

UC Irvine

UC Irvine Previously Published Works

Title

The outcomes of continuous ambulatory and automated peritoneal dialysis are similar

Permalink

<https://escholarship.org/uc/item/6pm2544k>

Journal

Kidney International, 76(1)

ISSN

0085-2538

Authors

Mehrotra, Rajnish
Chiu, Yi-Wen
Kalantar-Zadeh, Kamyar
et al.

Publication Date

2009-07-01

DOI

10.1038/ki.2009.94

Copyright Information

This work is made available under the terms of a Creative Commons Attribution License, available at <https://creativecommons.org/licenses/by/4.0/>

Peer reviewed

see commentary on page 12

The outcomes of continuous ambulatory and automated peritoneal dialysis are similar

Rajnish Mehrotra^{1,2}, Yi-Wen Chiu^{1,3}, Kamyar Kalantar-Zadeh^{1,2} and Edward Vonesh⁴

¹Los Angeles Biomedical Research Institute at Harbor-UCLA, Torrance, California, USA; ²David Geffen School of Medicine at UCLA, Los Angeles, California, USA; ³Kaohsiung Medical University, Kaohsiung, Taiwan and ⁴Northwestern University, Chicago, Illinois, USA

Recent reports indicate a decreased mortality risk for patients on chronic peritoneal dialysis in the United States. We sought to determine whether a higher use of automated versus continuous ambulatory peritoneal dialysis was associated with this improvement. Analyses were carried out using data from the United States Renal Data System on 66,381 incident patients on chronic peritoneal dialysis in the years 1996–2004 that were adjusted for demographic, clinical, laboratory and dialysis facility characteristics. Patients were followed until the time of transfer to other modes of dialysis, transplant, or death, whichever occurred first, or until their last follow-up through September 2006. Over time, the risks were substantially reduced such that the adjusted hazard ratios for death or technique failure of these patients in the 2002–2004 period were 0.55 (0.53, 0.57) and 0.62 (0.59, 0.64), respectively, compared with those of incident patients during the years 1996–1998. The risk improvements for both modes of dialysis were, however, found to be similar. Under intent-to-treat, time-dependent, and as-treated analysis, there was little or no difference in risk for death or in technique failure. Thus, the improved chronic peritoneal dialysis outcomes cannot be attributed to a greater use of automated peritoneal dialysis.

Kidney International (2009) **76**, 97–107; doi:10.1038/ki.2009.94; published online 1 April 2009

KEYWORDS: automated peritoneal dialysis; continuous ambulatory peritoneal dialysis; end-stage renal disease; mortality; technique survival

Since 1996, the proportion of end-stage renal disease patients undergoing peritoneal dialysis (PD) in the United States has declined; during the same period, although the 1-year outcomes of PD patients have improved, those of maintenance hemodialysis patients have remained largely unchanged.¹ It is unclear what changes in practice, if any, have led to improvements in the outcomes of PD patients. Over this period, there have been important changes, each of which has the potential to reduce the overall death risk, for example, decrease in infectious complications in many centers, increased use of automated PD (APD), and publication of clinical practice guidelines that may have improved prescription management.^{2–4}

In the 1980s and the early 1990s, APD was largely used to optimize volume status in high-average and high transporters. With the introduction of smaller, portable machines, in many centers the increased APD use has been fueled by patient and by physician choice, irrespective of the transport type. Even though many epidemiological studies have considered continuous ambulatory PD (CAPD) and APD to be equivalent, several lines of investigations have questioned that premise. On the one hand, most studies have shown that APD patients have a lower peritonitis risk.⁵ On the other hand, some studies have raised concern that the daily sodium removal may be lower in APD patients.⁴ However, the data are inconsistent whether this lower sodium removal with APD is associated with worse volume and blood pressure control.^{5,6} Furthermore, some single-center studies have shown a more rapid loss of residual renal function in APD patients; these findings have not been confirmed in larger, multi-center studies.⁶ Finally, a larger number of PD exchanges during the night-time cycling may be associated with higher daily protein losses.⁷ These differences highlight the need to compare the outcomes of CAPD and APD patients. At least three studies have compared the probability of transfer to maintenance hemodialysis (technique failure) and death in CAPD and APD patients, with inconsistent results.^{8–10}

