Nephrol Dial Transplant (2012) 27: 3568–3575
doi: 10.1093/ndt/gfr674
Advance Access publication 5 March 2012

Original Articles

NDT
Nephrology Dialysis Transplantation

Hemodialysis and peritoneal dialysis are associated with similar outcomes for end-stage renal disease treatment in Canada

Karen Yeates[1], Naisu Zhu[2], Edward Vonesh[3], Lilyanna Trpeski[4], Peter Blake[5] and Stanley Fenton[6]

[1]Department of Medicine, Queen's University, Kingston, Ontario, Canada, [2]Canadian Institute for Health Information, Ottawa, Ontario, Canada, [3]Department of Preventive Medicine, Feinberg School of Medicine, Northwestern University, Chicago, IL, USA, [4]The Renal Disease Registry, Toronto, Ontario, Canada, [5]Department of Medicine, The University of Western Ontario, London Health Sciences Centre, London, Ontario, Canada and [6]Division of Nephrology, University Health Network, Department of Medicine, University of Toronto, Toronto, Canada

Correspondence and offprint requests to: Karen Yeates; E-mail: yeatesk@queensu.ca

Abstract

Background. There were 35 265 patients receiving renal replacement therapy in Canada at the end of 2007 with 11.0% of patients on peritoneal dialysis (PD) and 48.9% on hemodialysis (HD) and a remaining 40.1% living with a functioning kidney transplant. There are no contemporary studies examining PD survival relative to HD in Canada. The objective was to compare survival outcomes for incident patients starting on PD as compared to HD in Canada.

Methods. Using data from the Canadian Organ Replacement Register, the Cox proportional hazards (PH) model was employed to study survival outcomes for patients initiating PD as compared to HD in Canada from 1991 to 2004 with follow-up to 31 December 2007. Comparisons of outcomes were made between three successive calendar periods: 1991–95, 1996–2000 and 2001–04 with the relative risk of death of incident patients calculated using an intent-to-treat (ITT) analysis with proportional and non-PH models using a piecewise exponential survival model to compare adjusted mortality rates.

Results. In the ITT analysis, overall survival for the entire study period favored PD in the first 18 months and HD after 36 months. However, for the 2001–04 cohort, survival favored PD for the first 2 years and thereafter PD and HD were similar. Among female patients > 65 years with diabetes, PD had a 27% higher mortality rate.

Conclusions. Overall, HD and PD are associated with similar outcomes for end-stage renal disease treatment in Canada.

Keywords: hemodialysis; outcomes; peritoneal dialysis; survival

Introduction

Peritoneal dialysis (PD) is an effective form of renal replacement therapy (RRT) that has been in widespread use since the 1980s. Despite a number of studies that describe PD as conferring similar or superior patient outcomes when compared to hemodialysis (HD), the number of incident PD patients has fallen in the USA and Europe, leaving HD as the prominent modality [1–3]. In comparison, the incidence of PD in Canada has remained relatively stable over time; however, proportionally, PD as an initial dialysis modality has declined from 37% in 1991 to 18% in 2007 in Canada [4]. PD has emerged as a reliable and effective modality in many other parts of the world including Asia and Central and South America [5–8]. There were an estimated 35 265 patients receiving RRT in Canada at the end of 2007 with 11.0% of patients on PD and 48.9% on HD. Among 5256 incident patients on dialysis in 2007, 18.1% initiated dialysis on PD [4]. The falling incidence of PD in some developed countries may be due to a variety of causes including (i) historical survival comparisons [9–11] suggesting PD survival is inferior to HD especially in certain subgroups such as people with diabetes, (ii) changes over time in nephrology fellowship training program content of PD and exposure to varying dialysis practice patterns among nephrologists in HD intensive centers, (iii) changes in patient case-mix with increasing co-morbidity level and prevalence of diabetes mellitus (DM) as well as age among incident patients starting dialysis and (iv) rising availability of HD satellite units allowing delivery of this modality of RRT closer to the patients' homes.

Although assigning patients to a dialysis modality is not a random process, statistical comparisons can attempt to minimize confounding through the use of appropriate statistical models. However, older methods did not always account for incident and prevalent patients, dialysis modality switches or even baseline co-morbidity. Newer statistical methods, especially those using time-dependent covariates allow for more robust survival comparisons but do not replace a head-to-head comparison of a randomized controlled trial in PD versus HD survival. A prior

attempt at such a randomized trial failed [12] and it is unlikely that subsequent attempts will occur given that for many patients starting RRT, the important element of patient choice cannot be disregarded especially for those patients who have no contraindications to either modality.

In one Canadian study published > 10 years ago, PD was found to have a significant survival advantage to HD overall [13]. This survival benefit was most prominent in younger patients within the first 2 years of therapy. A subsequent Canadian cohort study showed that among the 822 patients enrolled between March 1993 and November 1994 (with follow-up to 1998) that after adjustment for important covariates, there was no difference in survival between PD and HD [14]. No subsequent contemporary studies have been published regarding PD survival as compared to HD in Canada in the current era.

Despite the knowledge that home dialysis therapies such as PD may provide improved quality of life [15] with potential for reduced cost in Canada [16]; given secular trends and the changing case-mix of dialysis patients in Canada who tend to be older and carry higher co-morbidity levels, we hypothesized that PD survival, as compared to HD, may have worsened in the study period and in particular during the most contemporary cohort selected. Using data from the Canadian Organ Replacement Register (CORR), we present survival outcomes for incident patients initiating PD as compared to HD in Canada from 1991 to 2004 with follow-up to 31 December 2007.

