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Home Hemodialysis and Peritoneal Dialysis Patient and Technique Survival in Canada

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Introduction: As interest for home dialysis is growing, knowledge of comparative clinical outcomes between peritoneal dialysis (PD) and home hemodialysis (HHD) would help to better inform shared decision making with patients and caregivers during modality discussion. This study aimed to assess differences in risk of mortality and technique failure in an incident home dialysis cohort and, specifically, to assess change in this association through eras.

Methods: All adults patients initiating PD or HHD, in Canada (excluding Quebec), within 365 days after kidney replacement therapy (KRT) initiation between 2000 and 2013 were included (administrative censoring 31 December 2014). Mortality and treatment failure (transfer to another modality for >90 days or death) were assessed in a multivariable Cox proportional hazard model, with prespecified stratification based on the year of KRT initiation.

Results: The study included 959 HHD and 15,469 PD patients. Compared with incident PD, incident HHD was associated with a lower risk of mortality (adjusted hazard ratio [aHR] = 0.64, 95% confidence interval [CI] = 0.53−0.78), and treatment failure (aHR = 0.52, 95% CI = 0.45−0.60). These lower risks of mortality with HHD were more pronounced for older cohorts (2000−2005: aHR = 0.47, 95% CI = 0.31−0.70; 2006−2010: aHR = 0.70, 95% CI = 0.54−0.89) and not significantly different in the most recent era (2011−2013: aHR = 0.86, 95% CI = 0.51−1.47).

Conclusion: In Canadian incident KRT patients, HHD was associated with appreciably lower risks of mortality and treatment failure compared to PD, although this association appeared to be attenuated in the most contemporary era.

Kidney Int Rep (2020) **5,** 1965–1973; https://doi.org/10.1016/j.ekir.2020.08.020
KEYWORDS: home dialysis; home hemodialysis; mortality; peritoneal dialysis; technique failure

Dialysis modality selection is a cornerstone of advanced chronic kidney disease (CKD) management. Queries from patients and caregivers about the optimal modality, notably in relation to patient and technique survival but also regarding lifestyle differences, are frequent and strongly influence modality choice.[1−3] Although quality of life and personal life goals should be the most central factors guiding dialysis modality selection, mortality and technique failure remain important considerations for home dialysis patients, as reported by the Standardised Outcomes in Nephrology-Peritoneal Dialysis (SONG-PD) initiative.[3,4] As interest in home dialysis increases in Canada and internationally, the dilemma about whether to initiate with peritoneal dialysis (PD) or home hemodialysis (HHD) is commonplace.[5,6] Eligibility criteria for treatment with HHD has also expanded with consideration of this modality for more vulnerable patients, including those with higher comorbidity burden and older age.[7,8]

However, the comparative outcomes of incident PD and HHD remain uncertain because of the availability of only a limited number of studies,[9−11] which have yielded conflicting results, ranging from a nearly 50% lower mortality risk with HHD compared to PD in an Australia and New Zealand Dialysis and Transplantation (ANZDATA) registry study[9] to similar mortality in an incident home dialysis study in the United States.[10] However, none of these studies reported data on potential changes

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Received 11 May 2020; revised 13 July 2020; accepted 18 August 2020; published online 26 August 2020

Table 1. Baseline characteristics

Characteristic	PD (n = 15,469)	HHD (n = 959)	*P*	Missing data
Age, yr	63 (51–73)	54 (45–63)	<0.001	6 (<1)
Sex, male	9119 (59)	656 (68)	<0.001	0
Race			<0.001	0
Caucasian	10367 (67)	697 (73)		
Black	572 (4)	63 (7)		
Asian	1401 (9)	57 (6)		
Other	3129 (20)	142 (15)		
Primary kidney disease			<0.001	558 (3)
Glomerulonephritis	3018 (20)	223 (24)		
Diabetes	5806 (39)	278 (30)		
Hypertension	2749 (18)	109 (12)		
Other	2271 (23)	316 (34)		
Cardiovascular disease	6061 (42)	299 (33)	<0.001	1035 (6)
Diabetes	7096 (48)	371 (40)	<0.001	866 (5)
Body mass index			<0.001	1130 (7)
<20 kg/m^2	1023 (7)	68 (8)		
20–24.9 kg/m^2	4768 (33)	225 (25)		
25–29.9 kg/m^2	4928 (34)	247 (28)		
≥30 kg/m^2	3696 (26)	343 (38)		
Late nephrology referral, <3 mo	2425 (18)	174 (20)	<0.001	2403 (14)
eGFR, ml/min	8.8 (6.7–11.6)	8.4 (6.3–11.1)	0.002	
Delay before home dialysis initiation, d	0 (0–27)	77 (7–177)	<0.001	0
KRT initiation era			<0.001	0
2000–2005	6183 (40)	170 (18)		
2006–2010	5700 (37)	417 (43)		
2011–2013	3586 (23)	372 (39)		
Region			<0.001	2594 (16)
West	5001 (39)	231 (26)		
Ontario	6745 (52)	621 (71)		
Atlantic	1166 (9)	26 (3)		
Other	42 (<1)	2 (<1)		0
Home dialysis center size[a]			<0.001	
Small	1712 (11)	105 (11)		
Medium	4333 (28)	204 (21)		
Large	9424 (61)	650 (68)		

