated that overall patient survival rates in PD and HD are similar (3,4), although PD has a survival advantage in the first 2 years of dialysis, especially in diabetic and older patients (2,5). Furthermore, it is generally recognized that the clinical course of dialysis in a patient with ESRD is not limited to a single modality. It is reported that about 10% – 20% of PD patients annually may transfer to HD because of technique failure (6). And in many PD centers, a significant percentage of patients, ranging from 15% to 25%, have been transferred from HD (6–8). Any timely transfer between modalities would be expected to improve the survival rate of ESRD patients (9,10).

In the model of dialysis, the effect on survival outcomes of initial dialysis modality and of modality switches is infrequently reported and not well-defined. Previous studies have shown no significant differences in hospitalization or uremic symptoms between HD patients and those transferred from HD to PD (11). The survival rate was also reported to be higher in integrated care patients than in PD patients (12). However, only a few reports in the literature have so far assessed rates of overall survival and technique success in patients after transfer from HD to PD, and the influence of initial dialysis modality on prognosis is unclear.

In the present matched case-control study, we retrospectively compared patient and technique survival for PD patients transferred from initial HD to PD and for patients who started with and remained on PD.

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METHODS

PATIENTS

All patients who received PD treatment in our unit between June 2002 and June 2007 were screened for the study. The patients included were those at least 18 years of age who had been closely followed, who had intact clinical records, and who had survived for at least 6 months after starting RRT. Patients were excluded if they had been on PD therapy for less than 3 months, had transferred between dialysis modalities two or more times, or had undergone transplantation. Eligible patients were divided into two groups: a transfer group (patients initially treated with HD for at least 3 months and then transferred to PD) and a no-transfer group (patients started on and continuing with PD). Because transfer from HD to PD was rare and the number of transfer patients was small at our center, we conducted a matched case-control study to identify risk factors for clinical outcome in PD patients transferred from HD. The ratio of the transfer group to the no-transfer group was 1:2. The patients were matched for age, sex, primary renal disease, and cardiovascular disease. The recruited patients were followed from the start of PD therapy until 30 June 2009.

DATA COLLECTION

In a review of clinical records, the following patient data were collected: demographic details, underlying cause of ESRD, initial modality of dialysis, date of first dialysis, causes of modality transfer, general information about PD therapy and dialysis prescription, presence and duration of diabetes, presence or history of hypertension, residual urinary output, biochemical data, and patient outcome. Baseline biochemical data collected included hemoglobin, serum albumin, total cholesterol, triglycerides, corrected (for protein) serum calcium, and phosphate.

Clinical outcomes in the present study included actuarial patient and technique survival. In the patient survival analysis, only death was considered a final event. Transplantation was censored. If a patient died within 60 days after transfer to HD, the death was attributed to PD. Technique survival was defined as the percentage of patients who remained alive and on PD therapy (13). For both of the foregoing outcomes, survival was calculated from the date of commencement of PD therapy to the date of death, transfer to HD, transplantation, recovered renal function, loss to follow-up, or 30 June 2009. Cardiovascular disease was defined as the presence of one or more definite manifestations of coronary

artery disease (angina pectoris, coronary insufficiency, myocardial infarction, and sudden or non-sudden death as consequence of coronary disease), congestive heart failure, stroke, transient ischemic attack, and intermittent claudication (14).

STATISTICAL ANALYSIS

Continuous data are expressed as mean $\pm$ standard deviation or median and interquartile range (IQR), and categorical data are expressed as frequencies and percentages. Demographic characteristics were compared using the Student t-test or Wilcoxon rank sum test for continuous data and the chi-square test for categorical data. Univariate Cox proportional hazards regression was applied to estimate the individual odds for patient death, which are expressed as hazard ratios (HRs) with 95% confidence intervals (CIs). The significant variables ($p < 0.05$) in the univariate analysis were put into a final multivariate Cox model. Stepwise regression, with adjustment for confounders, was used to identify factors that predicted death. The survival curves were generated using Kaplan-Meier survival analysis, and the log-rank test was used to test differences in predicted mortality in the final Cox proportional hazards regression model. All statistical assessments were two-sided and evaluated at the 0.05 level of significant difference. The analyses were performed using the SPSS statistics software (version 15.0: SPSS, Chicago, IL, USA).

