CLINICAL OUTCOME OF HOME HEMODIALYSIS IN PATIENTS WITH PREVIOUS PERITONEAL DIALYSIS EXPOSURE: EVALUATION OF THE INTEGRATED HOME DIALYSIS MODEL

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♦ **Background:** Home dialysis is a cost-effective modality of renal replacement therapy associated with excellent outcomes. Peritoneal dialysis (PD) is the most common home-based modality, but technique failure remains a problem. Transfer from PD to home hemodialysis (HHD) allows the patient to continue with a home-based modality, but the outcomes of patients transitioning to HHD after PD are largely unknown.

♦ **Methods:** In a retrospective cohort study, including all consecutive HHD patients between January 1996 and December 2011, we evaluated the outcomes of patients with previous PD exposure compared to those without. The primary outcome was the cumulative patient and technique survival. Secondary outcomes included time to first hospitalization and hospitalization rate. Data were compared using the log-rank test and a multivariable Cox proportional hazards model.

♦ **Results:** Among our cohort of 207 consecutive HHD patients, 35 (17%) had previous exposure to PD. Median renal replacement therapy (RRT) vintage (12.3 years, interquartile range (IQR) 8.5 – 18.9 vs 0.9 years, IQR 0.2 – 7.5, $p < 0.001$) and Charlson comorbidity index (CCI) (4, IQR 2 – 6 vs 3, IQR 2 – 4, $p = 0.044$) were higher among patients with PD exposure than those without. Despite the difference in vintage, cumulative patient and technique survival was similar in the two groups, in both unadjusted (log-rank $p = 0.893$) and Cox adjusted models (hazard ratio (HR) 1.15, 95% confidence interval (CI) 0.51 – 2.59) for patients with PD exposure compared to those without. The time to first hospitalization was shorter in patients with previous PD exposure compared to PD-naïve patients (log-rank $p = 0.021$). This association was preserved in the Cox proportional model (HR 1.65, 95% CI 1.08 – 2.54).

♦ **Conclusion:** Despite a higher burden of comorbidity, patients with previous PD exposure had similar cumulative patient and technique survival on HHD compared to those without PD exposure. Whenever possible, HHD should be considered in PD patients in need of a new dialysis modality.

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Home dialysis is promoted in many countries for both patient outcomes and financial considerations (1–5). Although peritoneal dialysis (PD) is by far the most common home dialysis modality used internationally, home hemodialysis (HHD) is slowly becoming more accessible (6). Until now, most of the studies evaluating dialysis modalities have focused on comparison between PD and conventional hemodialysis (CHD). Overall, survival is similar in patients initiating dialysis with PD or CHD (1). Nonetheless, some observational studies have reported a modest benefit for PD during the first several years after dialysis initiation (7). Better preservation of residual kidney function also favors patients undergoing PD rather than CHD (8). Furthermore, PD is considered the most economic dialysis modality in most countries (2,9). When patients need to shift from one dialysis modality to another, better outcomes have been shown among those transferring from PD to CHD compared to transfer in the opposite direction (10). Interestingly, one study also reported similar survival in a cohort of PD patients between those switching to CHD and those remaining on PD (11).

There is a paucity of data about dialysis modality transition in home-based therapies. In most cases, patients have successively been treated with PD and then HHD rather than with HHD first and PD second (12). Successful transition between home modalities (PD to HHD) have been reported in two small case series with patients from Toronto (13,14) and in another case series from Japan (15). However, none of these studies have evaluated the outcomes of PD patients once they start HHD.

The purpose of the present study was to assess the clinical outcomes associated with previous PD exposure in

a HDD cohort. We hypothesized that patients with previous PD exposure would have a shorter cumulative patient and HDD technique survival, and would be at higher risk of hospitalization (given their longer vintage), compared to patients without PD exposure.