Results are presented as count (percentage) for categorical variables and median (interquartile range) for continuous variables.
[a]Center size: small, <15 new home dialysis patients per year; medium, 15–25 new home dialysis patients per year; large, ≥25 new home dialysis patients per year.
eGFR, estimated glomerular filtration rate; HHD, home hemodialysis, KRT, kidney replacement therapy; PD, peritoneal dialysis.

in this comparative association through different eras, as home dialysis patient characteristics and perceived eligibility may evolve over time.[7,8]

The aim of this registry study was to compare patient and technique survival for HHD and PD in the Canadian dialysis population and specifically to assess any change of this association over time. It was postulated that HHD would be associated with a lower mortality risk, although it was expected that this association would vary over time, with a less pronounced effect in more contemporary eras, in which selection for HHD has become less restrictive and outcomes in PD have improved.[12,13]

MATERIALS AND METHODS

Study Design and Population

This observational registry study included all adult patients initiated on home dialysis within 365 days of kidney replacement therapy (KRT) start, in Canada, between January 2000 and December 2013. Patients receiving KRT in Quebec and those initiated on KRT outside of Canada were excluded. Patients with <90 days of KRT and those with a previous kidney transplant were also excluded because of the expected influence of the failed transplant on the subsequent risk of death. Data were obtained through the Canadian Organ Replacement Register (CORR), a validated registry of incident KRT therapy initiation in Canada (excluding Quebec).[14]

Exposure and Outcome Assessment

Patients were defined based on the first home dialysis modality (PD or HHD). The primary outcome was mortality. Patients were followed from start of home dialysis until death, irrespective of modality transfer. The secondary outcome, treatment failure, was the

Table 2. Baseline characteristics by era and home dialysis modality

Characteristics	PD 2000–2005 n = 6183	PD 2006–2010 n = 5700	PD 2011–2013 n = 3580	P	HDD 2000–2005 n = 170	HDD 2006–2010 n = 417	HDD 2011–2013 n = 372	P
Age	63 (50–73)	63 (51–73)	63 (52–73)	0.02	52 (43–61)	54 (46–63)	54 (46–64)	0.12
Sex, male	57%	59%	61%	<0.001	74%	67%	68%	0.20
Race				<0.001				0.18
Caucasian	69%	68%	62%		78%	73%	70%	
Black	3%	4%	4%		5%	5%	9%	
Asian	8%	8%	11%		5%	6%	7%	
Other	20%	19%	23%		11%	15%	15%	
Kidney disease				<0.001				0.06
Glomerulonephritis	22%	19%	19%		27%	25%	22%	
Diabetes	37%	38%	42%		21%	30%	34%	
Hypertension	18%	20%	17%		13%	10%	13%	
Other	23%	23%	21%		38%	35%	31%	
Cardiovascular disease	46%	40%	38%	<0.001	37%	32%	31%	0.39
Diabetes	45%	49%	52%	<0.001	31%	40%	45%	0.01
Body mass index, kg/m^2	26 (23–29)	27 (23–31)	27 (23–31)	<0.001	27 (23–32)	28 (23–34)	28 (24–34)	0.43
Late referral	23%	17%	15%	<0.001	27%	22%	16%	0.01
Vintage at home dialysis start, days	0 (0–19)	0 (0–36)	0 (0–29)	<0.001	110 (11–212)	89 (0–202)	62 (7–133)	0.001
Home dialysis center size[a]				<0.001				0.22
Small	11%	11%	12%		10%	10%	12%	
Medium	26%	29%	30%		22%	18%	24%	
Large	63%	60%	59%		68%	71%	64%	
Intensive HHD at start, >18 h					39%	38%	35%	0.51

HHD, home hemodialysis; KRT, kidney replacement therapy; PD, peritoneal dialysis.
[a]Small center: <15 new home dialysis patients per year; medium: 15–25 new home dialysis patients per year; and large: ≥25 new home dialysis patients per year.
Results are presented as percentage for categorical variables and median (interquartile range) for continuous variables.

composite of technique failure (defined as transfer to any other modality for 90 consecutive days) and death (during home dialysis or within 90 days of transfer to another modality).[15] In all analyses, data were censored at time of kidney transplantation, kidney function recovery, loss to follow-up, and end of the study (31 December 2014). Any event occurring <90 days after a dialysis modality switch was attributed to the previous modality.