RESULTS

BASELINE CHARACTERISTICS OF THE PATIENTS

We screened 475 patients for the study, of whom 33 (6.95%) were transferred from HD and 442 (93.05%) were started on and continued with PD. From among the 442 patients, 66 matching the transferred patients were selected. Tables 1 and 2 set out the baseline demographic and clinical characteristics of the patients in the two groups. The groups were well matched in terms of age, sex, time of PD follow-up [median: 17 months vs 18 months (IQR: 9 – 41 months vs 10 – 31 months), $p = 0.973$], ratio of diabetes as the underlying disease, and body mass index (20.14 ± 2.67 kg/m² vs 21.55 ± 3.47 kg/m², $p = 0.077$). No significant differences between the groups were observed in comorbidities at the start of PD therapy, including diabetes and cardiovascular diseases. However, compared with the no-transfer group, the transfer group was characterized by a significantly lower initial daily residual urinary output [0 mL vs 850 mL (IQR: 0 – 775 mL vs

TABLE 1
Baseline Demographic Characteristics^a of the Dialysis Patients

Characteristic	Transfer group (n=33)	No-transfer group (n=66)	p Value
Age (years) ^b	65 (52–69)	64 (49–70)	0.849
Sex [n (%) men] ^c	28 (42.4)	28 (45.4)	0.774
PD follow-up (months) ^b	17 (9–41)	18 (10–31)	0.937
Cause of renal failure [n (%)] ^c			0.660
Diabetes	10 (30.3)	23 (34.8)	
Glomerulonephritis	13 (39.4)	26 (39.4)	
Hypertension	7 (21.2)	15 (22.7)	
Others	3 (9.1)	2 (3.0)	
Body mass index (kg/m ²) ^d	20.4±2.7	22.5±3.8	0.077
Comorbidities [n (%)] ^c			
Diabetes	13 (39.4)	27 (40.9)	0.885
Cardiovascular disease	7 (21.2)	11 (16.7)	0.580

^a Continuous data are expressed as mean ± standard deviation or median (interquartile range). Categorical data are expressed as frequency and percentage.

^b By Wilcoxon rank sum test.

^c By chi-square test.

^d By Student t-test.

TABLE 2
Baseline Clinical Characteristics^a of the Dialysis Patients

Characteristic	Transfer group (n=33)	No-transfer group (n=66)	p Value
Hemoglobin (g/L) ^b	95.0±18.8	92.1±17.9	0.453
Serum albumin (g/L) ^b	36.8±5.5	35.9±5.4	0.496
Potassium (mmol/L) ^c	3.5 (3.1–3.9)	3.9 (3.5–4.3)	0.027
Sodium (mmol/L) ^c	140.0 (137.9–142.2)	140.4 (138.0–141.8)	0.818
Chlorine (mmol/L) ^b	100.9 (98.6–103.9)	102.2 (99.7–105.0)	0.242
Total cholesterol (mmol/L) ^c	4.8 (3.9–5.7)	5.0 (4.5–5.8)	0.325
Triglycerides (mmol/L) ^c	1.7 (1.1–2.5)	1.5 (1.2–2.2)	0.613
High-density lipoprotein (mmol/L) ^c	1.1 (0.9–1.3)	1.2 (0.9–1.4)	0.323
Low-density lipoprotein (mmol/L) ^c	2.4 (1.9–3.2)	2.6 (2.2–3.3)	0.351
Ca×P product (mg ² /dL ²) ^c	44.6 (37.3–58.1)	42.1 (35.5–50.7)	0.354
Intact PTH (pg/mL) ^c	195.7 (150.3–376.9)	236.8 (88.8–420.6)	0.663
Residual urinary output (mL/d) ^c	0 (0–775)	750 (600–1250)	0.002

PTH = parathyroid hormone.