Materials and methods

Data source

The de-identified data (data set with patient names removed and coded to ensure confidentiality) for all incident dialysis patients over a 17-year period—1991 through 2007—were obtained from the CORR a clinical register of the Canadian Institute for Health Information. CORR is a population-based national registry that includes all reported cases of RRT as well as baseline demographic data (age, gender, location of dialysis centre, self-reported race) and baseline co-morbidities (presence of diabetes, cardiovascular disease, cerebrovascular disease, pulmonary disease, hypertension, peripheral vascular disease, malignancy, smoking history) in addition to primary renal diagnosis and modality on individual patients at the time of dialysis initiation. All data are collected and submitted by the treatment center. Dates of death, dialysis modality switches, renal transplantation or withdrawal from dialysis are updated annually by the dialysis centers and submitted to the CORR.

Definitions

For an intent-to-treat (ITT) analysis, the dialysis modality 90 days after the first service date was considered to be the initial modality. Thus, patients who died or were censored prior to Day 90 would be excluded from the ITT analysis. For a time-dependent as-treated (AT) analysis, patients were assigned to their initial modality (PD versus HD) based on their first service date and were reclassified to be on a new modality whenever a switch was made. For patients whose last date of follow-up was < 60 days following a change to their modality, the event (death) was attributed to the patient's prior modality. For these analyses, PD and HD patients include patients dialyzed in hospital, community dialysis center (satellite unit) or at home with total self-care or limited self-care. Patients under 18 years of age, having pre-emptive renal transplant or extra-renal transplant were excluded.

Covariates

Hazard ratios (HR) and corresponding 95% confidence intervals (CI) were adjusted for case-mix differences in cohorts, region, age, gender, race, cause of primary renal disease, diabetes and co-morbidity as measured by the Charlson Index [17, 18].

Statistical analyses

Baseline characteristics of PD and HD patients were compared using Pearson's chi-square tests for categorical variables and the Student's *t*-test for continuous variables. Patients were followed until the time of transplant, death, loss to follow-up or 31 December 2007, whichever happened first. Proportional hazards (PH) and non-PH models using a piecewise exponential survival model were used to compare case-mix adjusted mortality rates between PD and HD at successive 6-month intervals through the first 60 months [19–21]. Average or time-independent HR of death for PD compared to HD patients were estimated using a PH model, while time-dependent HR and cumulative hazard ratios (CHR) were estimated with a non-PH model. All analyses were done using the SAS statistical software package version 9.2 (SAS, Inc., Cary, NC); in particular, the GENMOD procedure was used to fit the data using a piecewise exponential survival model (both PH and non-PH) as implemented via interval Poisson regression. As has been demonstrated previously, these results will be nearly identical with those obtained under the Cox model [19]. The advantage of the piecewise exponential survival model over the Cox model is that under the ITT analysis, it can be used to provide an adjusted population-averaged ITT survival curve for PD and HD patients that corresponds directly with the time-dependent CHR obtained from the more realistic and flexible non-PH model.

The primary analysis was carried out using an ITT approach in which death was assigned to a patient's initial treatment modality regardless of a change in therapy during the course of follow-up. A time-dependent AT analysis was also performed in which death was assigned to the modality the patient was on at the time of the event or to the patient's prior modality in those cases where the patient switched from PD to HD or vice versa, within 60 days of dying. In this latter case, any event (i.e. death, transplant or loss to follow-up) that occurred within 60 days following a change in modality was attributed to the prior treatment modality. Actuarial technique survival by modality was calculated for each cohort. Finally, adjusted population-averaged survival curves were computed using an adaptation of the direct-adjusted survival curve approach described by Zhang *et al.* [22]. Specifically, we computed population-averaged estimates of the adjusted cumulative hazard function which, when exponentiated, yields direct-adjusted survival curve estimates. From these, adjusted median life expectancies were computed using life table methodology [23]. We also compute an adjusted CHR, defined as the ratio of the adjusted cumulative hazard functions for PD versus HD. Under a non-PH model, the CHR is a moving average of the time-specific HR. As such, it provides a measure of the cumulative treatment effect over time for PD versus HD in an ITT analysis. Moreover, 95% CI on the CHR provides a direct test of whether the survival curves between PD and HD are significantly different from one another at a particular moment in time. For example, if the 95% CI on the CHR at 1 year includes the value of 1.0, then this indicates that there is no significant difference in 1-year survival between PD and HD. The estimated CHR under the piecewise exponential non-PH model is similar to that presented by Wei and Schaubel [24] for the Cox non-PH model. It should be noted that neither the adjusted CHR nor the adjusted survival curves may be computed under an AT analysis where treatment modality serves as time-dependent internal covariate [25]. CI and P-values for select subgroup analyses were adjusted for multiple comparisons using Sidak's method [26]. This included examining mortality differences in patients with diabetes over time as calculated through the ITT model. In addition, survival was also calculated under a PH model for diabetes and gender. The study protocol was reviewed and approved by the Institutional Review Board at Queen's University, Kingston, Ontario.

Results

Patient characteristics

There were a total of 46 839 patients who started RRT on PD or HD during the study time period. Of these, 32 531 (69.5%) were incident on HD and 14 308 (30.5%) were incident on PD. Table 1 displays demographic and clinical characteristics of the study patients. The study subjects were more likely to be male and over the age of 65 years.