We undertook this study to compare the risk for death and technique failure among incident CAPD and APD patients in the United States using the data from the United States Renal Data System (USRDS). We also sought to determine whether the improvement in PD outcomes can be attributed to a greater use of APD.

Correspondence: Rajnish Mehrotra, Division of Nephrology and Hypertension, Los Angeles Biomedical Research Institute, 1124 W. Carson Street, Torrance, California 90502, USA. E-mail: rmehrotra@labiomed.org

Received 3 November 2008; revised 10 February 2009; accepted 17 February 2009; published online 1 April 2009

RESULTS

Patient characteristics

Over the 9-year period, starting in 1996, there were 66,381 incident PD patients in the United States. The proportion of PD patients undergoing APD on day 90 of end-stage renal disease increased from 30% during 1996–1998 to 40% during 2002–2004 (Table 1). The mean age of APD patients was 0.7 years greater than that of CAPD patients; the former were also more likely to be male and White. There were small differences in the prevalence of other coexisting illnesses—APD patients had a higher prevalence of cardiac arrest or dysrhythmia, cerebrovascular disease, and malignant neoplasm, but had a lower prevalence of chronic obstructive pulmonary disease and current smoking. Owing to the large sample size and increased statistical power, there were a number of statistically significant differences in laboratory variables reported on Medical Evidence form 2728; however, none of them were clinically meaningful (Table 1).

There were significant differences in the characteristics of the facilities where the patients received their care. Summarized in Table 1 are the mean and median numbers of patients for the facilities where the CAPD and APD patients were treated in the United States. Among 41,265 incident CAPD patients with facility-linked census data, the average APD census count was 15.5 patients per facility (or 41% of the average PD census count) compared with that of 25.4 patients per facility (or 68% of the average PD census count) among the 22,574 incident APD patients with facility-linked census data ($P < 0.001$, Table 1).

Patient survival

Patients were followed up to the time of death, transfer to in-center maintenance hemodialysis, home hemodialysis, or 'other' PD or renal transplantation (Table 2). The median follow-up period for CAPD and APD patients was 18.3 and 17.6 months, respectively.

On the basis of an intent-to-treat (ITT) analysis, the adjusted risk for death among incident PD patients during 1999–2001 and 2002–2004 was 14 and 45% lower, respectively, when compared with that among incident patients in the 1996–1998 period (Table 3 and Figure 1). The adjusted median life expectancy for incident CAPD and APD patients in 1996–1998 was 49.6 and 48.4 months, respectively. For incident CAPD and APD patients during 1999–2001, the adjusted median life expectancy improved to 57.6 and 57.2 months, respectively. Owing to the shorter period of follow-up, life expectancies could not be computed for the 2002–2004 cohort period, although the 45% reduction in adjusted mortality rates for this cohort compared with those for 1996–1998 suggests a further improvement in median life expectancy. As shown below, the improvement in outcomes over time was similar for both CAPD and APD, and there was no significant interaction between modality and cohort period ($P = 0.96$).