Covariates Assessment

Demographics, comorbidities, cause of primary kidney disease, body mass index (BMI), region, era, and late nephrology referral were determined at time of KRT initiation. End-stage kidney disease (ESKD) vintage and dialysis center were defined at home dialysis start. Race was categorized as Caucasian, black, Asian, or other. Late referral was defined as referral to a nephrologist <3 months before KRT initiation. Primary kidney disease was categorized as glomerulonephritis, diabetes, hypertensive disease, and "other/unknown." Estimated glomerular filtration rate (eGFR) was calculated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula, with adjustment for black race.[16] Center size was based on the mean number of incident home dialysis patient per year. Region was defined as Ontario, West (British Columbia, Alberta, Manitoba, and Saskatchewan), Atlantic (Nova Scotia, New Brunswick, Prince Edward Island, Newfoundland, and Labrador) and "other." Home hemodialysis was subdivided based on total weekly hours during the initial HHD period, with intensive HHD defined as >18 hours per week.

Statistical Analysis

Unadjusted survival curves were compared using the Kaplan–Meier product limit and log-rank test. The primary statistical approach was a multivariable Cox proportional hazard model, with robust standard error to account for data clustering in dialysis centers. Covariates were selected *a priori* based on previous literature and biological plausibility and included age, sex, race, diabetes, cardiovascular disease, primary kidney disease, BMI, ESKD vintage, era, region, and center size.[9,17] Prespecified 2-way interactions were tested between dialysis modality and the following covariates: age, race, diabetes, era, vintage, and center size. Interaction effects were assessed with likelihood ratio. Subgroup analysis was planned with interactions with a P value <0.10 and prespecified for era. A time-varying effect of dialysis modality on outcomes was also assessed with the likelihood ratio test. The proportional hazards assumption was visually assessed with log-minus-log plots, observed (Kaplan–Meier) and predicted (Cox) graphs and plotting of Schoenfeld residuals.

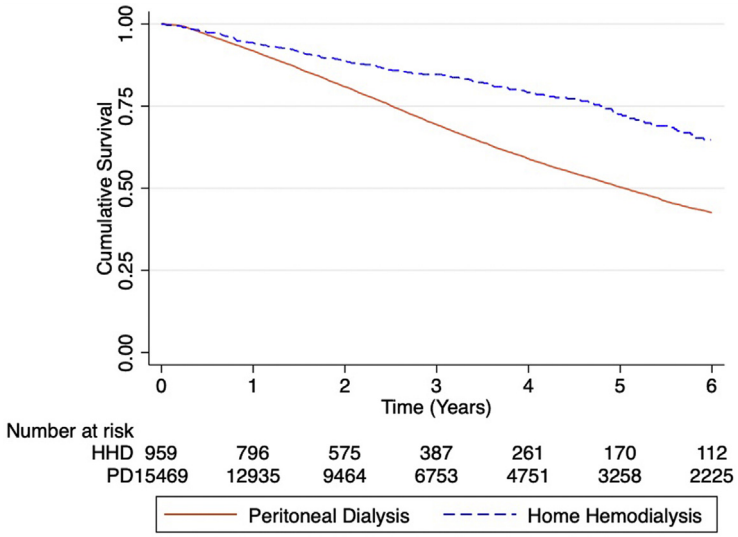

Figure 1. Kaplan–Meier in incident home hemodialysis and peritoneal dialysis patients in Canada (2000–2013).

Propensity score (PS) matching was used as a second statistical approach to compare outcomes in PD and HHD cohorts. Probability of HHD therapy was predicted using logistic regression with inclusion of all baseline characteristics listed in Table 1 and interaction terms based on previous publication and biological plausibility (age * sex, age*cardiovascular disease, race*cardiovascular disease, race*BMI, diabetes*BMI, diabetes*era, era*center size). The PS obtained from this logistic regression model was evaluated with a receiver operating characteristic curve (area under curve [AUC] = 0.84) and for covariate balance within quintiles of PS. The continuous PS was used to perform 1:1 nearest neighbor matching without replacement.[18] Survival times for the matched dialysis modality groups were compared using Cox proportional hazards models with robust standard errors. Standardized differences before and after matching were calculated (Supplementary Figure S1).

Third, Fine, and Gray multivariable competing risk survival models[19] were performed with transplantation as the competing event. Fourth, an analysis with chained multiple data imputation (n = 5) was performed to assess the influence of any missing data.[20,21]

In addition, an analysis was conducted using a 3-category home modality variable (intensive HHD vs. nonintensive HHD vs. PD) to account for potential differences based on HHD treatment prescriptions.