Table 1. Patient characteristics

Category	HD n	HD %	PD n	PD %	P-value
All	32 531	100	14 308	100	
Aqnge					
18–34	1943	6.0	1234	8.6	<0.0001
35–44	2450	7.5	1599	11.2	
45–54	4242	13.0	2322	16.2	
55–64	6496	20.0	3142	22.0	
65–74	9592	29.5	3836	26.8	
75–84	6888	21.2	1976	13.8	
85+	920	2.8	199	1.4	
Gender					
Female	13 108	40.3	6171	43.1	<0.0001
Male	19 423	59.7	8137	56.9	
Racial Origin					
Caucasian	24 449	75.2	10 637	74.3	<0.0001
Aboriginal	1663	5.1	573	4.0	
Asian	1430	4.4	1016	7.1	
Black	998	3.1	441	3.1	
Other	3991	12.3	1641	11.5	
Region					
0	10 474	32.2	4239	29.6	
1	2908	8.9	1723	12.0	
2	5812	17.9	2251	15.7	
3	13 337	41.0	6095	42.6	
Incident year					
1991–95	6760	20.8	5327	37.2	<0.0001
1996–2000	12 527	38.5	5128	35.8	
2001–04	13 244	40.7	3853	26.9	
Primary renal primary renal diagnosis					
Glomerulonephritis	4676	14.4	2798	19.6	<0.0001
Diagnosis					
Diabetes	10 477	32.2	4806	33.6	
Vascular	6865	21.1	2629	18.4	
Others	10 513	32.3	4075	28.5	
Diabetes status					
Diabetic	13 205	40.6	5615	39.2	0.033
Non-diabetic	19 326	59.4	8693	60.8	
Charlson co-morbidity index					
2	11 037	33.9	6430	44.9	<0.0001
3	7299	22.4	3253	22.7	
4–5	8862	27.2	3185	22.3	
≥6	5333	16.4	1440	10.1	

Patients aged ≥65 years made up 53.5% of the patients initiating dialysis on HD and 42% of those initiating PD during the study period. Patients with diabetes accounted for 40% of patients on HD and 39.2% of those on PD. The majority of study subjects were Caucasian (75.2% on HD and 74.3% on PD).

Overall comparison of outcomes of incident HD and PD patients by cohort period

Table 2 displays the adjusted HR under a PH model for the ITT and AT analyses for the entire study population as well as by the three cohort periods, 1991–95, 1996–2000 and 2001–04. These time-independent HR suggest a trend of improving outcomes on PD versus HD as reflected by the lack of an overall difference in the HR for the 2001–04 cohort compared to prior cohort periods. However, a better indication of the differences in the risk of death between PD and HD is presented in Figure 1 wherein the CHR from an ITT analysis is plotted against time for the entire population as well as the three cohort periods. The adjusted CHRs are computed under a non-PH model and, as depicted in Figure 1, reflect the early survival advantage associated with PD through 2 years of follow-up after which there is a survival advantage associated with HD. As with the time-independent HR shown in Table 2, the trend in the CHR across the cohort periods suggests that based on the most recent CORR data (i.e. the 2001–04 cohort), patients receiving PD as their initial therapy are associated with better 2-year survival compared to HD after which survival is no longer different between PD and HD patients. These trends are also reflected in the adjusted population-averaged survival curves shown in Figure 2. Figure 3 displays actuarial technique survival by cohort period and overall for all cohorts for the follow-up period of 60 months. An early separation of technique survival occurs between the two modalities with PD technique survival beginning to fall at 10 months.

Table 2. Adjusted HRs (PD:HD) under a PHs model[a]

Group	HR ITT (95% CI)	HR AT (95% CI)
Overall (1991–2004)	1.08 (1.04–1.11)**	1.08 (1.05–1.11)**
1991–95	1.08 (1.02–1.15)*	1.10 (1.03–1.17)*
1996–2000	1.13 (1.07–1.20)**	1.15 (1.08–1.22)**
2001–04	0.99 (0.92–1.06)^{NS}	0.98 (0.92–1.05)^{NS}

[a]NS, not significant (P > 0.05).
*P-value < 0.05, **P-value < 0.001.

Outcome of incident HD and PD patients stratified by age and diabetes status for the ITT and AT models

Table 3 displays the adjusted HR from a PH model for the ITT analysis and the AT analyses for the diabetic and non-diabetic subgroups by age group. In the overall ITT model, for the 18–44 years age group without diabetes, there is a 25% lower mortality rate, on average, for PD versus HD (HR = 0.75, CI: 0.57–0.99, P < 0.05). Similarly, in the same group for the AT analysis, there is a 30% lower mortality rate for PD compared to HD (HR = 0.70, CI: 0.53–0.93, P < 0.05). For the 45–64 years non-diabetic subgroup, there was no statistically significant difference between PD and HD survival in the ITT analysis (HR = 0.90, CI: 0.79–1.01), but in the AT analysis of the same subgroup, there was a 15% lower mortality rate, on average, for PD versus HD (HR: 0.85, CI: 0.75–0.96, P < 0.05). For the non-diabetic over 65 years of age subgroup, there were no differences in survival between PD and HD in both the ITT and AT analyses. For patients with diabetes, there was no difference in survival between PD and HD in the 18–44 years age group (HR = 0.99, CI 0.81–1.23. However, for patients with diabetes in both the 45–64 years and the > 65 years age groups, there was an 11 and 19% higher rate of mortality, on average, for PD, respectively, as compared to HD (HR = 1.11, CI: 1.02–1.22, P < 0.05) and (HR = 1.19, CI: 1.11–1.29, P < 0.001).