METHODS

SELECTION AND DEFINITIONS

We conducted a single-center retrospective cohort study including all consecutive patients who completed HDD training between 1 January 1996 and 31 December 2011. Outcomes were captured from the time patients completed HDD training and initiated dialysis at home. Patients were defined as having previous PD exposure if they had any PD therapy before the initiation of HDD, regardless of the time and duration of the PD exposure. All the other patients were defined as not having had any PD exposure, in other words, PD-naïve.

Our primary outcome was cumulative patient and technique survival. Secondary outcomes included the time to first hospitalization and the hospitalization rate. Both elective and non-elective hospitalizations were included. Data were collected using a combination of electronic and paper chart review. Patients were censored at the time of loss to follow-up, transplantation or the end of the follow-up period (1 July 2012). HDD technique failure was defined as a permanent change in dialysis modality with a transition to in-center HD, facility HD or peritoneal dialysis.

DATA COLLECTION

Baseline characteristics including patients' demographics, comorbidities, causes of end-stage renal disease (ESRD) and vintage were collected at the time of HDD initiation. For patients with more than one period of PD, we included the total PD exposure time in the PD vintage calculation. We combined individual comorbidities into a Charlson comorbidity index (CCI). This index has been validated in dialysis patients (16) and assigns points to several medical conditions to determine a global comorbidity score. Higher scores have been shown to predict mortality (17). For patients with previous PD exposure, the reason for PD cessation and the next renal replacement therapy (RRT) modality were identified. If a patient had more than one exposure to PD, only the last one was considered. Causes of PD cessation were classified as kidney transplantation, peritonitis, ultrafiltration or clearance problem, encapsulating peritoneal sclerosis, abdominal surgery, leak and other PD-related mechanical

issues. Patients who underwent less than 90 days of CHD between PD and HDD were considered as a direct transition to HDD. Reasons for first hospitalization were identified through electronic discharge summaries.

STATISTICAL ANALYSIS

Data are reported as counts and percentages for categorical variables, mean $\pm$ standard deviation for normally distributed continuous variables, and median and interquartile range for non-normally distributed continuous variables. Categorical variables were compared between the group with and without PD exposure using Fisher's exact test. Continuous variables were analyzed with *t*-test and Wilcoxon rank sum test for normally and non-normally distributed variables, respectively. The cumulative survival and hospitalization-free survival were graphically displayed using the Kaplan-Meier product limit method. Unadjusted survival functions were compared through the log-rank test. Adjusted hazard ratios with 95% confidence intervals (CI) were calculated with a multivariable Cox proportional hazards model. Variables included in the multivariable models were based on recognized predictors in the literature and clinical judgment of the authors (16,18). To evaluate hospitalization rates, we compared groups with an unadjusted incidence rate ratio (IRR) and calculated the adjusted IRR using a binomial regression model. A sensitivity analysis was performed in order to attenuate the difference in RRT vintage among our groups. In this sensitivity analysis, the group without PD exposure was subdivided in two groups, the first included patients with another RRT modality before HDD initiation (without PD) and the second represented incident HDD patients. Statistical analyses were performed using Stata IC, version 12 (StataCorp, College Station, TX, USA). A two-tailed *p* value < 0.05 was considered statistically significant.

RESULTS

Our global cohort included 207 consecutive HDD patients among whom 35 had previous PD exposure and 172 were PD-naïve (Figure 1). Demographic characteristics were similar in the two groups with a mean age of approximately 45 years at HDD initiation (Table 1). Patients with previous PD exposure had a longer renal replacement therapy vintage (median 12.3 years) compared to the other patients (0.9 years). The burden of comorbidity was also higher among patients with previous PD with a higher frequency of coronary artery disease, stroke and a median Charlson comorbidity index (CCI) of 4 (2 – 6) vs 3 (2 – 4).

Figure 1 — Trajectory before HHD initiation stratified by PD exposure. Dashed arrow: direct transition from one modality (or CKD) to another or transition through other RRT modalities. Solid arrow: direct transition from one modality to another. HHD = home hemodialysis; CHD = conventional home dialysis; PD = peritoneal dialysis; RRT = renal replacement therapy; CKD = chronic kidney disease.

