Changes in Patient and Technique Survival over Time among Incident Peritoneal Dialysis Patients in Canada

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Summary

Background and objectives In the last 15 years in Canada, there have been less stringent guidelines for peritoneal dialysis (PD) adequacy, availability of novel PD solutions, and lower PD-related peritonitis rates. Effects of these changes on outcomes of incident patients treated with PD during this period are unknown.

Design, setting, participants, & measurements Risk of PD technique failure and mortality were compared among three incident cohorts of PD patients who initiated dialysis during the following periods: 1995–2000, 2001–2005, and 2006–2009. A multivariable model was used to evaluate time to PD technique failure using inverse probability of treatment and censoring weights accounting for changing survival and transplantation rates.

Results Between 1995 and 2009,13,120 incident adult PD patients were identified from the Canadian Organ Replacement Register. Compared with the 1995–2000 cohort (*n*=5183), the risk of PD technique failure was lower among patients between 2001 and 2005 (*n*=4316) but similar among incident patients between 2006 and 2009 (*n*=3621). Cause-specific PD technique failure revealed no difference in PD peritonitis-related technique failure over time. PD technique failure due to inadequate PD was initially higher in the 2001–2005 cohort but lower in the 2006–2009 cohort compared with the 1995–2000 cohort. Relative to incident patients between 1995 and 2000, adjusted mortality was lower among incident patients between 2001 and 2005 and 2006 and 2009.

Conclusions Survival on PD continues to improve with only modest changes in PD technique failure. Peritonitis remains an ongoing and modifiable source of PD technique failure.

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Introduction

The prevalence of ESRD continues to rise in Canada and worldwide. Increasing the use of home-based peritoneal dialysis (PD) is an attractive strategy to target increasing dialysis-related health care costs. Consistently, PD has been demonstrated to be a more cost-effective therapy compared with facility-based conventional hemodialysis (CHD) with annualized costs for therapy that are approximately 60%–70% that of CHD (2). Moreover, recent Canadian comparisons between incident PD and CHD patients indicate that after accounting for the selection bias and the use of tunneled venous catheters, overall survival is similar between the two therapies (3,4). Yet, despite similar outcomes as well as the potential fiscal and lifestyle benefits offered by PD, the last 15 years have shown a steady decline in incident PD use in Canada (Figure 1) (5) as well as other countries (6,7).

Although Canadian policy makers and healthcare providers continue to focus on increasing incident PD use, less attention is focused on the effect of time spent on PD therapy, the costs associated with the development of PD technique failure, and the effect of such a change in dialysis modality on patient outcomes. Patients on PD experience significantly shorter technique survival compared with patients on hemodialysis (8,9). If technique survival on PD were to continue to improve over time, then it would be possible to improve upon prevalent PD utilization in the absence of changes in incident PD use. Similarly, if increasing incident PD use were to be accompanied by a higher rate of PD technique failure, then its effect on increasing PD utilization would be significantly attenuated.

PD-related infections, catheter complications, inadequate peritoneal ultrafiltration, inadequate small solute clearance, and psychosocial barriers continue to remain important causes of PD technique failure (10). Over time, changes in PD connectology and practices aimed at the prevention of PD-related infections have translated into lower rates of PD peritonitis (11,12). Increasing availability of novel PD solutions such as icodextrin has provided an additional tool to enhance peritoneal ultrafiltration, particularly among long-term PD patients (13,14). Lastly, a shift in recent Canadian and international PD guidelines that has lowered targets for small solute clearance may reduce the number of patients transferred to hemodialysis for failure to meet adequacy guidelines (15,16). We hypothesized that these favorable changes in practice

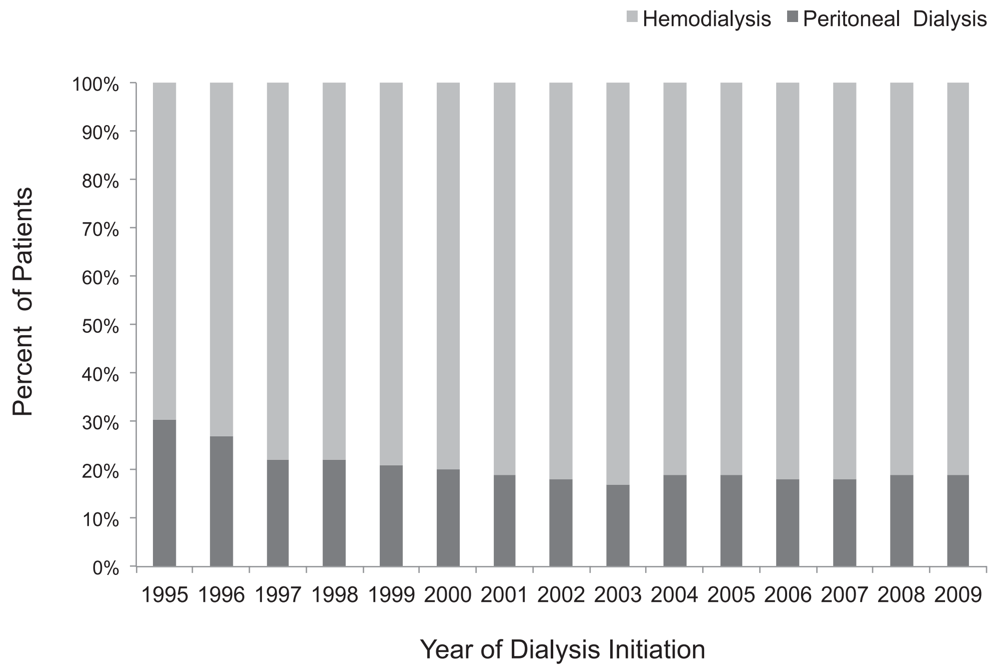

Figure 1. | **Distribution of incident dialysis modality in Canada from 1995 to 2009.** $P<0.001$ by Cochrane Armitage trend test. Dark gray bar, percentage of incident peritoneal dialysis patients; light gray bar, percentage of incident hemodialysis patient by year of dialysis initiation.

patterns would translate into improvements in PD technique survival in Canada over time.