Table 4 displays the adjusted HRs estimated from a PH model for patients with diabetes for both the ITT and AT analyses by gender and age grouping. In the ITT analysis, the 18–64 age group, there was no survival difference between

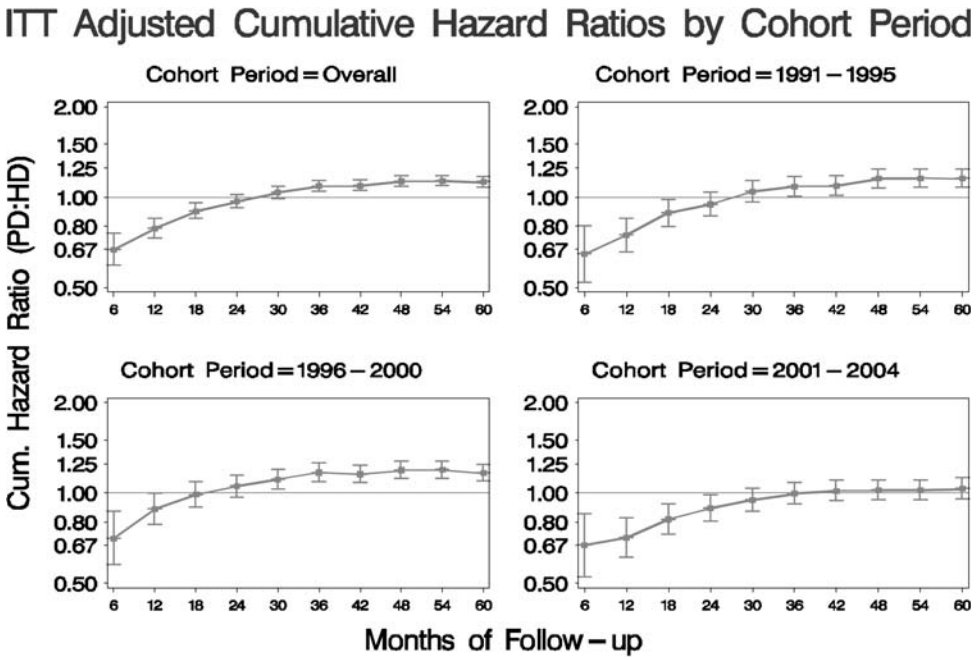

Fig. 1. ITT adjusted cumulative HRs by cohort period.

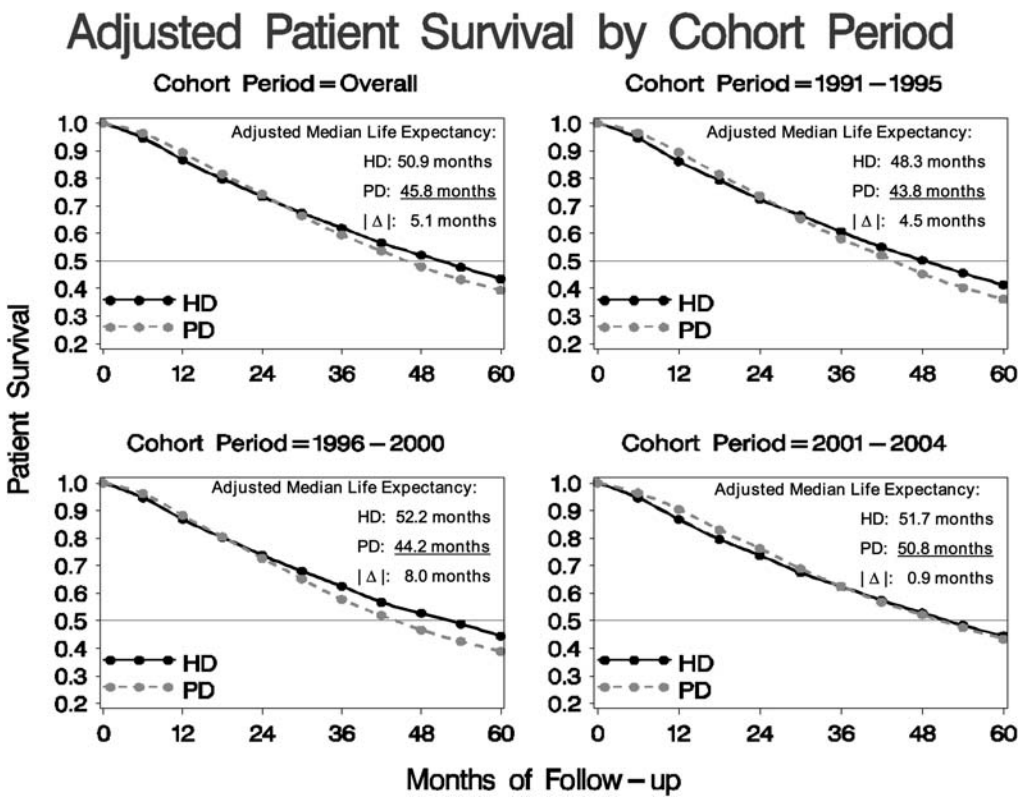

Fig. 2. Adjusted patient survival by cohort period.

HD or PD survival for males or females with diabetes. For the AT analysis, there was a 23% increased mortality ($P < 0.001$) for females with diabetes in this age group. For patients with diabetes in the 65 years and older age groups, there was increased mortality for PD as compared to HD for both males and females in both the ITT and AT analyses.