TABLE 1
Baseline Characteristics Stratified by Presence or Absence of PD Exposure

Characteristics	Previous PD exposure (n=35)	No PD exposure (n=172)	p
Age, mean±SD	44.7±12.6	44.5±13.7	0.833
Caucasian, n (%)	20 (57)	108 (63)	0.570
Male, n (%)	19 (54)	111 (65)	0.257
ESRD etiology, n (%)			
Diabetic nephropathy	3 (9)	24 (14)	0.582
Glomerulonephritis	14 (40)	64 (37)	0.849
PKD	3 (9)	19 (11)	1.000
Comorbidities, n (%)			
Diabetes	8 (23)	39 (23)	1.000
Coronary artery disease	11 (31)	14 (8)	<0.001
Peripheral artery disease	3 (9)	10 (6)	0.465
Stroke	6 (17)	9 (5)	0.024
CCI, median (IQR)	4 (2–6)	3 (2–4)	0.044
Previous kidney transplantation	28 (80)	51 (30)	<0.001
RRT vintage (years), median (IQR)	12.3 (8.5–18.9)	0.9 (0.2–7.5)	<0.001
PD vintage (years), median (IQR)	3.0 (1.2–4.8)	0	
Permanent vascular access ^a at HHD initiation, n (%)	15 (43)	88 (51)	0.459

PD = peritoneal dialysis; SD = standard deviation; ESRD = end-stage renal disease; PKD = polycystic kidney disease; CCI = Charlson comorbidity index; IQR = interquartile range; RRT = renal replacement therapy; HHD = home hemodialysis.

^a Includes arteriovenous fistula and graft.

Among patients with previous PD who ultimately entered the HHD cohort, the median time spent specifically on PD was 3.0 years (1.2 – 4.8). Reasons for PD cessation and the next RRT modality after PD are described in Table 2. Aside from kidney transplant, peritonitis (34%) was the main reason for stopping PD. Only nine (26%) patients went directly from PD to HHD while 13 (37%) patients underwent kidney transplantation and 13 (37%) patients were transferred to CHD (for more than 90 days) before entering the HHD program.

PRIMARY OUTCOME

In the primary analysis, 52 events were identified during a total follow-up time of 811 patient-years. Thirty of these events were patient deaths, and 22 events were related to

HHD technique failure. The cumulative patient and technique survival was similar for both groups (HHD patients with and without previous PD) in the unadjusted analysis (log rank $p=0.893$) with a 1-, 3- and 5-year survival of 91%, 88% and 66% in a PD exposure group and 92%, 80% and 72% among patients without previous PD. The Cox-adjusted model showed similar results (hazard ratio (HR) 1.15, 95% CI 0.51 – 2.59, $p=0.742$) (Table 3). Kaplan Meier and Cox-adjusted curves are shown in Figure 2. Our model included age, CCI, RRT vintage and diabetes as ESRD etiology. Age was the only variable associated with the primary outcome in our multivariable model (HR 1.03 per year, 95% CI 1.01 – 1.05, $p=0.001$).

SECONDARY OUTCOME

Patients who underwent PD at any time before HHD initiation had a shorter time to first hospitalization compared to PD-naïve patients (log-rank $p=0.021$). This association was preserved in a Cox proportional model (HR 1.65, 95% CI 1.08 – 2.54, $p=0.022$) (Table 4). Kaplan Meier and Cox-adjusted curves for the hospitalization-free survival can be found in Figure 3. Reasons for first admission stratified by infections, dialysis-related events, cardiovascular events or others were not different between the two groups (Table 5).

The unadjusted hospitalization rate was also higher for patients with PD exposure compared to those without (0.63 per year vs 0.35 per year) with an IRR of 1.84 (95% CI 1.43 – 2.34, $p<0.001$). However, the association became non-significant after adjustment for age, diabetes, ESRD, RRT vintage and CCI (IRR 1.43, 95% CI 0.87 – 2.36, $p=0.157$).