^a Continuous data are expressed as mean ± standard deviation or median (interquartile range).

^b By Student t-test.

^c By Wilcoxon rank-sum test.

600 – 1250 mL), $p < 0.001$]. There were no significant differences between the groups with regard to other patient characteristics at the start of PD therapy. The reasons for transfer from HD to PD were cardiovascular disease (45.45%), vascular access problems (24.24%), patient choice (15.15%), and others (15.15%). The cardiovascular problems that were the main

cause of transfer in chronic HD patients included systemic hypotension (2 of 15, 13.33%), intradialytic hypotension (4 of 15, 26.67%), heart failure (3 of 15, 20%), ischemic heart disease (5 of 15, 33.33%), arrhythmia (4 of 15, 26.67%), and other unacceptable symptoms (5 of 15, 33.33%). The median time on HD before transfer to PD was 7 months (range: 3 – 187 months).

PATIENT SURVIVAL

Of the 99 patients, 35 (35.4%) died and 64 (64.6%) survived during follow-up, with the mean survival time being 49.5 months (95% CI: 39.7 to 59.3 months). For transfer and no-transfer patients, the mean survival time was 42.7 months and 54.5 months respectively. Figure 1 shows the associated Kaplan–Meier survival curve. The cumulative survival rate during 7 years of follow-up was not significantly different between the no-transfer and transfer groups ($p = 0.278$). The overall survival rates at 1, 3, and 5 years were 80.0%, 53.7%, and 27.6% in the transfer group, and 89.7%, 60.2%, and 43.1% in the no-transfer group. The main causes of death in the 35 patients who died were cardiovascular disease (57.1%) and infection (34.3%). Table 3 shows the causes of death for patients in the two groups.

TECHNIQUE SURVIVAL

The overall mean expected technique survival was 47.3 months (95% CI: 37.8 to 56.7 months). The mean expected technique survival was 38.6 months in the transfer group and 53.5 months in the no-transfer group. The cumulative technique survival rates for years 1, 3, and 5 were 74.2%, 41.1%, and 18.1% in the transfer group and 86.4%, 56.3%, and 36.0% in the no-transfer group (Figure 2), which did not differ

significantly between the groups ($p = 0.076$). The major reasons for technique failure were death and peritonitis. In the transfer group, 8 patients (11 episodes) and, in the no-transfer group, 13 patients (17 episodes) experienced peritonitis during follow-up, which did not differ significantly between the groups ($p = 0.602$). The mean duration from PD start to the development of peritonitis was 18.43 ± 11.75 months.

TABLE 3
Causes of Death in the Two Groups

Characteristic	Transfer group (n=33)	No-transfer group (n=66)	p Value
Death ^a	15	20	0.137
Cardiovascular disease ^a	8	9	0.940
Coronary artery disease	4	2	
Congestive heart failure	2	5	
Stroke	2	2	
Infection ^b	4	8	0.489
Severe malnutrition ^b	1	0	0.429
Malignant disease ^b	0	2	0.496
Other (for example, treatment withdrawal) ^b	2	1	0.565

^a By Pearson chi-square test.

^b By Fisher exact test.

Patients at risk, n

Non-transfer group	66	39	20	10	5	4	3	2	1
Transfer group	33	18	11	7	5	2	1	0	0

Figure 1 — Kaplan–Meier survival analysis of survival status, comparing cumulative survival rate (survival time, months) based on hemodialysis groups (transfer and no-transfer). The 1-, 3-, and 5-year survival rates were 89.7%, 60.2%, and 43.1% in the no-transfer group, and 80.0%, 53.7%, and 27.6% in the transfer group. The cumulative survival between did not reach significance between the groups (log-rank $p = 0.278$).

Patients at risk, n

Non-transfer group	66	39	20	11	5	4	3	2	1
Transfer group	33	19	11	8	5	2	1	0	0

Figure 2 — Kaplan–Meier survival analysis of technique status (failure or success), comparing cumulative survival rates (survival time, months) based on hemodialysis groups (transfer and no-transfer). The 1-, 3-, and 5-year survival rates were 86.4%, 56.3%, and 36.0% in the no-transfer group, and 74.2%, 41.1%, and 18.1% in the transfer group. The cumulative survival rate did not reach significance between the groups (log-rank $p = 0.076$).