Finally, sensitivity analyses were performed to compare home dialysis outcomes in incident cohorts with very early (within 90 days of KRT start) and moderately early (within 180 days of KRT start) home dialysis initiation. The analyses were also repeated in a restricted cohort including centers with a mean annual number of new HHD patients >3 and new PD >20 during the study period, to attenuate potential practice pattern bias. All analyses were performed using Stata SE, version 15 (StataCorp, College Station, TX).

RESULTS

Overall, 959 HHD and 15,469 PD patients were included in the study. Their baseline characteristics are presented in Table 1. The HHD patients were younger, had fewer comorbidities, and were less likely to have home dialysis as their first KRT modality compared to PD patients. There was, however, a change in baseline characteristics over time, with patients in more recent eras being more likely to be older and to have diabetes, diabetic nephropathy, and a shorter KRT vintage at home dialysis start (Table 2).

Patient Survival

Crude patient survival was higher in HHD compared to PD with a respective 1-, 2-, and 5-year survivals of 94%, 89%, and 73% for HHD patients and 92%, 81%, and 50% for PD patients (log-rank $P < 0.001$) (Figure 1). Incident HHD was associated with a lower mortality (adjusted hazard ratio [aHR] = 0.64, 95% CI = 0.53–0.78, $P < 0.001$) compared to PD after adjustment for demographic characteristics, comorbidities, primary kidney disease, BMI, vintage, era, region, and center size in the Cox proportional hazard multivariable model. Similar findings were observed with data imputation Cox proportional hazard analysis and competing risk model (Table 3). There was a small attenuation in the effect size in the propensity score matched analysis (aHR = 0.74, 95% CI = 0.58–0.95, $P = 0.02$).

Table 3. Adjusted mortality risk for incident HHD compared to incident PD

Statistical model	HR	95% CI	*P*
Multivariable Cox PH model, n = 10,717	0.64	0.53–0.78	<0.001
Data imputation model, n = 16,428	0.65	0.56–0.75	<0.001
Competing risk model, n = 10,717	0.63	0.51–0.77	<0.001
PS matching model, n = 1384	0.74	0.58–0.95	0.02
Sensitivity analysis (multivariable Cox PH regressions)			
90 days, n = 8982	0.54	0.40–0.73	<0.001
180 days, n = 9968	0.62	0.49–0.78	<0.001
Restricted to large HHD and PD centers, n = 2736[a]	0.70	0.53–0.93	0.02
Stratification by era of KRT initiation (multivariable Cox PH regressions)[b]			
2000–2005, n = 3,341	0.47	0.31–0.70	<0.001
2006–2010, n = 4,391	0.70	0.54–0.89	0.004
2011–2013, n = 2,985	0.86	0.51–1.47	0.59

CI, confidence interval; HHD, home hemodialysis; HR, hazard ratio; KRT, kidney replacement therapy, PD, peritoneal dialysis; PH, proportional hazard; PS, propensity score.
[a]Large HHD, >3 new patients yearly; large PD, >20 new patients yearly.
[b]*P* for interaction = 0.10.

Era Effect and Comparative Mortality Risk

Crude mortality rates decreased with peritoneal dialysis over subsequent years. In contrast, mortality rates appeared mostly stable with HHD (Figure 2 and Supplementary Figure S2). The mortality risk of HHD compared with PD became less pronounced with home dialysis initiation in more recent eras (2000−2005: aHR = 0.47, 95% CI = 0.31−0.70; 2006−2010: aHR = 0.70, 95% CI = 0.54−0.89) and was not statistically significant in the most recent era (2011−2013: aHR = 0.86, 95% CI = 0.51−1.47, *P* for interaction = 0.10, using the main Cox proportional hazards analysis) (Table 3, Figure 3). Of note, median follow-up time was 2.6 (1.4−4.5) years for the 2000 to 2005 cohort, 3.4 (1.7−4.9) years for the 2006 to 2010 cohort, and 1.6 (1.0−2.3) years for the 2011 to 2013 cohort. The adjusted HR for death and treatment failure with HHD compared to PD, stratified by years of KRT initiation, are displayed in Table 4.

Subgroup Analysis

There was no statistically significant interaction between home dialysis modality and prespecified covariables. However, era, center size, time on facility hemodialysis before home dialysis start, and follow-up duration after home dialysis start showed a marked interaction trend. Specifically, the association between HHD and lower mortality was more marked with earlier era, small center size, shorter time on facility hemodialysis prior to home dialysis, and longer follow-up duration (Figure 3).