Table 5 displays the overall adjusted HR (PD:HD) under a PH model by diabetes status and gender. For patients without diabetes, there was no difference in survival for PD as compared to HD in both the ITT and AT analyses. In patients with diabetes, significant differences in survival in both males and females were noted in both

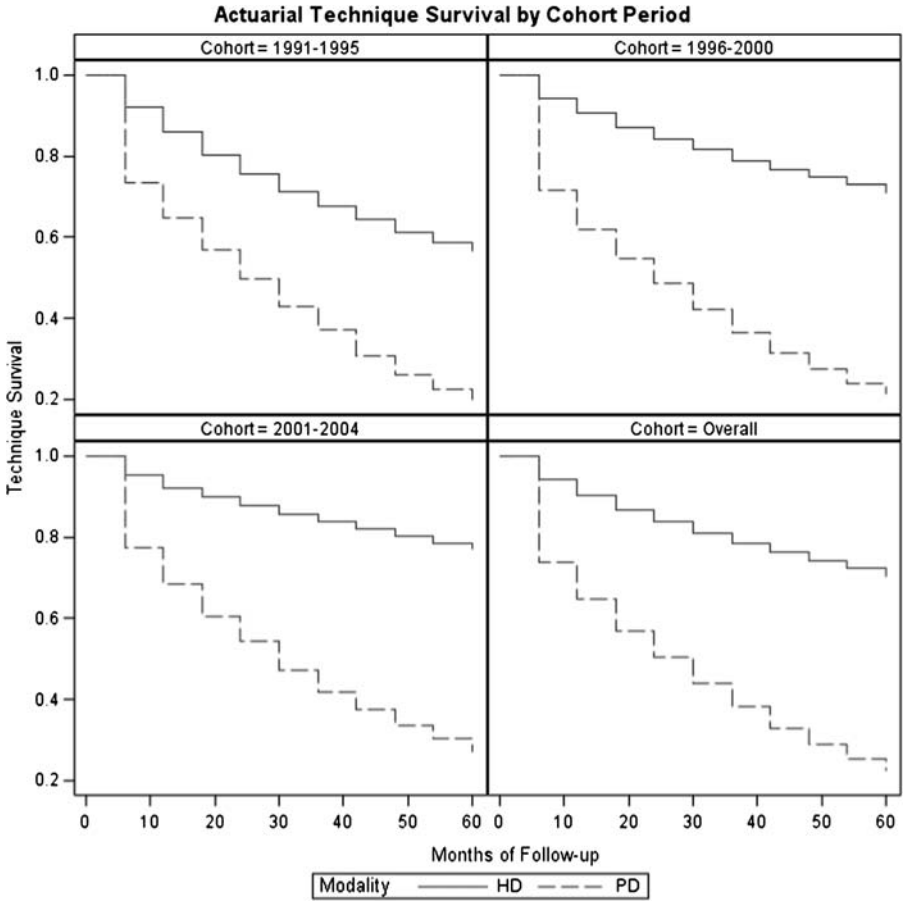

Fig. 3. Actuarial technique survival by cohort period.

Table 3. Adjusted HRs (PD:HD) under a PHs model results by type of patient and age[a]

Patient type	Age	HR ITT (95% CI)	HR AT (95% CI)
Non-DM	18–44	0.75 (0.57–0.99)*	0.70 (0.53–0.93)*
	45–64	0.90 (0.79–1.01)^{NS}	0.85 (0.75–0.96)*
	65+	1.05 (0.98–1.12)^{NS}	1.04 (0.97–1.11)^{NS}
DM	18–44	0.99 (0.81–1.23)^{NS}	0.91 (0.74–1.12)^{NS}
	45–64	1.11 (1.02–1.22)*	1.20 (1.09–1.31)**
	65+	1.19 (1.11–1.29)**	1.26 (1.16–1.36)**

[a]NS, not significant ($P > 0.05$).
*P-value < 0.05, **P-value < 0.001.

models. For the ITT and AT models, respectively, males on PD had a 12% overall higher mortality when compared to males on HD and females had a 19 and 33% higher mortality when compared to females with diabetes on HD.

Table 6 displays the evolution of mortality differences by gender in patients with diabetes over the selected time periods using the ITT model. For the overall period of 1991–2004, significantly higher mortality was seen in both females (28%) and males (19%) with diabetes on PD as compared to HD. In general, when observing the mortality trends over each successive time period, females with diabetes had higher mortality than males on PD when compared to people with diabetes on HD in that same time period.

Discussion

This is the largest contemporary comparison of survival to date in Canadian RRT patients who began treatment with HD as compared to those who began treatment with PD. Contrary to our hypothesis that overall, survival has worsened for PD as compared to HD in Canada over the study period from 1991 to 2004, we showed that, based on an ITT analysis using a PH model, overall adjusted survival for the most recent cohort (2001–04) remains similar for PD and HD with an average HR of 0.99 (CI: 0.92–1.06). This is in keeping with results from similarly conducted analyses that include historical Canadian survival data [13] and previous results from other countries including the USA and Denmark [27–29]. Moreover, when we applied an ITT analysis using a non-PH model, our examination of adjusted CHRs comparing PD versus HD over time and by calendar cohort period showed that for the most recent cohort of 2001–04, patients receiving PD were associated with significantly better survival during the first 2 years of dialysis and that long-term survival (3–5 years) was similar for PD and HD patients. Technique survival was also examined for each cohort and overall and, as expected, highlights the significant issue of lower technique survival in PD versus HD. There was a small improvement in technique survival in PD from the 1991 to 1995 cohort as compared to the 2001 to 1004 cohort.

Table 4. Adjusted HRs (PD:HD) under a PHs model results for DM patients by age and gender[a]

Age	Gender	HR ITT (95% CI)	HR AT (95% CI)
18–64	Male	1.08 (0.98–1.20)^{NS}	1.08 (0.97–1.21)^{NS}
	Female	1.10 (0.98–1.25)^{NS}	1.23 (1.09–1.39)**
65+	Male	1.14 (1.04–1.26)*	1.15 (1.04–1.27)*
	Female	1.27 (1.13–1.42)**	1.41 (1.26–1.58)**

[a]NS, not significant (P > 0.05).
*P-value < 0.05, **P-value < 0.001.