Our primary objective was to examine national trends over time in PD technique survival among incident Canadian PD patients while accounting for temporal trends in mortality and transplantation rates over time. Secondary objectives were to examine trends over time in cause-specific PD technique failure and to assess trends over time in PD patient survival among incident Canadian PD patients.

Materials and Methods

Study Design, Data Source, Definitions, and Collection

This prospective observational cohort study of consecutive adults (≥18 years of age), who initiated PD between January 1, 1995 and December 31, 2009, was performed using data from the Canadian Organ Replacement Register (CORR). CORR is a national registry that has recently been validated and captures the incidence, prevalence, treatment changes, and outcomes of >99% of chronic dialysis and solid organ transplant patients in Canada and is described in detail elsewhere (1,17,18). We included both continuous ambulatory PD (CAPD) and automated PD (APD) patients.

The era of PD initiation was the primary exposure of interest. Eligible patients included those who were on PD 60 days after chronic dialysis initiation. To examine trends over time, three incident cohorts of PD patients were established: 1995–2000, 2001–2005, and 2006–2009. The rationale for the selection of these three cohort periods was based on major updates in national and international PD guidelines that took place during each of these three periods (15,19,20).

Information on the presence or absence of coronary artery disease (CAD), peripheral vascular disease (PVD), hypertension, diabetes mellitus, and cerebrovascular disease were categorized as "yes," "no," and "unknown." The unknowns were combined into the "no" group. Diabetes was adjusted for both as a cause of ESRD and as a comorbidity. Current smokers were documented as those having smoked in the last 3 months. Comorbidities were included in the determination of a validated comorbidity index for each patient (21). Late referral was defined as never having been seen by a nephrologist before dialysis initiation or first seeing a nephrologist within 3 months before starting dialysis. Body mass index (BMI) was calculated using the height and weight collected at the start of dialysis. Baseline laboratory parameters included hemoglobin, serum albumin, and serum creatinine measured as the value closest to but preceding the initial dialysis treatment and were available only from 2001 and onward. The estimated GFR before the start of dialysis was calculated using the four-variable Modification of Diet in Renal Disease equation (22).

Outcomes

The primary outcome was time to PD technique failure. Secondary outcomes included cause-specific technique failure and overall mortality. PD technique failure was defined as a transfer to hemodialysis for ≥90 days. Causes of PD technique failure were categorized as follows: peritonitis, inadequate PD (which included inadequate peritoneal ultrafiltration and/or inadequate small solute clearance), and other causes. The "other causes" category included abdominal and/or PD-related complications, patient/family unable to cope, transfer to originally intended treatment, recovery of kidney function, and unknown causes. For analyses examining time to technique failure, patients were censored at death, kidney transplantation, and loss to follow-up or at the end of the observation period (December 31, 2010).

In the analyses examining cause-specific technique failure, patients were additionally censored for all other causes of technique failure. For the secondary analyses examining time to death, analyses were performed with and without censoring at technique failure. In all analyses of time to death, patients were censored at kidney transplantation.

Statistical Analyses

Categorical variables were compared using the chi-squared test. The Kruskal–Wallis test was used to analyze differences between continuous variables. Prespecified interactions with the exposure of interest and the risk of all-cause technique failure included age (<65 versus ≥65 years), sex, the presence or absence of diabetes, the presence or absence of any comorbidities, and being obese versus nonobese (BMI >29.9 kg/m^2 versus ≤29.9 kg/m^2).

Two-year unadjusted transplantation, death, and technique failure rates by year of dialysis initiation were calculated to ensure equal follow-up time across each cohort. To examine adjusted survival, proportional and nonproportional piecewise exponential survival models were used to compare mortality between patients among the three cohort periods within sequential 12-month intervals during the first 60 months. Average or time-independent hazard ratios of death were estimated using a proportional hazards model. Time-dependent relative risks were estimated using a nonproportional hazards model. All models were adjusted for case-mix differences in the cohorts including the following: age, sex, race, cause of ESRD, weighting of comorbidities (diabetes mellitus, CAD, PVD, malignancy, lung disease, pulmonary edema) based on a validated ESRD comorbidity index (21), BMI (as a continuous variable), province of treatment, and PD center size (as previously described) (21,23).

In addition, we used a marginal structural model with inverse probability of treatment and censoring weighting (IPTCW) to examine the risk of PD technique failure and mortality. Using this technique (described in detail elsewhere) allowed us to adjust for all measured covariates in a single summary weight and to adjust for the effect of informative censoring due to differences in the rates of death and kidney transplantation between PD patients over the three time periods (24–26). Propensity scores (PSs) estimated each study participant's probability of initial cohort period assignment and were calculated using all available covariates in two separate multivariable logistic regression models ([1995–2000 versus 2001–2005] and [1995–2000 versus 2006–2009]). Area under receiver operating characteristic (ROC) curves tested the discriminatory capacity of each model. Stabilized censoring weights were created by estimating the following: (*1*) the probability of remaining transplant free for each individual in successive 1-year time intervals and (*2*) the probability of remaining alive in successive 1-year time intervals. Each observation was then weighted both by the inverse probability of initial cohort assignment (1/PS) and then by the stabilized censoring weights. In analyses of mortality, IPTCW analyses were weighted both by the propensity to remain transplant free and technique failure free. Analyses were performed using SAS software (version 9.1.3; SAS Institute, Cary, NC).

Results

Baseline Characteristics

Between 1995 and 2009, 13,120 incident chronic PD patients were registered in CORR, including 5183 patients initiating PD in 1995–2000, 4316 patients in 2001– 2005, and 3621 patients in 2006–2009. As seen in Figure 1, the percentage of incident PD utilization declined over time from 29.3% of new cases of ESRD in 1995 to 18.7% in 2009 ($P<0.001$).

Table 1 lists the baseline characteristics of the study population. Compared with patients who initiated PD between 1995 and 2000, patients in more contemporary cohorts were more likely to be older, had a higher frequency of diabetes mellitus as a comorbidity, and had a higher BMI. The frequency of CAD and PVD was lower in more contemporary cohorts. One or more missing values for comorbidities occurred in 3.5%, 2.5%, and 3.4% of patients from the 1995–2000, 2001–2005, and 2006–2009 cohort periods, respectively.