SENSITIVITY ANALYSIS

In a sensitivity analysis, we subdivided our group without previous PD exposure into incident HHD patients and

TABLE 2
Characteristics of Peritoneal Dialysis
Transition Period ($n=35$)

Characteristics	N (%)
First modality after peritoneal dialysis	
Kidney transplant ^a	13 (37)
Conventional hemodialysis	13 (37)
Home hemodialysis ^b	9 (26)
Reasons for peritoneal dialysis cessation	
Transplantation	13 (37)
Peritonitis	11 (31)
Ultrafiltration or clearance problem	4 (11)
Abdominal surgery	2 (6)
Encapsulating peritoneal sclerosis	2 (6)
Leak	1 (3)
Other PD-related mechanical issues	2 (6)

PD = peritoneal dialysis.

^a Includes deceased and living donors.

^b Includes <90 days of conventional hemodialysis.

TABLE 3
Univariable and Cox Proportional Model for Patient and Technique Survival ($n=52$)

Variable	Univariable		Cox model ^a	
	HR (95% CI)	p	HR (95% CI)	p
Age	1.03 (1.01–1.05)	0.001	1.03 (1.01–1.05)	0.005
CCI	1.12 (1.01–1.4)	0.025	1.07 (0.95–1.21)	0.279
RRT vintage	0.98 (0.96–1.02)	0.305	0.99 (0.95–1.03)	0.565
PD exposure	1.05 (0.53–2.09)	0.893	1.15 (0.51–2.59)	0.742
DM ESRD	1.93 (0.94–3.97)	0.075	1.24 (0.56–2.76)	0.601

HR = hazard ratio; CI = confidence interval; CCI = Charlson comorbidity index; RRT = renal replacement therapy; PD = peritoneal dialysis; DM = diabetes mellitus; ESRD = end-stage renal disease.

^a Factors in the model include age, CCI, RRT vintage, PD exposure status and ESRD secondary to diabetes.

Figure 2 — Primary outcome: Cumulative patient and technique survival. A: Unadjusted Kaplan-Meier curve, B: Cox proportional curve. Other variables in model include: age, renal replacement therapy vintage, Charlson comorbidity index, diabetic nephropathy as etiology of end-stage renal disease. PD = peritoneal dialysis; HR = hazard ratio.

TABLE 4
Univariable and Cox Proportional Model for Time to First Hospitalization ($n=126$)

Variable	Univariable		Cox model ^a	
	HR (95% CI)	<i>p</i>	HR (95% CI)	<i>p</i>
Age	1.01 (1.00–1.03)	0.087	1.01 (0.99–1.02)	0.352
CCI	1.12 (1.05–1.20)	0.001	1.06 (0.99–1.15)	0.105
RRT vintage	1.00 (0.98–1.02)	0.805	1.00 (0.97–1.02)	0.820
PD exposure	1.65 (1.08–2.54)	0.022	1.70 (1.02–2.84)	0.042
DM ESRD	2.19 (1.33–3.60)	0.002	1.90 (1.09–3.31)	0.024

HR = hazard ratio; CI = confidence interval; CCI = Charlson comorbidity index; RRT = renal replacement therapy; PD = peritoneal dialysis; DM = diabetes mellitus; ESRD = end-stage renal disease.

^a Factors in the model include age, CCI, RRT vintage, PD exposure status and ESRD secondary to diabetes.

patients with other previous RRT modalities (but excluding PD). When divided in three groups, 35 patients had previous PD exposure, 110 patients had other RRT before HHD initiation but no PD exposure and 62 patients had HHD as their first RRT modality. Baseline characteristics stratified by these three groups are displayed in Table 6. For both our primary and secondary outcomes, the results were similar in direction, and effect estimate was consistent with the original analysis.