RISK FACTORS FOR PD PATIENT SURVIVAL AND TECHNIQUE SURVIVAL

Table 4 shows the univariate Cox proportional hazards analysis for patient survival based on each potential risk factor. Age (per 10 years), Ca×P product, serum albumin, and high-density lipoprotein were identified as significant factors ($p < 0.05$). Table 5 shows the results of the multivariate Cox proportional hazards regression analysis, which evaluated factors that predicted death. For each 10 years of age, the HR for death increased by a factor of 1.08 (95% CI: 1.04 to 1.15; $p < 0.001$). In addition, patients with a higher serum albumin had a lower HR for death. These results suggest that patient age (per 10 years) and low serum albumin are independent predictors of survival in long-term PD patients. However, compared with the no-transfer group, the relative risk of death was not significantly greater in patients transferred from HD. None of the included variables significantly influenced technique survival (data not shown).

DISCUSSION

Although the number of patients transferring to PD after HD failure is growing, little is known about clinical outcomes in those patients. The present matched case-control study assessed patient and technique survival in patients transferred from HD to PD and in patients who started and remained on PD at our unit between June 2002 and June 2007. The data show that the two populations experienced similar actual patient and technique survival. Patient age (per 10 years) and low serum albumin were independent predictors of mortality risk in long-term PD patients. The relative risks of death and technique failure were not significantly increased in patients transferred from HD compared with patients starting and remaining on PD.

It is generally believed that integrated dialysis care (transfer between HD and PD after a failed RRT) increases patient survival (8,11). During their time on dialysis, patients with ESRD will most likely be treated with more than one RRT modality. Selection of the first RRT modality should be based on a strategy that optimizes the use of each treatment modality. More importantly, the HD and PD modalities are more complementary than competitive. Previously, several studies showed that patient survival was improved by timely transfer to HD of patients experiencing problems on PD (11,15). Although only a few published studies have compared outcomes in PD patients transferred from HD with outcomes of patients starting and remaining on PD, discrepancies can be seen in the findings (6,7,16–19).

TABLE 4
Univariate Analyses for Factors Influencing Survival Among Patients by Cox Proportional Hazards Regression

Characteristic	HR	95% CI	p Value
Age (each 10 years)	1.08	1.04 to 1.13	<0.001
Male sex	1.28	0.65 to 2.52	0.475
Body mass index (kg/m ²)	1.03	0.89 to 1.19	0.684
Diabetes	1.51	0.77 to 2.97	0.232
Transfer	1.35	0.69 to 2.18	0.383
Hemoglobin (g/L)	0.98	0.96 to 1.00	0.042
Potassium (mmol/L)	1.07	0.58 to 1.95	0.837
Ca×P product (mg ² /dL ²)	0.97	0.95 to 0.99	0.031
Intact PTH (pg/mL)	0.99	0.99 to 1.00	0.427
Serum albumin (g/L)	0.95	0.89 to 1.00	0.057
Total cholesterol (mmol/L)	0.77	0.56 to 1.06	0.104
Triglycerides (mmol/L)	0.94	0.72 to 1.23	0.673
Low-density lipoprotein (mmol/L)	0.83	0.53 to 1.30	0.417
High-density lipoprotein (mmol/L)	0.27	0.09 to 0.85	0.026
Residual urinary output (mL/d)	1.00	0.99 to 1.00	0.926
Cardiovascular disease	1.01	0.36 to 2.90	0.979

HR = hazard ratio; CI = confidence interval; PTH = parathyroid hormone.

TABLE 5
Multivariate Analyses for Factors Influencing Survival Among Patients by Cox Proportional Hazards Regression

Characteristic	HR	95% CI	p Value
Age (each 10 years)	1.08	1.04 to 1.15	<0.001
Serum albumin (g/L)	0.92	0.85 to 1.00	0.040

HR = hazard ratio; CI = confidence interval.