All-Cause PD Technique Failure by Era of Dialysis Initiation

A total of 4318 (33%) patients experienced PD technique failure over the course of follow-up. Among these patients, the median time to technique failure was 1.9, 2.2, and 1.7 years for patients initiating PD between 1995 and 2000, 2001 and 2005, and 2006 and 2009, respectively. When patients were stratified by the period of dialysis initiation (Table 2), those initiating PD between 2001 and 2005 had a lower adjusted risk of technique failure (adjusted hazard ratio [AHR], 0.89; 95% confidence interval [95% CI], 0.82–0.98) compared with those initiating PD between 1995 and 2000. Patients initiating PD between 2006 and 2009 had a similar risk of technique failure compared with patients initiating PD between 1995 and 2000 (AHR, 0.95; 95% CI, 0.85–1.06). Among both contemporary cohort periods, relative to 1995–2000, there was a trend toward a reduction in technique failure in the third year on PD in the 2001–2005 cohort (AHR, 0.84; 95% CI, 0.70–1.02) and in the 2006–2009 cohort (AHR, 0.80; 95% CI, 0.63–1.02).

Cause-Specific PD Technique Survival by Era of Dialysis Initiation

Table 3 summarizes the results of cause-specific PD technique failure stratified by era of PD initiation. Compared with patients initiating PD between 1995 and 2000, there was no reduction in the risk of technique failure due to peritonitis among those initiating PD between 2001 and 2005 (AHR, 1.21; 95% CI, 0.99–1.48) and 2006 and 2009 (AHR, 1.19; 95% CI, 0.94–1.51). Patients initiating PD between 2001 and 2005 had a higher risk of technique failure due to inadequate PD compared with incident PD patients treated between 1995 and 2000 (AHR, 1.21; 95% CI, 1.0–1.46). However, those treated between 2006 and 2009 had a lower risk of technique failure due to inadequate PD (AHR, 0.69; 95% CI, 0.54–0.90). Relative to patients initiating PD in 1995–2000, the risk of technique failure due to other causes was lower in 2001–2005 (AHR, 0.68; 95% CI, 0.60–0.77) and similar in 2006–2009 (AHR, 0.95; 95% CI, 0.83–1.10).

All-Cause Mortality by Era of PD Initiation

A total of 4158 patients (32%) died over the course of follow-up. Figure 2 demonstrates 2-year mortality rates by

Table 1. Patient characteristics at PD initiation in Canada: 1995–2009

	Year of Dialysis Initiation			*P* Value
	1995–2000 (*n*=5183)	2001–2005 (*n*=4316)	2006–2009 (*n*=3621)	
Age group (yr)				
18–44	20.6	15.9	14.7	<0.001
45–54	16.6	17	16.7	
55–64	20.9	22.5	24.4	
65–74	26.5	25.3	24.9	
≥ 75	15.5	19.3	19.2	
Race				
Caucasian	71.3	70.9	67.9	<0.001
Asian	7.7	8.7	9	
black	3.5	3.4	3.9	
other	10	12.8	13.6	
unknown	7.5	4.2	5.7	
Female	43.1	42.5	42.5	0.77
Primary diagnosis				
GN	18.8	17.4	16.2	<0.001
diabetes	34.2	36.6	35.4	
renal vascular disease	18.3	17.3	17.5	
polycystic kidney disease	5.1	6.9	6.8	
other	10.6	9.6	12.9	
unknown	13	12.2	11.1	
Comorbid conditions				
diabetes[a]	5.7	5.7	8.3	<0.001
coronary artery disease[b]	29.8	26.1	21	<0.001
peripheral vascular disease	13.7	13.9	11.1	<0.001
malignancy	6.6	6.8	7.6	0.18
lung disease	7.2	6.7	5.4	0.003
pulmonary edema	22.8	13.8	9.6	<0.001
hypertension	81.5	87.8	82.7	<0.001
current smoker	12.2	12.4	11.8	0.69
Automated PD (%)	29.1	28.4	26.5	0.03
Body mass index (kg/m^2)	24.6 (6.0)	25.7 (6.4)	26.6 (7.3)	<0.001
Late referral (%)[c]	—	17.7	11.1	<0.001
Hemoglobin (g/L)[c]	—	111 (21)	111 (18)	0.42
Estimated GFR (ml/min/1.73 m^2)[c,d]	—	8.9 (4.7)	9.6 (5.0)	<0.001
Albumin (g/L)[c]		36 (7)	37 (8)	<0.001
Prevalent PD center size[e]	25 (52)	26 (37)	27 (49)	—

Data are presented as a percentage or as the median (interquartile range). PD, peritoneal dialysis.
[a]Diabetes as a comorbidity but not a cause of ESRD.
[b]Coronary artery disease was determined from the presence of at least one of the following: a history of coronary artery bypass grafting, previous myocardial infarction, or previous angina.
[c]Not available before 2001.
[d]Determined by the Modification of Diet in Renal Disease formula.
[e]More than 95% of facilities the same across cohort periods.

year of PD initiation compared with transplantation and technique failure rates. When PD patients were stratified by the period of dialysis initiation, those initiating PD between 2001 and 2005 (AHR, 0.69; 95% CI, 0.63–0.76) and between 2006 and 2009 (AHR, 0.55; 95% CI, 0.49–0.62) had a significantly lower adjusted risk of death compared with patients initiating PD between 1995 and 2000 (Table 4).

Prespecified Interactions

Figure 3 demonstrates the results of the prespecified subgroup analyses. With the exception of age, the effect of era of PD initiation on the risk of technique failure was not modified among any of the subgroups examined. There was a significant interaction between age and era of PD initiation. Whereas patients <65 years of age experienced no difference in technique failure risk by period of PD initiation, those >65 years of age had a significantly lower risk of technique failure between 2001 and 2005 (AHR, 0.86; 95% CI, 0.75–0.97) and between 2006 and 2009 (AHR, 0.80; 95% CI, 0.69–0.93) relative to those >65 years of age who initiated PD between 1995 and 2000.