DISCUSSION

In this study, we have shown that patients with previous PD had similar cumulative patient and technique survival on HHD compared to patients without previous PD exposure. The hospitalization-free period was, however, shorter among patients with PD exposure. Furthermore, we identified that only 9 (26%) patients

transitioned directly from PD to HHD while 13 (37%) patients were directed to CHD and 13 (37%) patients received a kidney transplant before ultimately coming to HHD (Figure 1).

The feasibility of HHD in patients with PD failure has been described in two small studies from Toronto (13,14), but, unlike the current study, they did not examine the outcome of these patients on HHD. Cinà *et al.* recently characterized 12 patients with PD failure who were transitioned to HHD. Compared to patients transferred to CHD, those directed to HHD were younger, tended to live further from the hospital and were less likely to have an infection as the precipitating cause of PD cessation (14). Similarly, the young mean age of 45 years in our cohort probably reflects a selection process among patients who were eventually referred to HHD after PD, knowing that patients 65 years and older represent 45% of PD prevalent population in Canada (19). Excluding

Figure 3 — Secondary outcome: Time to first hospitalization. A: Kaplan-Meier unadjusted curve B: Cox proportional curve. Other variables in model include: age, renal replacement therapy vintage, Charlson comorbidity index, diabetic nephropathy as etiology of end-stage renal disease. PD = peritoneal dialysis; HR = hazard ratio.

TABLE 5
Reasons for First Admission after HHD Initiation

Admission reason	Previous PD exposure (n=27)	No PD exposure (n=99)	p
Infection (access or other)	5 (19)	29 (29)	0.807
Dialysis-related (non-infection)	5 (19)	12 (12)	0.174
Cardiovascular	3 (11)	9 (9)	0.431
Other	14 (52)	49 (49)	0.226

HHD = home hemodialysis; PD = peritoneal dialysis.
Data are presented as numbers with percentages in brackets.

the 13 (37%) patients who ceased PD for kidney transplantation, peritonitis was the most frequent reason precipitating a change in dialysis modality in our cohort, which differed from the study published by Cinà *et al.* Furthermore, in our cohort two patients successfully initiated HHD after PD cessation precipitated by encapsulating peritoneal sclerosis.

Our study also showed that 9 (26%) patients were directly referred to HHD after PD cessation while 13 (37%) spent more than 3 months in CHD before eventually initiating HHD. The length of time spent on CHD has previously been associated with patients' interest in initiating HHD (20). Hence, patients with long CHD exposure after PD cessation are probably less likely to initiate HHD subsequently. Although, in our cohort, 13 patients successively transitioned from PD to CHD and then HHD, we speculate that a larger number of patients

with PD failure were potential HHD candidates had they not been first referred to CHD.

Our primary outcome, cumulative patient and technique survival, was similar in patients with and without PD exposure. This cumulative survival is comparable overall to what has been reported in previous studies, especially knowing that we included all HHD (18). Considering that patients with previous PD had longer RRT vintage and a higher burden of comorbidity, a poorer outcome on HHD might have been expected in this group (18,21). It is reasonable to hypothesize that patients with prior PD exposure may have gained prior education in self-management, which may facilitate transition from one form of home dialysis to another home-based renal replacement therapy (10,11). Our primary outcome results support the extension of the concept of "integrated dialysis," previously described for PD and CHD (10), to patients specifically undergoing home-based dialysis (22–24).