In an unadjusted ITT analysis, mortality rates of CAPD and APD were similar over time (APD versus CAPD

unadjusted hazard ratios and corresponding 95% CI: 0–6 months, 0.98 (0.93, 1.04); 6–12 months, 1.13 (1.06, 1.20); 12–18 months, 1.06 (0.99, 1.14); 18–24 months, 1.07 (0.99, 1.16); 24–30 months, 1.01 (0.92, 1.11); 30–36 months, 1.00 (0.90, 1.11); 36+ months, 1.00 (0.93, 1.08)). Similarly, the frequency of patients according to their modality at day 90 and their outcomes were also similar, although overall statistical significance was reached owing to the large numbers of patients (Table 2). Using an ITT non-proportional hazards model, there were no significant differences in adjusted mortality rates (adjusted for demographic, clinical, laboratory, and facility characteristics) in patients treated with CAPD or APD for virtually all the time periods examined (Table 3, Figure 2a). Similarly, there were little or no differences in the adjusted mortality rates for any of the time periods in incident patients treated with CAPD or APD under a time-dependent as-treated analysis (Figure 2b). The hazard ratios for the confounding variables under the as-treated analysis were almost identical to those shown in Table 3 for the ITT analysis (data not shown). Figure 3 shows the population-averaged adjusted ITT patient survival curves for CAPD and APD patients. These survival curves correspond to the time-dependent hazard ratios shown in Figure 2a, for APD versus CAPD. Included in Figure 3 is the time-independent or average adjusted hazard ratio of 1.03 (95% CI: (0.99, 1.06)) obtained under a proportional hazards model (adjusted for demographic, clinical, laboratory, and facility characteristics) and indicates a similar risk of death with APD and CAPD (Figure 3). As indicated in Table 3, there was a trend toward improved survival among centers with larger numbers of period-prevalent hemodialysis or PD patients, although the overall P -value comparing the five hemodialysis center census categories did not reach significance ($P = 0.07$), nor did the overall P -value for comparing the four PD center census categories ($P = 0.23$). Note that the category listed as 'Facility count = 0' under hemodialysis center census corresponds to patients from a PD-only facility.

Technique failure

The adjusted risk for technique failure (transfer to maintenance hemodialysis for >60 days, censoring for death) among incident CPD patients during 1999–2001 and 2002–2004 was 10 and 38% lower, respectively, than that among incident patients in the 1996–1998 period (Table 4). The improvement in outcomes over time was similar for both CAPD and APD, and there was no significant interaction between modality and cohort period.

On the basis of unadjusted outcomes, a larger proportion of CAPD patients transferred to maintenance hemodialysis, compared with APD patients (Table 2). However, under an ITT non-proportional hazards regression analysis, there were no significant differences in either the time-dependent or overall relative risk for technique failure (adjusted for demographic, clinical, laboratory, and facility characteristics) between CAPD and APD patients (Table 4, Figures 4 and 5a).

Table 1 | Select characteristics of patients undergoing CAPD and APD on day 90 of end-stage renal disease