Discussion

This large observational study of Canadian patients initiating PD between 1995 and 2009 demonstrates an

Table 2. Results of the piecewise proportional hazards model for all-cause PD technique failure

	Hazard Ratio (95% Confidence Interval)		
	Univariate	Multivariate[a]	IPTCW[b]
Overall (*n*=13,120)			
1995–2000	1.0	1.0	1.0
2001–2005	0.91 (0.84, 0.98)	0.91 (0.83, 0.99)	0.89 (0.82, 0.98)
2006–2009	0.95 (0.87, 1.04)	0.91 (0.82, 1.01)	0.95 (0.85, 1.06)
Year 1 (*n*=13,120)			
1995–2000	1.0	1.0	1.0
2001–2005	0.91 (0.80, 1.03)	0.91 (0.80, 1.04)	0.90 (0.78, 1.03)
2006–2009	1.03 (0.90, 1.17)	0.99 (0.86, 1.14)	1.03 (0.88, 1.19)
Year 2 (*n*=11,283)			
1995–2000	1.0	1.0	1.0
2001–2005	0.93 (0.81, 1.07)	0.93 (0.81, 1.07)	0.93 (0.80, 1.08)
2006–2009	0.96 (0.83, 1.12)	0.92 (0.79, 1.08)	0.96 (0.81, 1.14)
Year 3 (*n*=8369)			
1995–2000	1.0	1.0	1.0
2001–2005	0.89 (0.76, 1.03)	0.88 (0.75, 1.03)	0.84 (0.70, 1.02)
2006–2009	0.79 (0.65, 0.96)	0.75 (0.62, 0.92)	0.80 (0.63, 1.02)

PD, peritoneal dialysis; IPTCW, inverse probability of treatment and censoring weighting.
[a]Adjusted for age, race, sex, body mass index, ESRD comorbidity index, primary diagnosis, PD modality (automated PD versus continuous ambulatory PD), province, and PD center size. Number of patients in analysis in year 1: 5183 in 1995–2000, 4316 in 2001–2005), and 3621 in 2006–2009; in year 2: 4329 in 1995–2000, 3744 in 2001–2005, and 3210 in 2006–2009; in year 3: 3364 in 1995–2000, 3021 in 2001–2005, and 1984 in 2006–2009.
[b]Adjusted as above but weighed for treatment era, and inverse probablity of death and transplantation.

Table 3. Results of the piecewise proportional hazards model for cause-specific PD technique failure

	Hazard Ratio (95% Confidence Interval)		
	Inadequate PD	Peritonitis	Other Causes
Overall (*n*=13,120)			
1995–2000	1.0	1.0	1.0
2001–2005	1.21 (1.00, 1.46)	1.21 (0.99, 1.48)	0.68 (0.60, 0.77)
2006–2009	0.69 (0.54, 0.90)	1.19 (0.94, 1.51)	0.95 (0.83, 1.10)
Year 1 (*n*=13,120)			
1995–2000	1.0	1.0	1.0
2001–2005	1.38 (1.03, 1.85)	1.14 (0.81, 1.60)	0.69 (0.58, 0.82)
2006–2009	0.86 (0.59, 1.25)	1.21 (0.83, 1.76)	1.00 (0.83, 1.20)
Year 2 (*n*=11,283)			
1995–2000	1.0	1.0	1.0
2001–2005	1.12 (0.83, 1.52)	1.23 (0.90, 1.68)	0.72 (0.59, 0.88)
2006–2009	0.58 (0.39, 0.87)	1.10 (0.78, 1.55)	1.04 (0.83, 1.31)
Year 3 (*n*=8369)			
1995–2000	1.0	1.0	1.0
2001–2005	1.11 (0.78, 1.59)	1.28 (0.89, 1.83)	0.60 (0.46, 0.78)
2006–2009	0.62 (0.36, 1.07)	1.29 (0.86, 1.94)	0.72 (0.51, 1.02)

All models performed using inverse probability of treatment and censoring weighting. Adjusted for age, race, sex, body mass index, ESRD comorbidity index, primary diagnosis, PD modality (automated PD versus continuous ambulatory PD), province, and PD center size. Number of patients in analysis in year 1 model: 5183 in 1995–2000, 4316 in 2001–2005, and 3621 in 2006–2009; in year 2 model: 4329 in 1995–2000 *n*=, 3744 in 2001–2005, and 3210 in 2006–2009; in year 3: 3364 in 1995–2000, 3021 in 2001–2005, and 1984 in 2006–2009. PD, peritoneal dialysis.

improvement in PD patient survival over time, but only small changes in PD technique survival. In particular, there was a significant reduction in technique failure over time among the subgroup of patients >65 years of age, but not among younger PD patients. Although there was no reduction in peritonitis-related technique failure over time, there was an improvement in technique failure due to inadequate PD in the most contemporary cohort.