Compared to PD, initiation of dialysis with intensive HHD was associated with the lowest mortality risk (aHR = 0.56, 95% CI = 0.37−0.85), although "non-intensive" HHD was also significantly associated with a lower risk of mortality (aHR = 0.67, 95% CI = 0.54−0.83), and confidence intervals were mostly similar (Supplementary Figure S3).

Sensitivity Models

To address the possibility of survivor bias (i.e., selective inclusion of patients who survived the high-risk post-KRT period and initiated home dialysis later), the analyses were restricted to those who started on home dialysis <90 days and <180 days after KRT inception, and yielded globally consistent findings (Table 3). Specifically, for patients who started very early (<90 days after KRT) on home dialysis, the point estimate was lower, showing a stronger association between HHD and lower risk of death The association between HHD and lower mortality was also comparable when restricting the analysis to larger dialysis centers with a mean annual number of new patients of >3 for HHD and >20 for PD during the study period (aHR = 0.70, 95% CI = 0.53−0.93, *P* = 0.02).

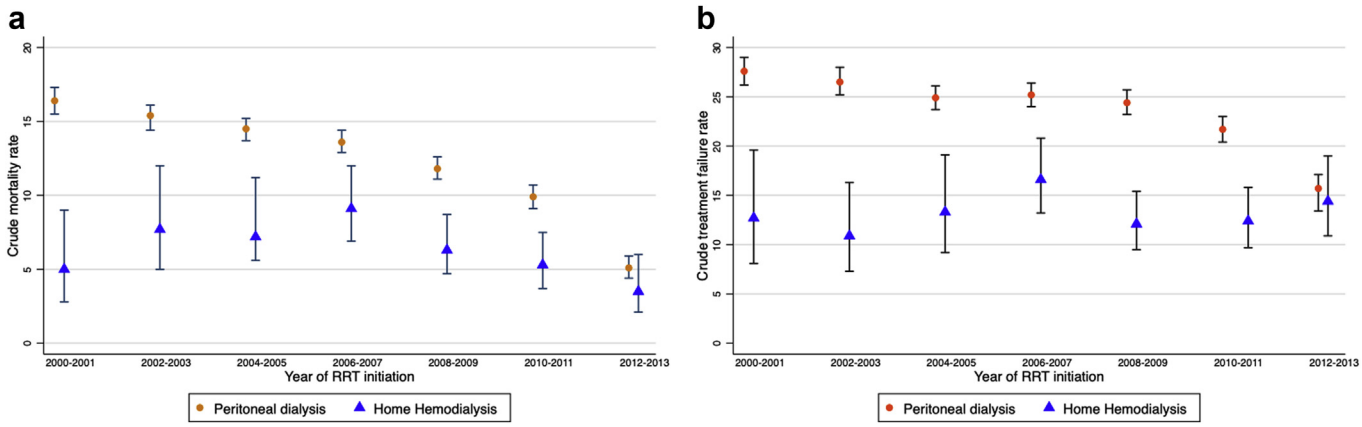

Figure 2. Crude mortality and treatment failure rates in incident home hemodialysis and peritoneal dialysis, stratified by year of kidney replacement therapy initiation from 2000 to 2013. RRT, renal replacement therapy.

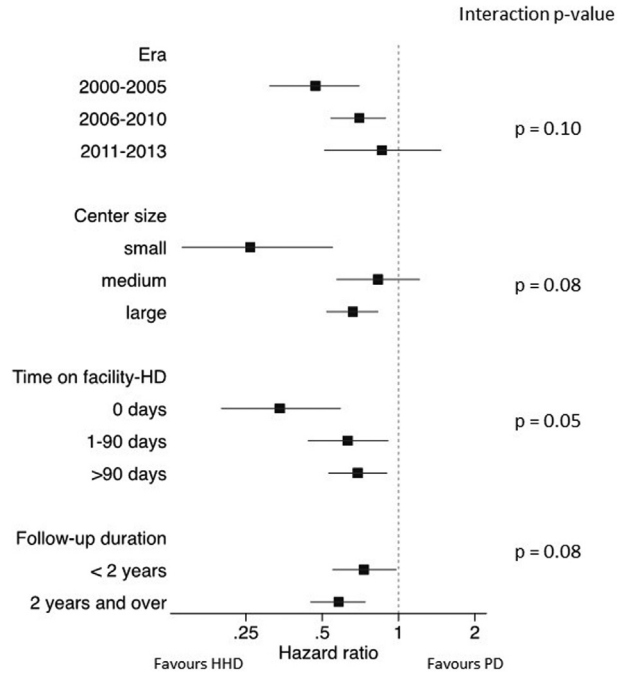

Figure 3. Adjusted hazard ratios for patient mortality in home hemodialysis compared to peritoneal dialysis (reference) between 2000 and 2013, in prespecified subgroup analysis, using multivariable Cox proportional hazard regressions (era, center size, time on facility hemodialysis) and a multivariable time-dependent Cox proportional hazard regression (follow-up duration).