	CAPD (n = 42,942)	APD (n = 23,439)	P-value
<i>Cohort period, n</i>			
1996–1998	17,174	7243	
1999–2001	13,619	7967	
2002–2004	12,149	8229	
Age, years	56.4 ± 15.1	57.1 ± 15.6	< 0.001
Gender, % male	52.6	55.6	< 0.001
<i>Race, %</i>			
Whites	72.2	74.5	< 0.001
Blacks	20.8	19.6	
Asians	4.5	3.2	
Others	2.5	2.7	
<i>Cause of end-stage renal disease</i>			
Diabetes	46.1	45.4	< 0.05
Hypertension	21.6	21.9	
Glomerulonephritis	14.9	14.6	
Others	17.3	18.1	
Cardiac arrest or dysrhythmia, %	4.9	5.3	< 0.05
Cerebrovascular disease, %	6.4	6.9	< 0.01
Congestive heart failure, %	22.2	21.5	NS
Ischemic heart disease or myocardial infarction, %	21.7	22.0	NS
Peripheral vascular disease, %	11.2	11.3	NS
Limited activities of daily living, %	1.3	1.5	< 0.05
Chronic obstructive pulmonary disease, %	4.5	4.1	< 0.05
Current smokers, %	6.2	5.4	< 0.001
Diabetes (primary or secondary), %	47.2	46.5	NS
Malignant neoplasm, %	3.5	3.9	< 0.01
Body mass index, kg/m ²	26.9 ± 6.5	26.8 ± 6.4	NS
Hemoglobin, g per 100 ml	10.3 ± 1.8	10.3 ± 1.8	< 0.001
Serum albumin, g per 100 ml	3.5 ± 0.7	3.5 ± 0.7	NS
Blood urea nitrogen, mg per 100 ml	83.2 ± 29.3	83.8 ± 29.3	< 0.01
Serum creatinine, mg per 100 ml	7.5 ± 3.3	7.5 ± 3.3	NS
Estimated glomerular filtration rate, ml/min per 1.73 m ²	8.8 ± 4.0	8.9 ± 4.0	< 0.001
<i>Center census period-prevalent patient numbers</i>			
	(n = 41,265)	(n = 22,574)	
<i>All dialysis patients</i>			
mean ± s.d. ^a	135.0 ± 73.2	133.5 ± 75.7	< 0.001
median (range) ^b	124 (2, 478)	119 (1, 478)	< 0.05
<i>Peritoneal dialysis patients</i>			
mean ± s.d.	38.2 ± 28.0	37.3 ± 30.2	< 0.001
median (range)	31 (1, 202)	28 (1, 202)	< 0.001
<i>CAPD patients</i>			
mean ± s.d.	22.7 ± 19.7	12.0 ± 14.3	< 0.001
median (range)	17 (0, 135)	7 (0, 135)	< 0.001
<i>APD patients</i>			
mean ± s.d.	15.5 ± 15.6	25.4 ± 22.7	< 0.001
median (range)	11 (0, 121)	18 (0, 128)	< 0.001

APD, automated peritoneal dialysis; CAPD, continuous ambulatory peritoneal dialysis.

^aValues represent the average facility count among patients with linked facility-level data.

^bP-values based on the Wilcoxon rank sum test.

Table 2 | Unadjusted outcomes of patients undergoing CAPD and APD on day 90 of end-stage renal disease

Event	CAPD (n = 42,942)		APD (n = 23,439)		Pearson's χ^2 P-value
	n	% Patients	n	% Patients	
Treated with same PD modality	6929	16.1	4214	18.0	< 0.001
Death	14,189	33.0	7626	32.5	
Transfer to in-center HD	13,295	31.0	6760	28.8	
Transfer to home HD/other PD	1374	3.2	812	3.5	
Transplant	7155	16.7	4027	17.2	

APD, automated peritoneal dialysis; CAPD, continuous ambulatory peritoneal dialysis; HD, hemodialysis; PD, peritoneal dialysis.

Table 3 | Summary of overall, ITT, non-proportional hazard regression for mortality in incident chronic PD patients between 1996 and 2004 (CAPD, n = 42,803; APD, n = 23,345)