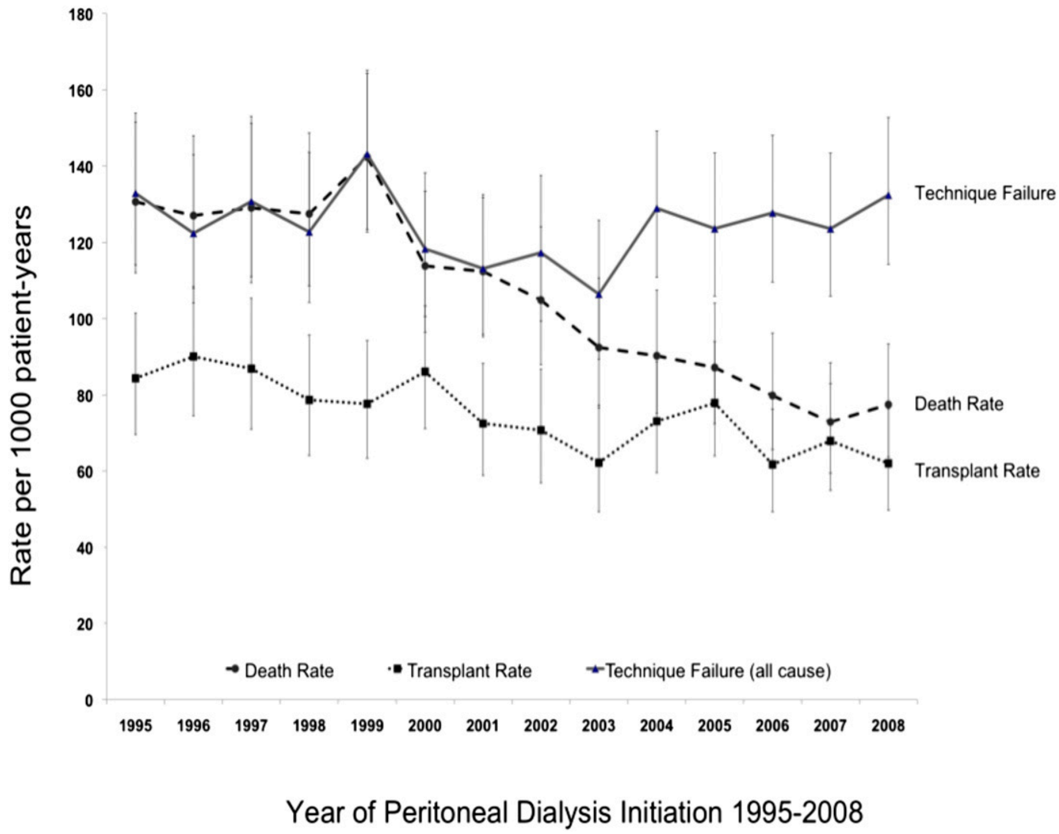

Figure 2. | Two-year mortality, technique failure, and transplantation rates among incident PD patients by year of dialysis initiation. Rates are unadjusted and presented per 1000 patient-years by year of dialysis initiation along with 95% confidence intervals. Solid line, technique failure rate; long-dashed line, death rate; short-dashed line, kidney transplantation rate. PD, peritoneal dialysis.

The improvement in patient survival on PD over time is substantial, with a 31% decline in all-cause mortality in 2001–2005 and a 45% decline in all-cause mortality in 2006–2009 compared with 1995–2000, and is in keeping with prior studies (6,27–29). Explanations for the improvement in patient survival could be differences in patient selection over time due to declining PD utilization or the decreasing transplant rate over time in Canada, resulting in healthier transplant-eligible patients remaining on PD for longer periods of time. However, we partially accounted for this using an IPTCW approach. Moreover, given that patients in the most contemporary era were older and more likely to have diabetes, the contribution of healthier and transplant-eligible patients to the improved survival in recent years is likely minor. More plausibly, the improving patient survival may reflect better management of patients on PD, including improved treatment of their comorbid illnesses as well as improvements in PD as a therapy.

There are limited data on the relationship between era of PD initiation and technique failure. One single-center study from Korea reported a significant reduction in technique failure among patients initiating PD in 1993–2005 relative to 1981–1992 (27). More recently, Mehrotra *et al.*, using data from the US Renal Data Service data, demonstrated improving PD technique survival between 1996 and 2004 (29). In our study, in contrast to the clear improvement in PD patient survival over time, the effect of era on PD technique survival was more complex. The 2001–2005 cohort demonstrated a small decrease in technique failure relative to the 1995–2000 cohort (consistent with the findings of Mehrotra *et al.*), yet there was no decrease in technique failure in the 2006–2009 cohort. When the timing of the technique failure was taken into account, it seemed that in both of the more recent cohorts, there was a trend toward reduced technique failure in the third year on PD. In other words, any small improvements in technique failure were predominantly driven by a reduction in late rather than early technique failure.

To better understand the basis for the changes in technique failure over time, we examined cause-specific PD technique failure over the three eras. Importantly, despite the fact that PD-related infection typically accounts for the largest proportion of technique failure, we found that PD peritonitis as a cause of technique failure did not decline over time. In fact, there was a trend toward more peritonitis-related technique failure in the two more contemporary eras. This is an interesting finding when one considers that PD peritonitis rates have declined over time (12,30,31). This apparent discrepancy is likely related, in part, to our improving success in the prevention of peritonitis caused by indolent organisms, such as coagulase-negative *Staphylococcus*, that are less likely to lead to technique failure (32,33). In contrast, severe peritonitis episodes, such as

Table 4. Results of the piecewise proportional hazards model for all-cause mortality

	Hazard Ratio (95% Confidence Interval)			
			IPTCW	
	Univariate	Multivariate[a]	Technique Failure Uncensored	Technique Failure Censored
Overall (*n*=13,120)				
1995–2000	1.0	1.0	1.0	1.0
2001–2005	0.77 (0.71, 0.84)	0.73 (0.66, 0.80)	0.73 (0.67, 0.79)	0.69 (0.63, 0.76)
2006–2009	0.61 (0.55, 0.67)	0.57 (0.50, 0.64)	0.58 (0.52, 0.65)	0.55 (0.49, 0.62)
Year 1 (*n*=13,120)				
1995–2000	1.0	1.0	1.0	1.0
2001–2005	0.77 (0.67, 0.89)	0.73 (0.63, 0.85)	0.74 (0.64, 0.85)	0.75 (0.65, 0.88)
2006–2009	0.61 (0.52, 0.72)	0.59 (0.50, 0.71)	0.60 (0.51, 0.71)	0.63 (0.53, 0.76)
Year 2 (*n*=11,283)				
1995–2000	1.0	1.0	1.0	1.0
2001–2005	0.74 (0.64, 0.84)	0.69 (0.60, 0.79)	0.75 (0.66, 0.85)	0.64 (0.56, 0.75)
2006–2009	0.57 (0.48, 0.67)	0.54 (0.45, 0.64)	0.58 (0.49, 0.68)	0.49 (0.41, 0.60)
Year 3 (*n*=8369)				
1995–2000	1.0	1.0	1.0	1.0
2001–2005	0.83 (0.71, 0.96)	0.76 (0.65, 0.89)	0.78 (0.68, 0.89)	0.70 (0.59, 0.82)
2006–2009	0.66 (0.54, 0.80)	0.59 (0.48, 0.72)	0.64 (0.54, 0.76)	0.54 (0.43, 0.67)

IPTCW, inverse probability of treatment and censoring weighting; PD, peritoneal dialysis.
[a]Adjusted for age, race, sex, body mass index, ESRD comorbidity index, primary diagnosis, PD modality (automated PD versus continuous ambulatory PD), province, and PD center size. Number of patients in analysis in year 1 by cohort: 5183 in 1995–2000, 4316 in 2001–2005, and 3621 in 2006–2009; in year 2: 4329 in 1995–2000, 3744 in 2001–2005, and 3210 in 2006–2009; and in year 3: 3364 in 1995–2000, 3021 in 2001–2005, and 1984 in 2006–2009.