In terms of secondary outcomes, time to first hospitalization was shorter in patients with previous PD. These patients might have been at higher risk of admission due to the condition that precipitated their PD cessation (for instance a higher risk of infection in a patient with a severe peritonitis or an intestinal obstruction following encapsulating peritoneal sclerosis). Although differences in hospitalization-free survival persisted after adjustment, we could speculate that discrepancy in comorbidities, ESRD vintage and other unmeasured confounders may explain in part the present finding. Comorbidity burden has been associated with a higher rate of hospitalization early during CHD therapy (25). In

TABLE 6
Baseline Characteristics Stratified by Patients with Previous PD Exposure, Patients with Exposure to Other RRT Modalities Before HHD (without PD) and Incident HHD Patients

Characteristics	Previous PD exposure (n=35)	Other RRT modalities without PD (n=110)	Incident HHD (n=62)	p
Age, mean, (SD)	44.7 ± 12.6	43.6 ± 13.2	46.0 ± 14.5	0.532
Caucasian, n (%)	20 (57)	73 (66)	35 (56)	0.531
Male, n (%)	19 (54)	66 (60)	45 (73)	0.133
ESRD etiology, n (%)				
Diabetic nephropathy	3 (9)	11 (10)	13 (21)	0.101
Glomerulonephritis	14 (40)	41 (37)	23 (37)	0.961
PKD	3 (9)	8 (7)	11 (18)	0.099
Comorbidities, n (%)				
Diabetes	8 (23)	22 (20)	17 (27)	0.531
Coronary artery disease	11 (31)	9 (8)	5 (8)	0.002
Peripheral artery disease	3 (9)	7 (6)	3 (4)	0.743
Stroke	6 (17)	5 (5)	4 (7)	0.050
CCI, median (IQR)	4 (2–6)	3 (2–4)	2 (2–4)	0.058
Previous kidney transplantation	28 (80)	51 (46)	0	<0.001
RRT vintage (years), median (IQR)	12.3 (8.5–18.9)	4.5 (1.0–13.3)	0.2 (0.1–0.3)	<0.001
Permanent vascular access ^a at HHD initiation, n (%)	15 (43)	55 (50)	33 (53)	0.616

PD = peritoneal dialysis; RRT = renal replacement therapy; HHD = home hemodialysis; SD = standard deviation; ESRD = end-stage renal disease; PKD = polycystic kidney disease; CCI = Charlson comorbidity index; IQR = interquartile range.

^a Includes arteriovenous fistula and graft.

contrast to the time to first hospitalization, the rate of hospitalization in the two groups was not different in the Cox proportional model, which notably included vintage and CCI. Furthermore, a large difference in RRT vintage was present between our two groups. Part of this longer RRT vintage among patients with previous PD is probably related to prior transplantation exposure, which in turn could have influenced hospitalizations.

This study has several limitations. Although we tried to adjust for differences in comorbidity with the CCI (16), RRT vintage and other baseline characteristics, our model might not have accounted for all differences between the two groups, resulting in unmeasured confounding. Transplantation history was more frequent in the group with PD exposure, which could have influenced our results. Little is known about outcome of HHD in patients with a failed renal allograft. It is reasonable to speculate that this group of patients may be at higher risk of hospitalization during the period before and after dialysis initiation (26). Furthermore, the heterogeneity of our group with PD exposure, which included patients with PD at any time (remote or near) before HHD initiation, also prevents us from drawing any firm conclusions. Immortal time bias could also have favored the group with PD exposure since they had to survive at least one renal

replacement therapy before initiating HHD. Mortality is known to be higher during the first weeks after dialysis initiation (27). However, whether or not this is also true for HHD remains uncertain. Nonetheless, their longer RRT vintage at time of HHD initiation also increases the possibility of a ‘survivor’ effect among the PD-exposed group. Immortal time bias has been identified as a major limitation in studies evaluating outcomes after dialysis initiation (28) and remains a significant limitation in our study. Finally, the retrospective single-center design prevents us from drawing any definitive conclusions for other centers that might have different dialysis practices or populations.

CONCLUSION

In conclusion, we identified that patients with previous PD exposure had similar overall and technique survival during HHD compared to those without PD exposure. These results support the idea of “integrated home dialysis” promoting the transition between PD and HHD. Novel approaches to operationalize the concept of integrated home dialysis require further investigation. In the mean time, HHD should be strongly considered for all patients in need of a new dialysis modality after PD.

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DISCLOSURE

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