Variable	Reference	Hazard ratio (95% confidence interval)	Overall P-value
<i>Cohort period</i>	1996–1998		< 0.0001
1999–2001		0.86 (0.83, 0.88)	
2002–2004		0.55 (0.53, 0.57)	
<i>Interval × modality (months)</i>	CAPD		0.03
0–6		0.98 (0.92, 1.04)	
6–12		1.12 (1.05, 1.20)	
12–18		1.05 (0.98, 1.13)	
18–24		1.06 (0.97, 1.15)	
24–30		1.00 (0.91, 1.10)	
30–36		0.97 (0.87, 1.09)	
36–161		0.97 (0.90, 1.05)	
<i>Age, years</i>	18–44 years		< 0.0001
45–64		2.07 (1.96, 2.19)	
65+		4.18 (3.96, 4.41)	
<i>Male gender</i>	Female	0.92 (0.89, 0.95)	< 0.0001
<i>Race</i>	White		< 0.0001
Asian		0.60 (0.55, 0.65)	
Black		0.77 (0.74, 0.80)	
Other/unknown		0.81 (0.74, 0.88)	
<i>Cause of ESRD</i>	Diabetes		< 0.0001
Hypertension		0.82 (0.78, 0.86)	
Glomerulonephritis		0.56 (0.53, 0.60)	
Other		0.82 (0.78, 0.87)	
Cardiac arrest or dysrhythmia	No	1.19 (1.13, 1.25)	< 0.0001
Cerebrovascular disease	No	1.27 (1.22, 1.33)	< 0.0001
Congestive heart failure	No	1.41 (1.36, 1.45)	< 0.0001
Ischemic heart disease or myocardial infarction	No	1.18 (1.14, 1.22)	< 0.0001
Peripheral vascular disease	No	1.16 (1.12, 1.21)	< 0.0001
Limited activities of daily living	No	2.04 (1.87, 2.22)	< 0.0001
Chronic obstructive pulmonary disease	No	1.19 (1.13, 1.26)	< 0.0001
Current smokers	No	1.07 (1.01, 1.14)	0.02
Diabetes (primary or secondary)	No	1.08 (1.03, 1.13)	0.0009
Malignant neoplasm	No	1.25 (1.17, 1.33)	< 0.0001
<i>Body mass index quintiles (kg/m²)</i>	< 21.88 kg/m ²		< 0.0001
21.88–24.61		0.90 (0.86, 0.94)	
24.61–27.43		0.82 (0.79, 0.86)	
27.43–31.37		0.86 (0.82, 0.90)	
> 31.37		0.94 (0.89, 0.98)	
Data missing		0.93 (0.89, 0.98)	
<i>Hemoglobin quintiles (g per 100 ml)</i>	< 8.9 g per 100 ml		< 0.0001
8.9–9.9		0.99 (0.95, 1.04)	
9.9–10.7		0.90 (0.86, 0.95)	
10.7–11.7		0.92 (0.88, 0.97)	
> 11.7		0.89 (0.84, 0.93)	
Data missing		0.92 (0.87, 0.97)	
<i>Serum albumin quintiles (g per 100 ml)</i>	< 2.9 g per 100 ml		< 0.0001
2.9–3.4		0.86 (0.82, 0.90)	
3.4–3.7		0.76 (0.72, 0.79)	
3.7–4.0		0.67 (0.63, 0.70)	
> 4.0		0.55 (0.52, 0.58)	
Data missing		0.78 (0.74, 0.81)	
<i>Blood urea nitrogen quintiles (mg per 100 ml)</i>	< 59 mg per 100 ml		< 0.0001
59–73		0.97 (0.93, 1.02)	
73–87		1.05 (0.99, 1.10)	
87–105		1.14 (1.09, 1.20)	
> 105		1.30 (1.24, 1.36)	
Data missing		1.05 (0.99, 1.12)	

Table 3 continued on following page

Table 3 | Continued

Variable	Reference	Hazard ratio (95% confidence interval)	Overall P-value
Glomerular filtration rate quintiles (ml/min per 1.73 m ²)	<5.65 ml/min per 1.73 m ²		<0.0001
5.65–7.18		1.11 (1.05, 1.16)	
7.18–8.84		1.18 (1.12, 1.24)	
8.84–11.41		1.27 (1.21, 1.34)	
> 11.41		1.60 (1.52, 1.68)	
Data missing		1.95 (1.77, 2.15)	
Type of center	For profit		0.89
Not for profit		1.01 (0.98, 1.04)	
Unknown		1.05 (0.79, 1.40)	
Period prevalent HD patient census (count)	1–35		0.07
36–59		0.97 (0.91, 1.04)	
60–90		0.95 (0.89, 1.01)	
> 90		0.93 (0.87, 0.99)	
Facility count = 0		0.95 (0.88, 1.02)	
Period prevalent PD patient census (count)	1–5		0.23
6–12		0.94 (0.87, 1.01)	
13–24		0.93 (0.86, 0.99)	
> 24		0.93 (0.87, 0.99)	

APD, automated peritoneal dialysis; CAPD, continuous ambulatory peritoneal dialysis; ESRD, end-stage renal disease; HD, hemodialysis; ITT, intention to treat; PD, peritoneal dialysis.