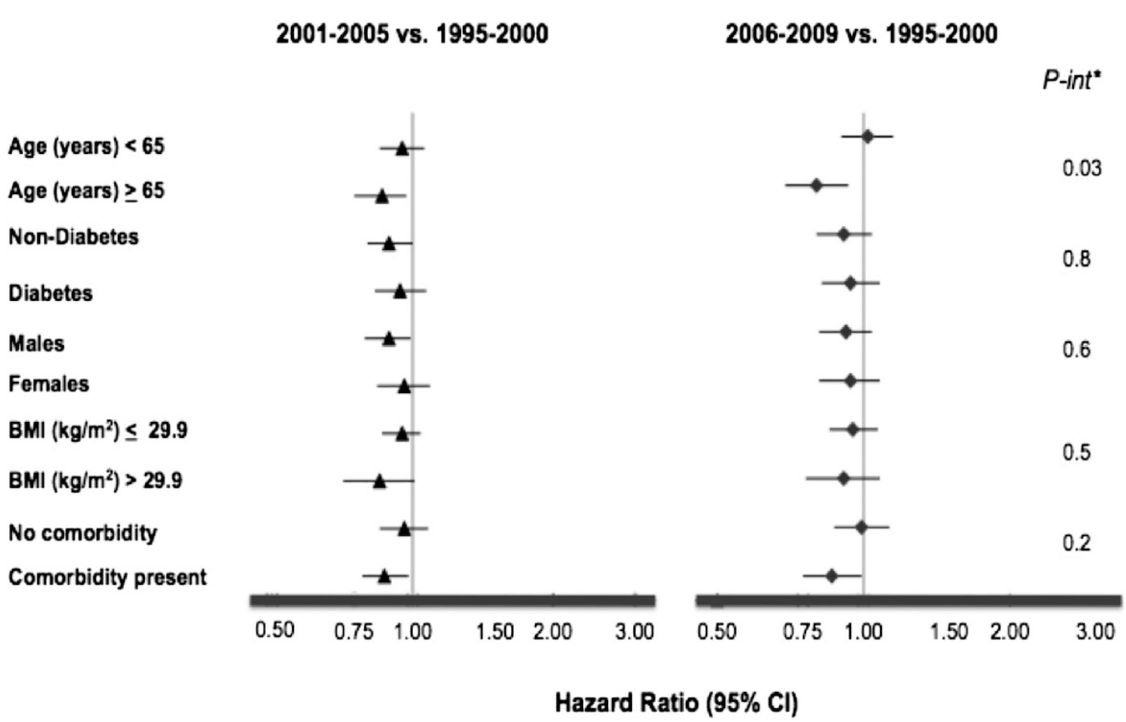

Figure 3. | Effect of era of PD initiation on the risk of all-cause peritoneal dialysis technique failure in selected subgroups. Adjusted for age, race, sex, BMI, ESRD comorbidity index, primary diagnosis, PD modality (automated PD versus continuous ambulatory PD), province and PD center size. Bars represent the hazard ratios and 95% confidence intervals among selected subgroups. PD, peritoneal dialysis; BMI, body mass index; P-*int*, *P* value for interaction term; CI, confidence interval.

those caused by enteric organisms, may not be adequately addressed by our current preventive strategies. An additional possibility is that we have become more proactive over time about catheter removal and transfer to hemodialysis for those peritonitis episodes caused by more aggressive organisms.

Whereas there was no reduction in technique failure due to PD peritonitis, technique failure due to inadequate PD did change over time. Specifically, there was an initial increase in technique failure due to inadequate PD in the 2001–2005 cohort followed by a decrease among those patients initiating PD more recently. One might hypothesize that fewer patients failing PD due to inadequate dialysis (including ultrafiltration failure) in recent years may relate to the use of alternate PD solutions including the glucose-based polymer icodextrin and increasing use of APD. However, incident APD use was similar, if not decreased, over time. Moreover, given that the use of novel PD solutions including glucose-based polymers has likely been steadily increasing since the late 1990s, it is unlikely for icodextrin use to explain an increase in technique failure due to inadequate dialysis in 2001–2005 followed by more recent improvement. More likely, the changes in technique failure due to inadequate dialysis over time may simply reflect changes in the PD adequacy guidelines over time. Specifically, the rise in technique failure due to inadequate dialysis seen in the 2001–2005 cohort corresponds to the publication of the Canadian Society of Nephrology guidelines in 1999 and the Kidney Disease Outcomes Quality Initiative (KDOQI) guidelines in 1997 and 2000 suggesting minimum Kt/V and creatinine clearance targets among PD patients (19,20,34). Subsequently, the decline in technique failure due to inadequate PD that occurred among patients initiating PD in the most contemporary cohort is likely due to the publication in 2006 of the revised, less stringent KDOQI adequacy targets based on the Adequacy of Peritoneal Dialysis in Mexico trial and other studies (15,35,36). If this is the case, it emphasizes the important effect that PD guidelines can have on management of PD patients. Despite the reduction in technique failure due to inadequate PD in the most contemporary cohort, the lack of improvement in technique failure due to all other causes contributed to an overall technique failure in 2006–2009 that was not significantly different from prior eras.

Interestingly, whereas patients <65 years of age showed no reduction in technique failure over time, those ≥65 years of age had a lower risk of technique failure in 2001–2005 and 2006–2009 relative to 1995–2000. Whereas the effect of era of PD initiation on risk of technique failure among elderly patients has not previously been reported, a recent study from the Australia and New Zealand Dialysis and Transplant Registry reported superior technique survival among PD patients >65 years of age relative to younger patients (37), although this has not been a consistent finding (38–41). In our analysis, the basis for better technique survival in more recent years among older but not younger patients is not clear. It was not driven by a reduction in technique failure due to peritonitis or due to inadequate PD but rather due to other causes of technique failure. This finding may relate to the increasing use of home-assisted PD for elderly patients across several regions in Canada (42). The improvement in PD technique failure among older patients is particularly relevant when one considers that the largest growth in the ESRD population over time has been among those >65 years of age (1).