Treatment Survival

Crude treatment survival was higher with HHD than with PD, with respective 1-, 2-, and 5-year technique survivals of 85%, 76%, and 53% in HHD patients and 82%, 64%, and 27% in PD patients. Treatment failure (defined as the composite of technique failure and death) was lower with incident HHD compared to incident PD, with a close to 50% risk reduction (aHR = 0.52, 95% CI = 0.45−0.60) (Table 3). Results were consistent when using other statistical approaches, including PS matching, data imputation, and competing risk model (Table 4).

The lower risk of treatment failure with HHD compared to PD also changed significantly over time and was attenuated in more recent eras (2000−2005: aHR = 0.34, 95% CI = 0.24−0.47; 2006−2010: aHR = 0.51, 95% CI = 0.42−0.62; 2011−2013: aHR = 0.75, 95% CI = 0.57−1.00, *P* for interaction <0.001) (Table 4, Figures 3 and 4). This era effect was apparently more related to lower rates of PD treatment failure over time, as HHD treatment failure rates remained globally stable or increased slightly (Figure 2).

DISCUSSION

In this registry study, incident HHD was associated with a 36% lower risk of death and a 48% reduction in treatment failure compared to incident PD. These associations were consistent through different statistical approaches and sensitivity models. Importantly, these associations were attenuated in more recent eras, such that mortality and treatment failure risks after incident HHD and PD were much more different in cohorts from earlier eras and more similar in recent years. The association between HHD and lower mortality was more pronounced in cohorts from smaller home dialysis centers and patients directly initiated on home dialysis at KRT start.

Globally, these study results are relatively consistent with findings from an ANZDATA registry study that reported a 53% reduction in mortality in 706 HHD patients compared with 10,710 PD patients.[9] However, this study was limited by the sole inclusion of patients started very early on home dialysis (within 90 days), which, especially for HHD, might have introduced a selection bias. In the present study, the primary analysis was conducted using a 365-day definition of incident home dialysis, which represents a more appropriate inclusion period considering that dialysis vintage at HHD start is frequently between 6 and 12 months.[22] In addition, the association of HHD with lower mortality compared to PD remained consistent when restricting the inclusion period to patients started on home dialysis <90 days after KRT start. Indeed, the effect size was more accentuated and closer to the 53% lower mortality reported in the ANZDATA registry study.

A recent small Swedish study also showed better survival with HHD compared to PD.[11] However, this study was limited by small sample size (152 HHD and 456 PD patients), inclusion of nearly half of the cohort before the year 2000, and a potential selection bias with very low comorbidity burden in the HHD cohort.[11]

In contrast, a study of USRDS data demonstrated lower mortality rates in 4201 prevalent HHD patients matched to 4201 PD patients, which was no longer statistically significant when the analysis was restricted

Table 4. Adjusted HR for treatment failure (including technique failure and death) in incident HHD compared to incident PD

Statistical model	HR	95% CI	*P*
Multivariable Cox PH model, n = 10,717	0.52	0.45–0.60	<0.001
Data imputation, n = 16,428	0.55	0.49–0.62	<0.001
Competing risk model, n = 10,717	0.54	0.47–0.63	<0.001
PS matching model, n = 1384	0.54	0.45–0.64	<0.001
Stratification by years of KRT start (multivariable Cox PH regressions)[a]			
2000–2005	0.34	0.24–0.47	<0.001
2006–2010	0.51	0.42–0.62	<0.001
2011–2013	0.75	0.57–1.00	0.05

CI, confidence interval; HHD, home hemodialysis; HR, hazard ratio; KRT, kidney replacement therapy; PD, peritoneal dialysis; PH, proportional hazard; PS, propensity score.
[a]*P* for interaction < 0.001.