Table 5. Overall adjusted HR (PD:HD) under a PH model results by diabetic status and gender[a]

Diabetic status	Gender	HR ITT (95% CI)	HR AT (95% CI)
Non-DM	Male	1.01 (0.96, 1.06)^{NS}	0.98 (0.93, 1.03)^{NS}
	Female	0.99 (0.92, 1.05)^{NS}	0.98 (0.92, 1.05)^{NS}
DM	Male	1.12 (1.06, 1.18)**	1.12 (1.06, 1.19)**
	Female	1.19 (1.12, 1.27)**	1.33 (1.24, 1.42)**

[a]NS, not significant (P > 0.05).
*P-value < 0.05, **P-value < 0.001.

Table 6. Evolution of mortality differences in diabetic patients ITT model[a]

	Risk ratio (PD:HD)	
Cohort	HR Female (95% CI)	HR Male (95% CI)
Overall (1991–2004)	1.28 (1.20–1.36)**	1.19 (1.13–1.26)**
1991–95	1.17 (1.04–1.31)*	1.04 (0.94–1.16)^{NS}
1996–2000	1.23 (1.11–1.36)**	1.19 (1.09–1.30)**
2001–04	1.17 (1.04–1.33)*	1.11 (1.00–1.22)*

[a]NS, not significant (P > 0.05).
*P-value < 0.05, **P-value < 0.001.

We speculate that this may be a reflection of improved catheter and exchange techniques over time.

Our examination of incident dialysis patients with diabetes is in keeping with previously published outcomes in the USA [9–11]. In the current analysis, in patients without diabetes, for all age groups, PD is associated with similar or better survival than HD. For those aged ≥45 years, PD has similar survival as compared to HD in the first 2 years of treatment. After 2 years, the survival advantage switches to HD. Furthermore, we show that the survival advantage of HD increases with increasing age groups in patients with diabetes, with the highest mortality on PD compared with HD seen in female patients with diabetes who are over the age of 65. These incrementally higher mortality rates seen in older female DM patients on PD were not seen to the same degree in older male patients with diabetes. This is in keeping with previous studies from the USA that have shown less favorable outcomes on PD compared with HD in patients with diabetes, ischemic heart disease and congestive heart failure [9–11]. When overall survival was compared specifically for males and females, mortality was significantly higher for PD in both genders for patients with diabetes. The analysis that compares male and female patients with diabetes in the < 65 and > 65 age groups again highlights that the lower survival of females with diabetes on PD versus HD is highly age dependent. Furthermore, when mortality differences were examined through the ITT model over time specifically for males and females with diabetes, a significant survival disadvantage existed for both female and male patients throughout the follow-up period and for virtually every cohort period except for males in the earliest period 1991–95. Furthermore, we did not observe improvement in outcomes by cohort periods for patients with diabetes that were observed for all patients overall.

Despite differences in previous studies that examined high-risk subgroups, it is noteworthy that our results are similar to a previous large study [27] that examined the interaction of age and diabetic status using United States Renal Data System data and similarly adjusted for cohort effect and found that among the patients with no significant co-morbidity, mortality rates for patients without diabetes were significantly higher for HD compared to PD for all age groups for the calendar period 1995–2000.

Historically, there have been conflicting results published with respect to mortality comparisons between PD and HD. Several previous studies using either large-scale registry data or prospective cohort studies have shown that HD has better outcomes than PD [9–11], while others have shown that PD and HD have comparable outcomes [27–30]. The variation in the findings from all these studies may partly reflect real international differences in patient case-mix, in patterns of modality allocation and in dialysis practices. However, differences in statistical analysis likely also contribute. Registry-based studies vary with regard to inclusion of prevalent versus incident patients, use of 'intent-to-treat' versus 'as-treated' analysis, correction for baseline demographics and co-morbidity, duration of follow-up and approach to modality switching. Key issues that must be considered are the realization that hazards do not stay proportionate with time and the consistent finding that there are interactions between survival by modality and age, co-morbidity and time on dialysis. These issues have been reviewed with respect to the USA (but still carry relevance for Canadian studies) by Vonesh *et al.*[31]. For example, in the Vonesh *et al.* comparison, they showed that the overall time-independent adjusted HR comparing PD to HD went from 1.07 (HR = 1.07, CI: 1.04–1.09, P < 0.001) for patients incident in 1995–97 to 1.01 (HR = 1.01, CI: 0.98–1.04, P = not significant) for patients incident from 1998–2000. Their result suggests that improvements in patient survival over time were significantly greater among PD patients compared to HD patients [31]. Accordingly, efforts have made to adjust for these factors in our analysis using techniques such as time-dependent covariate analysis.

It is important to highlight that we also found that there was an improvement in outcomes on PD relative to HD in the 2001–04 as compared to the prior cohorts. This strengthens the argument that differences in survival in previously published studies may, in part, be impacted by an overall trend in improved patient survival on PD compared to HD, especially in young patients and non-diabetic subgroups.

Our study has several limitations. First, the selection of subjects for our analysis is not random and provides

associative causality only. The lack of randomization does not allow us to adjust for all forms of potential bias. Second, the use of registry-based data, while providing for large study size and significant amounts of patient data to allow for adjustment of covariates and subgroup analyses, it provides us only with the specific clinical and demographic variables that are collected in CORR. Furthermore, these data elements are not current, but updated annually, and may be subject to error or missing data elements. In general, < 10% of data are missing and the missing data or error in data entry is likely to be non-systematic in nature. Third, mortality may be under reported, and, if so, we cannot determine if the underreporting is random or not. Additionally, the outcome variable is recorded as all causes of death and not renal-specific death. It is not known if the causes of death are evenly distributed in PD and HD patients. Fourth, our study findings may have been confounded by unmeasured laboratory tests, comorbidity or socio-economic factors not captured by CORR. Lastly, our statistical methods did not adjust for the probability of censoring. This lessens our ability to eliminate potential bias as the transplant rate for incident PD patients is higher than HD patients. A higher rate of renal transplantation in PD patients effectively removes healthier subjects from the analysis through censoring for renal transplant. For the purposes of our current analysis, adjusting for the probability of censoring for transplant would have only served to improve PD outcomes further.