Earlier studies on patient survival suggested that patients transferred from HD to PD had a poor clinical outcome (6,7,16–18). Furthermore, transfer to PD from HD was found to predict mortality (16). However, our findings are in line with a recent study (19) showing a nonsignificant difference in patient survival between transfer and no-transfer groups. These conflicting observations might be explained by differences in study design, an unsatisfactory match in the demographic and clinical characteristics of patients, or an unmatched sample size between the transfer and no-transfer groups. Our matched case-control study may therefore have reduced patient-to-patient outcome variability.

Our study also suggests that technique survival in transfer and no-transfer patients was similar. That finding is consistent with a previously reported study (6); however, other investigations revealed that technique survival was lower in transferred patients (18,19). Whether a history of HD therapy can or cannot influence peritoneal membrane function is still beyond our knowledge, but some evidence still indirectly favors our results to some extent. It has been well proved that peritoneal transport characteristics are closely associated with death and technique failure in PD patients (20,21). In addition, a large-scale study from the Australia and New Zealand Dialysis and Transplant Registry indicated that previous HD therapy is not predictive of either increased peritoneal transport category or dialysate-to-plasma ratio of creatinine at 4 hours (22). Those studies may explain the lack of a definite relationship between HD history and technique survival in PD patients.

Advanced age and lower serum album have been associated with decreased survival in dialysis patients (4,10). Elderly patients might have more comorbid conditions, including diabetes and cardiovascular and cerebrovascular diseases, the development of which might also be potentiated by hypoalbuminemia. In that respect, low serum albumin has been reported to be associated with increased oxidative stress, endothelial dysfunction, and the malnutrition-inflammation complex syndrome (23–25). Our univariate analysis also suggests that low albumin is an independent predictor of mortality in older patients.

Better preservation of residual renal function (RRF) has been reported to be associated with better clinical outcomes for HD and PD patients alike (9,10,26). Apart from providing small-solute clearance, RRF in dialysis patients continues to serve important metabolic, humoral, and hemodynamic functions. Those important parameters all contribute to the close association between RRF and survival. It is well known that RRF is preserved longer in PD patients than in HD patients. Patients on HD who are transferred to PD usually lack RRF, and PD adequacy is therefore more difficult to obtain. In the present study, we found that residual urinary output was significantly less in patients transferred from HD than in patients started and maintained on PD. However, in the present study, residual urinary output was not found to independently affect patient survival, which is inconsistent with other reports (27–29). That finding might be explained by the fact that the other studies focused mainly on RRF, but in our study, data on RRF was not available and was estimated by calculating the mean of renal clearances of urea and creatinine from a 24-hour urine collection. For some PD patients, residual urinary output can't entirely represent RRF. Therefore, that inconsistency might be

the delicate difference between RRF and residual urinary output that led to the disparity in results.

Peritonitis continues to be a major complication of PD. Peritonitis is not only the leading cause of technique failure, it also contributes to mortality (30,31). Peritonitis is responsible for 30% – 80% of permanent transfers to HD (32). Indeed, in the present study, nearly 60% of technique failure was a result of peritonitis. Peritonitis continues to be the leading cause of technique failure in our PD population. Interestingly, we observed no difference in technique survival between the transfer and no-transfer patients in our study.

As with any retrospective observational study, the present study has several limitations. First, recall and selection bias may be present. Second, data on dialysis adequacy, delivered dialysis dose, peritoneal equilibration test (PET) results, anemia management, and blood pressure control were not available. Third, we had data about comorbidity conditions at baseline only; we did not measure and monitor change in the comorbidity score, which may be a major marker of poor prognosis in PD patients. Fourth, cause and effect cannot be established.

CONCLUSIONS

Based on the results of the present study, we conclude that patients transferred from HD to PD have a prognosis on PD that is similar to the prognosis in patients who started with and remained on PD. Patient age (per 10 years) and low serum albumin might be factors contributing to increased mortality in the PD patient population.

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DISCLOSURES

The authors have no financial conflicts of interest to declare.

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