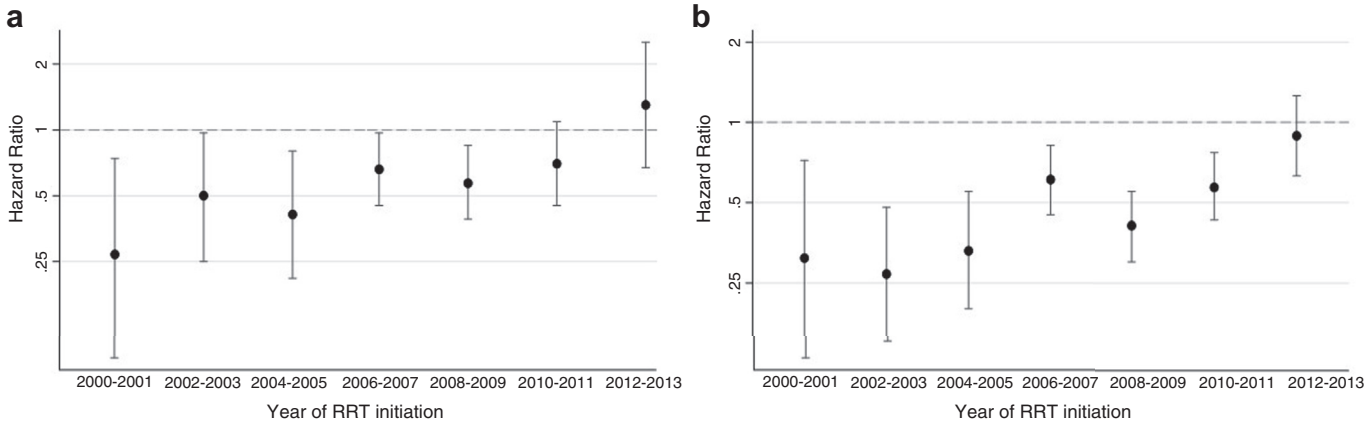

Figure 4. Adjusted hazard ratio for (a) mortality and (b) treatment failure in home hemodialysis compared to peritoneal dialysis (reference), stratified by year of renal replacement therapy (RRT) initiation from multivariable Cox proportional hazard regressions from 2000 to 2013.

to patients who started home dialysis within 6 months of KRT initiation.[10] It should also be noted that overall 1- and 2-year survival rates for incident home dialysis patients were much lower in this study (HHD: 89.1% and 79.7%, respectively; PD: 89.7% and 79.5%)[10] compared with the present study (HHD: 94% and 89%; PD: 92% and 81%). Other potential explanations for the apparent disparity in findings between the 2 studies may be related to differences in prescription patterns (short/daily vs. longer/nocturnal), modality (NxStage vs. standard hemodialysis), healthcare system structure, and patient characteristics.[1]

The present study showed that the lower mortality associated with incident HHD compared to PD was attenuated for the most contemporary cohorts. Although the interaction between years of dialysis start and modality did not reach statistical significance in the primary outcome analysis, it was statistically significant in the assessment of treatment failure. This is an important clinical finding when interpreting the result of this study for patients starting home dialysis, in whom the large survival benefit of HHD may not apply. Indeed, changes in HHD patient characteristics as HHD programs have become more confident with the modality and expanded may have underpinned the apparent convergence of outcomes between HHD and PD patients in more recent times. Perl *et al*. recently showed that HHD technique survival decreased in Canada during the years 2008 to 2012 compared to 2003 to 2007.[12] The authors reported a concurrent rise in patient age and changes in distribution of primary kidney disease and comorbidity through the years. Very similar findings were observed in the present study and are in line with greater accessibility of HHD therapy in Canada, a dialysis modality once reserved for exceptionally "healthy" patients. Changes in HHD prescription could also have contributed to this interaction with lower proportion of intensive hemodialysis in more recent cohorts. Of note, the percentages of intensive HHD in this cohort were 39%, 38%, and 35% in years 2000 to 2005, 2006 to 2010, and 2011 to 2013, respectively.

The survival differences reported in this study between incident HHD and PD are clinically significant. These findings should, however, be interpreted with caution and within their context, considering the observational nature of the data and the change over time. Specifically, duration of follow-up was shorter in the 2011 to 2013 cohort, which may have contributed to this finding. As reported in other home dialysis studies and represented in the baseline characteristics of this cohort, patients selecting PD and HHD are traditionally very different in terms of demographics and comorbidity burden, and statistical strategies may not always address these differences entirely.[9,17,23,24] In this study, the PS matching analysis showed a small attenuation in the protective association of HHD versus PD (aHR = 0.74 vs. 0.64 in the main model), which may validate this hypothesis. This small difference in effect size may also be related to the statistical approach specificity, whereby PS matching leads to estimation of the average treatment effect in the HHD population, rather than the average treatment effect in the incident home dialysis population. Likewise, centers with larger HHD programs (and offering both PD and HHD) also had a slight attenuation in the effect size associated with mortality on incident HHD compared to incident PD. The greater association of HHD with lower mortality compared to PD in smaller centers may involve stricter selection criteria favoring healthier patients for HHD in these centers less experienced with HHD therapy. Finally, cohorts initiated on home dialysis <90 days after KRT start had a stronger association with lower risk of death on HHD. This may be

the result of more optimal CKD follow-up and better preparation early initiation of HHD translating into an overall lower risk of death (i.e., indication bias).[9,25,26]