We believe that our study results are an important and timely contribution to currently available dialysis outcomes that exist in the literature today. These survival outcomes will provide Canadian nephrologists with a large, current, albeit, non-randomized study that should be easily generalized to their patient case-mix.

It is clear that patients who initiate dialysis on PD are, by nature, inherently different from those who initiate RRT on HD. However, our study attempts to adjust for some of these differences by accounting for modality switches. This is an important feature as it is known that most modality switches that occur reflect patient switches from PD to HD, an important issue that has previously not been accounted for in prospective studies.

Lastly, this study should reaffirm that there are survival advantages to PD therapy in many patients especially in the first 1–2 years of dialysis initiation. It also suggests that there may be an advantage to HD initiation at dialysis outset for specific patient subgroups, especially elderly female patients with diabetes. This contemporary look at PD versus HD survival outcomes should not stir further controversy but rather support the notion that PD and HD should be seen as complementary modalities that when selected with the individual patient in mind may result in better patient and technique survival while promoting informed patient modality choice and potential cost savings.

Acknowledgements. We would like to thank the Canadian Organ Replacement Register for provision of the data and analytical support (Naisu Zhu) for our collaboration. We would like also to acknowledge the whole-hearted support of CORR by members of the Canadian Society of Nephrology, The Canadian Society of Transplantation, the Canadian Association of Nephrology Nurses and Technologists for their participation in CORR and their voluntary reporting of the data on patients entering RRT therapy in Canada without which CORR would not exist. The study sponsors had no role in study design; in the collection, analysis, and interpretation of data; in the writing of the report; or in the decision to submit the paper for publication.

Funding. Funding for analytical support was provided by The Canadian Organ Replacement Register for N.Z. and L.T. E.V. received consulting fees from Baxter Corporation for statistical consulting.

Conflict of interest statement. None declared.

(See related article by Noordzij and Jager. Survival comparisons between haemodialysis and peritoneal dialysis. *Nephrol Dial Transplant* 2012; 27: 3385–3387.)

References

1. Mehrotra R. Changing patterns of peritoneal dialysis utilization in the United States. *Perit Dial Int* 2007; 27 (Suppl 2): 551–552.
2. Stenzel B, Billon S, van Dijk PC *et al*. Trends in the incidence of renal replacement therapy for end-stage renal disease in Europe, 1990-1999. *Nephrol Dial Transplant* 2003; 18: 1824–1833.
3. Feest TG, Rajamahesh J, Byrne C *et al*. Trends in adult renal replacement therapy in the UK: 1982-2000. *QJM* 2005; 98: 21–28.
4. Canadian Institute For Health Information. *Treatment of End-stage Organ Failure in Canada, 1998-2007 CORR Annual Report*. Ottawa, ON: CIHI, 2009.
5. Lo WK. Peritoneal dialysis in the far East—an astonishing situation in 2008. *Pert Dial Int* 2009; 29 (Suppl 2): S227–S229.
6. Yu AW, Chau KF, Ho YW *et al*. Development of the "peritoneal dialysis first" model in Hong Kong. *Perit Dial Int* 2007; 27 (Suppl 2): S53–S55.
7. Cucto-Manzano AM, Rojas-Campos E. Status of renal replacement therapy and peritoneal dialysis in Mexico. *Perit Dial Int* 2007; 27: 142–148.
8. Plecoits-Filho R, Abensus H, Cucto-Manzano AM *et al*. Overview of peritoneal dialysis in Latin America. *Perit Dial Int* 2001; 27: 316–321.
9. Bloembergen WE, Port FK, Mauger EA *et al*. A comparison of mortality between patients treated with hemodialysis and peritoneal dialysis. *J Am Soc Nephrol* 1995; 6: 177–183.
10. Ganesh SK, Hulbert-Shearon T, Port FK *et al*. Mortality differences by dialysis modality among incident ESRD patients with and without coronary artery disease. *J Am Soc Nephrol* 2003; 14: 415–424.
11. Stack AG, Molony DA, Rahman NS *et al*. Impact of dialysis modality on survival of new ESRD patients with congestive heart failure in the United States. *Kidney Int* 2003; 64: 1071–1079.
12. Korevaar JC, Feith GW, Dekker FW *et al*. Effect of starting with hemodialysis compared with peritoneal dialysis in patients new on dialysis treatment: a randomized controlled trial. *Kidney Int* 2003; 64: 2222–2228.
13. Fenton SS, Schaubel DE, Desmeules M *et al*. Hemodialysis versus peritoneal dialysis: a comparison of adjusted mortality rates. *Am J Kidney Dis* 1997; 30: 334–342.
14. Murphy SW, Foley RN, Barrett BJ *et al*. Comparative mortality of hemodialysis and peritoneal dialysis in Canada. *Kidney Int* 2000; 57: 1720–1726.
15. Ginieri-Coccossis M, Theofilou P, Synodinou C *et al*. Quality of life, mental health and health beliefs in haemodialysis and peritoneal dialysis patients: investigating differences in early and later years of current treatment. *BMC Nephrol* 2008; 9: 14.
16. Klarenbach S, Manns B. Economic evaluation of dialysis therapies. *Semin Nephrol* 2009; 29: 524–532.
17. Charlson ME, Pompei P, Ales KL *et al*. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis* 1987; 40: 373–383.
18. Jassal SV, Schaubel DE, Fenton SS. Baseline comorbidity in kidney transplant recipients: a comparison of comorbidity indices. *Am J Kidney Dis* 2005; 46: 136–142.