The strengths of this study are the large, multicenter cohort of patients and longitudinal follow-up. However, there are some limitations. First, the limited number of variables available in the CORR database, such as the absence of the estimated GFR in the earliest cohort or longitudinal measurements of residual kidney function in all groups, may have led to residual confounding that could have influenced the reported associations. Second, although causes of technique failure such as peritonitis and inadequate PD were clearly coded in the database, other reasons for technique failure were less well described and suffer from a lack of a standardized definition across the PD literature. Consequently, they had to be merged into an "other cause" category. As a result, we were unable to explore changing frequencies of these other causes of technique failure and how they might have influenced the risk of technique failure over time.

In conclusion, this study demonstrates that patient survival on PD has improved over time. In contrast, there have been only modest changes in technique failure over time, with a trend toward reduced late technique failure but no difference in early technique failure. There was an interaction between age and era, such that there was a significant reduction in technique failure over time among patients >65 years of age, but not among younger PD patients. Whereas there has been no reduction in peritonitis-related technique failure in more contemporary cohorts, there has been a reduction in technique failure due to inadequate PD in recent years, possibly driven by less stringent adequacy targets. Strategies aimed at prolonging PD technique survival will require an ongoing emphasis on reducing the risk of peritonitis-related technique failure as well as a better understanding of the contribution of each of the noninfectious causes of technique failure.

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References

1. Canadian Organ Replacement Register: *CORR Preliminary Report: Preliminary Statistics for Renal Failure and Solid Organ*