Of note, a previous ANZDATA study showed similar survival in patients treated directly with HHD and those initiated on PD and later switched to HHD, a sequence named the "integrated home dialysis model." This may reinforce the assumption that selection bias is involved in the remarkable survival differences reported in HHD versus PD studies.[27] It should also be recognized that modality selection should be based on an overall appreciation of the pros and cons of each modality and should include broader considerations such as lifestyle, quality of life, and specific individual goals.[3,4]

Finally, in this study cohort, the lower mortality observed with HHD compared to PD was more modest during the initial 2 years of home dialysis follow-up, and seemed more marked after 2 years. Trinh *et al*. recently reported a similar trend for death-censored technique failure in Canadian home dialysis patients.[17] Indeed, in this study, death-censored technique failure was similar for HHD and PD during the first year of dialysis, but the risk subsequently became lower for HHD than for PD. Variation in causes of home dialysis technique failure may be involved in this temporal association.[28,29] Ultimately, this association is consistent with the integrated home dialysis model assumption that, in patients who are candidates for both home modalities, start of dialysis with PD and subsequent transfer to HHD may be an optimal pathway.[27]

This study has several strengths. It is the first Canadian study to directly compare survival in PD and HHD with a prespecified era effect assessment, using several adjustment strategies and sensitivity analysis. It included all patients started on home dialysis within the first year of dialysis from a country renowned for its expertise with home dialysis. There are, however, significant limitations that should be acknowledged. First, it is important to recognize that results from registry data are always restricted by the observational nature of the data and constrained to collected information. This precluded consideration and adjustment for other variables such as socioeconomic status and psychosocial characteristics, and may have led to residual confounding. Despite different adjustment strategies, patients treated with different dialysis modalities are intrinsically different, and, as stated above, these differences may not be totally accounted for in the present study, potentially affecting the reported associations. The number of missing data was also relatively large in this registry study, which may have introduced a bias, although the analysis with data imputation yield to consistent results. Finally, it should be noted that the primary exposure was defined as home dialysis initiation as opposed to "intention to initiate or attempt at home dialysis training." It is possible that a number of individuals who were interested in PD or HHD either failed to complete training or were no longer deemed eligible. These patients may have been inconsistently included in either cohort. The effect of this could be more pronounced in HHD patients because of the duration and complexity of training.[30]

In conclusion, this Canadian registry study showed that incident HHD was associated with a 36% lower mortality and 48% lower treatment failure compared to incident PD. These differences were, however, attenuated in more contemporary cohorts, with mortality being not statistically different for PD and HHD in the 2011 to 2013 cohort. These findings may be possibly related to the inclusion of higher-acuity patients in HHD programs over time and simultaneous improvement in PD technique and patient survival, such that they should be confirmed in other contemporary cohorts.

DISCLOSURE

ACN-F has a scholarship from Les Fonds de la Recherche du Québec en Santé (FRQS) and has received previous speaker honoraria from Baxter and previous investigator-initiated grant support Baxter CEC grant. KKT, not relevant to the current submission, has received unrestricted grant funding from Otsuka, Canada and Astellas, Canada for investigator-initiated research projects, and has attended Advisory Boards for Otsuka, Astra-Zeneca, Baxter, and Janssen. JP has consulted for Baxter Healthcare, DaVita, and liberDi and has received speaker honoraria from Astra Zeneca, Baxter International, DaVita Healthcare partners, Dialysis Clinic Inc., Satellite Healthcare, and Fresenius Medical Care. JMB has been a Consultant for Baxter Canada and DaVita Healthcare Partners. DWJ has received personal fees from AWAK, Astra-Zeneca, Ono, Baxter Healthcare, and Fresenius Medical Care, and grant support from Baxter Extramural and Baxter CEC Grants. CT Chan holds the R Fraser Elliott Chair in Home Dialysis and has consulted for Baxter, Medtronic, and NxStage. He has also received investigator-initiated grant support from Baxter CEC grant program and Medtronic ERP program.

SUPPLEMENTARY MATERIAL

Supplementary File (PDF)

Table S1. Baseline characteristics in matched cohorts.

Table S2. Associations between covariates and mortality in incident home dialysis patients in the Cox proportional hazard model.

Table S3. Missing values in baseline characteristics.

Figure S1. Standardized differences before and after matching.

Figure S2. Crude mortality (A) and treatment failure (B) rates with fixed 3-year follow-up, stratified by year of kidney replacement initiation, per 100 patient-years.

Figure S3. Unadjusted survival with Intensive home hemodialysis versus "nonintensive" home hemodialysis versus peritoneal dialysis (log-rank $P < 0.001$).

STROBE Checklist.

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