19. Vonesh E, Schaubel DE, Hao W *et al*. Statistical methods for comparing mortality among ESRD patients: examples of regional/international variations. *Kidney Int Suppl* 2000; 54: S19–S27.
20. Holford TR. The analysis of rates and of survivorship using log-linear models. *Biometrics* 1980; 36: 299–305.
21. Allison PD. *Survival Analysis Using the SAS® System: A Practical Guide*. Cary, NC: SAS Institute, Inc., 1995.
22. Zhang X, Loberiza FR, Klein JP *et al*. A SAS macro for estimation of direct adjusted survival curves based on a stratified Cox regression model. Computer methods and programs in biomedicine. *Biometrics* 2007; 88: 95–101.
23. Lee ET. *Statistical Methods for Survival Data Analysis*. Belmont, CA: Lifetime Learning Publications. 1980.
24. Wei G, Schaubel DE. Estimating cumulative treatment effects in the presence of non-proportional hazards. *Biometrics* 2008; 64: 724–732.
25. Kalbfleisch JD, Prentice RL. *The Statistical Analysis of Failure Time Data*. New York: Wiley. 1980.
26. Sidak Z. Rectangular confidence regions for the means of multivariate normal distributions. *J Am Statistical Assoc* 1967; 62: 626–633.
27. Vonesh EF, Moran J. Mortality in end-stage renal disease: a reassessment of differences between patients treated with hemodialysis and peritoneal dialysis. *J Am Soc Nephrol* 1999; 10: 354–365.
28. Vonesh EF, Snyder JJ, Foley RN *et al*. The differential impact of risk factors on mortality in hemodialysis and peritoneal dialysis. *Kidney Int* 2004; 66: 2389–2401.
29. Heaf JG, Løkkegaard H, Madsen M. Initial survival advantage of peritoneal dialysis relative to haemodialysis. *Nephrol Dial Transplant* 2002; 17: 112–117.
30. Liem YS, Wong JB, Hunink MG *et al*. Comparison of hemodialysis and peritoneal dialysis survival in The Netherlands. *Kidney Int* 2007; 71: 153–158.
31. Vonesh EF, Snyder JJ, Foley RN *et al*. Mortality studies comparing peritoneal dialysis and hemodialysis: what do they tell us?. *Kidney Int Suppl* 2006; 103: S3–11. Review.

Received for publication: 15.2.2011; Accepted in revised form: 25.10.2011

Nephrol Dial Transplant (2012) 27: 3575–3581
doi: 10.1093/ndt/gfs081
Advance Access publication 18 April 2012

Anti-microbial locks increase the prevalence of *Staphylococcus aureus* and antibiotic-resistant *Enterobacter*: observational retrospective cohort study

John J. Dixon, Maggi Steele and A. David Makanjuola

South West Thames Renal and Transplantation Unit, St. Helier Hospital, Carshalton, Surrey, UK

Correspondence and offprint requests to: John J. Dixon; E-mail: johndixon3@nhs.net

Abstract

Background. Anti-microbial lock solutions (AML), in conjunction with systemic antibiotics, may successfully treat tunnelled haemodialysis catheter-related bloodstream infections (CR-BSI). It is unknown whether AML promote anti-microbial resistance.

Methods. This is a retrospective cohort study of all CR-BSI (2003–2006) in our dialysis unit. Controls ($n = 265$) were treated with systemic vancomycin and gentamicin. In addition to the systemic antibiotics, the study group ($n = 662$) received AML containing vancomycin and gentamicin during inter-dialytic periods. Antibiotic sensitivity/resistance profiles of all organisms were analysed. Changes in the incidence of infection (chi-square test) and resistant organisms (Fisher's exact test) were calculated.

Results. The incidence of CR-BSI decreased from 8.50/1000 catheter days (controls) to 3.80 (study group; $P < 0.0001$), and the incidence of relapses decreased ($P = 0.0027$). The number needed to treat to prevent subsequent bacteraemia using an AML adjunct is 3 ± 0.4. The proportion of Gram-positive cultures increased ($P < 0.0001$), including *Staphylococcus aureus* ($P = 0.03$), but the proportion of methicillin-resistant *S. aureus* ($P = 0.87$) and vancomycin resistance ($P = 0.90$) did not. Increased gentamicin resistance ($P < 0.0001$) and ciprofloxacin resistance ($P = 0.04$) were observed in Gram-negative cultures. Gentamicin resistance [relative risk (RR) > 15.29; $P < 0.0001$] and ciprofloxacin resistance ($RR = 6$; $P = 0.007$) increased in *Enterobacter* species, but not *Pseudomonas* or *Escherichia coli* species.

Conclusion. AML decrease CR-BSI incidence, although proportions of *S. aureus* and anti-microbial-resistant *Enterobacter* are increased.

Keywords: antibiotic resistance; haemodialysis catheter; line locks

Introduction

Tunnelled haemodialysis catheters (THC) are associated with increased bacteraemia when compared with arteriovenous fistulae [1]. Treatment of haemodialysis catheter-related bloodstream infections (CR-BSI) has significant financial costs [2] and associated morbidity [3]. Guidelines recommend empirical systemic treatment with vancomycin and an aminoglycoside for suspected CR-BSI, when THC