Transplantation in Canada. Ottawa, ON, Canadian Organ Replacement Register, 2008
2. Lee H, Manns B, Taub K, Ghali WA, Dean S, Johnson D, Donaldson C: Cost analysis of ongoing care of patients with end-stage renal disease: The impact of dialysis modality and dialysis access. *Am J Kidney Dis* 40: 611–622, 2002
3. Quinn RR, Hux JE, Oliver MJ, Austin PC, Tonelli M, Laupacis A: Selection bias explains apparent differential mortality between dialysis modalities. *J Am Soc Nephrol* 22: 1534–1542, 2011
4. Perl J, Wald R, McFarlane P, Bargman JM, Vonesh E, Na Y, Jassal SV, Moist L: Hemodialysis vascular access modifies the association between dialysis modality and survival. *J Am Soc Nephrol* 22: 1113–1121, 2011
5. Canadian Institute for Health Information: *Canadian Organ Replacement Register Annual Report: Treatment of End-Stage Organ Failure in Canada, 2000 to 2009*, Ottawa, ON, Canada, Canadian Institute for Health Information, 2011
6. Mehrotra R, Kermah D, Fried L, Kalantar-Zadeh K, Khawar O, Norris K, Nissenson A: Chronic peritoneal dialysis in the United States: Declining utilization despite improving outcomes. *J Am Soc Nephrol* 18: 2781–2788, 2007
7. Castledine CI, Caskey FJ, Tomson CR, Ansell D: Trends in renal replacement therapy and changes in peritoneal dialysis utilization in the United Kingdom. *Perit Dial Int* 31[Suppl 2]: S53–S57, 2011
8. Maiorca R, Vonesh E, Cancarini GC, Cantaluppi A, Manili L, Brunori G, Camerini C, Feller P, Strada A: A six-year comparison of patient and technique survivals in CAPD and HD. *Kidney Int* 34: 518–524, 1988
9. Serkes KD, Blagg CR, Nolph KD, Vonesh EF, Shapiro F: Comparison of patient and technique survival in continuous ambulatory peritoneal dialysis (CAPD) and hemodialysis: A multicenter study. *Perit Dial Int* 10: 15–19, 1990
10. Mujais S, Story K: Peritoneal dialysis in the US: Evaluation of outcomes in contemporary cohorts. *Kidney Int Suppl* 103: S21–S26, 2006
11. Nessim SJ, Bargman JM, Austin PC, Story K, Jassal SV: Impact of age on peritonitis risk in peritoneal dialysis patients: An era effect. *Clin J Am Soc Nephrol* 4: 135–141, 2009
12. Whaley-Connell A, Pavey BS, Satalowich R, Prowant BF, Misra M, Twardowski ZJ, Nolph KD, Khanna R: Rates of continuous ambulatory peritoneal dialysis-associated peritonitis at the University of Missouri. *Adv Perit Dial* 21: 72–75, 2005
13. Brown EA, Davies SJ, Rutherford P, Meeus F, Borras M, Riegel W, Divino Filho JC, Vonesh E, van Bree M, Group E; EAPOS Group: Survival of functionally anuric patients on automated peritoneal dialysis: The European APD Outcome Study. *J Am Soc Nephrol* 14: 2948–2957, 2003
14. Davies SJ, Woodrow G, Donovan K, Plum J, Williams P, Johansson AC, Bosselmann H-P, Heimbürger O, Simonsen O, Davenport A, Tranaeus A, Divino Filho JC: Icodextrin improves the fluid status of peritoneal dialysis patients: Results of a double-blind randomized controlled trial. *J Am Soc Nephrol* 14: 2338–2344, 2003
15. Peritoneal Dialysis Adequacy Work Group: Clinical practice guidelines for peritoneal dialysis adequacy. *Am J Kidney Dis* 48 [Suppl 1]: S98–S129, 2006
16. Blake PG, Bargman JM, Brimble KS, Davison SN, Hirsch D, McCormick BB, Suri RS, Taylor P, Zalunardo N, Tonelli M; Canadian Society of Nephrology Work Group on Adequacy of Peritoneal Dialysis: Clinical Practice Guidelines and Recommendations on Peritoneal Dialysis Adequacy 2011. *Perit Dial Int* 31: 218–239, 2011
17. Karamadoukis L, Ansell D, Foley RN, McDonald SP, Tomson CRV, Trpeski L, Caskey FJ: Towards case-mix-adjusted international renal registry comparisons: How can we improve data collection practice? *Nephrol Dial Transplant* 24: 2306–2311, 2009
18. Canadian Institute for Health Information: Data Quality Study on the Canadian Organ Replacement Register, Ottawa, ON, Canada, Canadian Institute for Health Information, 2009
19. National Kidney Foundation: II. NKF-K/DOQI clinical practice guidelines for peritoneal dialysis adequacy: Update 2000. *Am J Kidney Dis* 37[Suppl 1]: S65–S136, 2001
20. National Kidney Foundation: NKF-DOQI clinical practice guidelines for peritoneal dialysis adequacy. *Am J Kidney Dis* 30[Suppl 2]: S67–S136, 1997
21. Hemmelgarn BR, Manns BJ, Quan H, Ghali WA: Adapting the Charlson Comorbidity Index for use in patients with ESRD. *Am J Kidney Dis* 42: 125–132, 2003
22. Levey AS, Bosch JP, Lewis JB, Greene T, Rogers N, Roth D; Modification of Diet in Renal Disease Study Group: A more accurate method to estimate glomerular filtration rate from serum creatinine: A new prediction equation. *Ann Intern Med* 130: 461–470, 1999
23. Schaubel DE, Blake PG, Fenton SS: Effect of renal center characteristics on mortality and technique failure on peritoneal dialysis. *Kidney Int* 60: 1517–1524, 2001
24. Hernán MA, Brumback B, Robins JM: Marginal structural models to estimate the causal effect of zidovudine on the survival of HIV-positive men. *Epidemiology* 11: 561–570, 2000
25. Mehrotra R, Chiu YW, Kalantar-Zadeh K, Bargman J, Vonesh E: Similar outcomes with hemodialysis and peritoneal dialysis in patients with end-stage renal disease. *Arch Intern Med* 171: 110–118, 2011
26. van der Wal WM, Noordzij M, Dekker FW, Boeschoten EW, Krediet RT, Korevaar JC, Geskus RB: Comparing mortality in renal patients on hemodialysis versus peritoneal dialysis using a marginal structural model. *Int J Biostat* 6**:** Article 2, 2010
27. Han SH, Lee JE, Kim DK, Moon SJ, Kim HW, Chang JH, Kim BS, Kang SW, Choi KH, Lee HY, Han DS: Long-term clinical outcomes of peritoneal dialysis patients: Single center experience from Korea. *Perit Dial Int* 28[Suppl 3]: S21–S26, 2008
28. Guo A, Mujais S: Patient and technique survival on peritoneal dialysis in the United States: Evaluation in large incident cohorts. *Kidney Int Suppl* 88: S3–S12, 2003
29. Mehrotra R, Chiu YW, Kalantar-Zadeh K, Vonesh E: The outcomes of continuous ambulatory and automated peritoneal dialysis are similar. *Kidney Int* 76: 97–107, 2009
30. Brown F, Liu WJ, Kotsanas D, Korman TM, Atkins RC: A quarter of a century of adult peritoneal dialysis-related peritonitis at an Australian medical center. *Perit Dial Int* 27: 565–574, 2007
31. Wanten GJ, Koolen MI, van Liebergen FJ, Jansen JL, Wever J: Outcome and complications in patients treated with continuous ambulatory peritoneal dialysis (CAPD) at a single centre during 11 years. *Neth J Med* 49: 4–12, 1996
32. Kavanagh D, Prescott GJ, Mactier RA: Peritoneal dialysis-associated peritonitis in Scotland (1999-2002). *Nephrol Dial Transplant* 19: 2584–2591, 2004
33. Szeto CC, Kwan BC, Chow KM, Lau MF, Law MC, Chung KY, Leung CB, Li PK: Coagulase negative staphylococcal peritonitis in peritoneal dialysis patients: review of 232 consecutive cases. *Clin J Am Soc Nephrol* 3: 91–97, 2008
34. Bargman JM, Bick J, Cartier P, Dasgupta MK, Fine A, Lavoie SD, Spanner E, Taylor PA; Canadian Society of Nephrology: Guidelines for adequacy and nutrition in peritoneal dialysis. *J Am Soc Nephrol* 10[Suppl 13]: S311–S321, 1999
35. Paniagua R, Amato D, Vonesh E, Correa-Rotter R, Ramos A, Moran J, Mujais S; Mexican Nephrology Collaborative Study Group: Effects of increased peritoneal clearances on mortality rates in peritoneal dialysis: ADEMEX, a prospective, randomized, controlled trial. *J Am Soc Nephrol* 13: 1307–1320, 2002
36. Lo WK, Ho YW, Li CS, Wong KS, Chan TM, Yu AW, Ng FS, Cheng IK: Effect of Kt/V on survival and clinical outcome in CAPD patients in a randomized prospective study. *Kidney Int* 64: 649–656, 2003
37. Lim WH, Dogra GK, McDonald SP, Brown FG, Johnson DW: Compared with younger peritoneal dialysis patients, elderly patients have similar peritonitis-free survival and lower risk of technique failure, but higher risk of peritonitis-related mortality. *Perit Dial Int* 31: 663–671, 2011
38. De Vecchi AF, Maccario M, Braga M, Scalamogna A, Castelnovo C, Ponticelli C: Peritoneal dialysis in nondiabetic patients older than 70 years: Comparison with patients aged 40 to 60 years. *Am J Kidney Dis* 31: 479–490, 1998
39. Kadambi P, Troidle L, Gorban-Brennan N, Kliger AS, Finkelstein FO: APD in the elderly. *Semin Dial* 15: 430–433, 2002

40. Li PK, Law MC, Chow KM, Leung CB, Kwan BC, Chung KY, Szeto CC: Good patient and technique survival in elderly patients on continuous ambulatory peritoneal dialysis. *Perit Dial Int* 27 [Suppl 2]: S196–S201, 2007
41. Kotsanas D, Polkinghorne KR, Korman TM, Atkins RC, Brown F: Risk factors for peritoneal dialysis-related peritonitis: Can we reduce the incidence and improve patient selection? *Nephrology (Carlton)* 12: 239–245, 2007
42. Oliver MJ, Quinn RR, Richardson EP, Kiss AJ, Lamping DL, Manns BJ: Home care assistance and the utilization of peritoneal dialysis. *Kidney Int* 71: 673–678, 2007

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