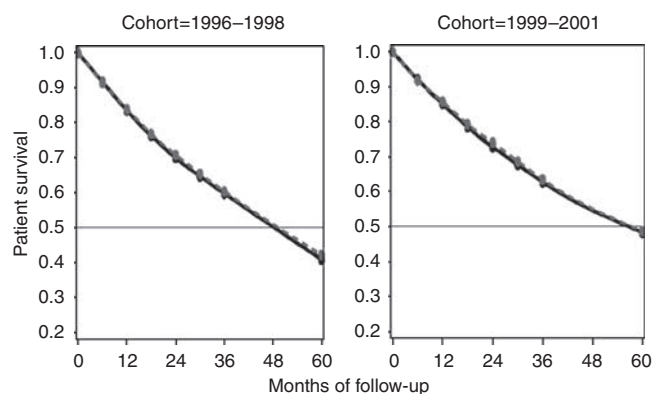


Figure 1 | Adjusted, intent-to-treat, patient survival among incident chronic peritoneal dialysis patients undergoing continuous ambulatory peritoneal dialysis or automated peritoneal dialysis in the United States in two cohort periods. Compared with 1996–1998 incident PD patients, the hazard ratio for death for the incident patients in the 1999–2001 cohort was 0.86 (0.83–0.88).

Under a time-dependent as-treated analysis, there were significant differences in technique failure rates over time. Among patients on APD at the time, the technique failure rate was significantly lower in the early (0–6) and later (30–36) months, but significantly higher in most of the intervening period (6–24 months) (Figure 5b). The hazard ratios for the confounding variables under the as-treated analysis were almost identical to that with the intention-to-treat analysis (data not shown). There was a graded, significant inverse relationship between the number of CPD patients and technique failure (Table 4).

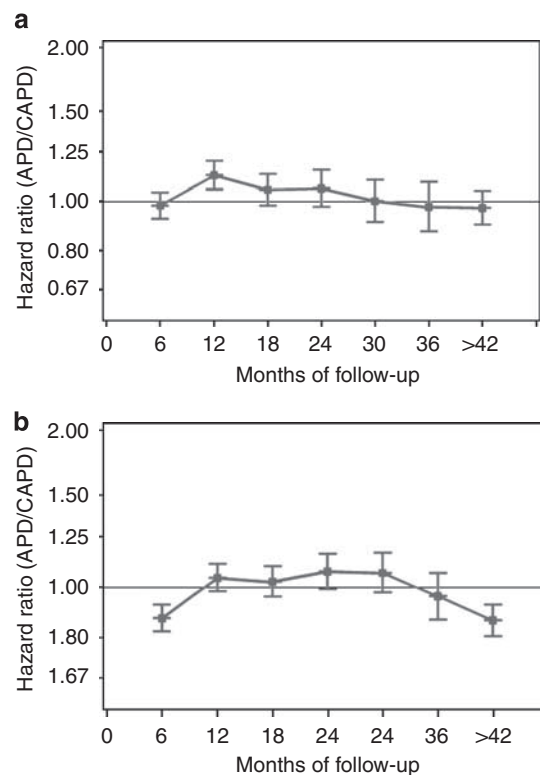


Figure 2 | Adjusted hazard ratio for death, using non-proportional hazards, among patients undergoing automated peritoneal dialysis compared with those undergoing continuous ambulatory peritoneal dialysis between 1996 and 2004. (a) Intent-to-treat and (b) as-treated analyses. Data are adjusted for cohort period, demographics, clinical, laboratory, and baseline facility characteristics.

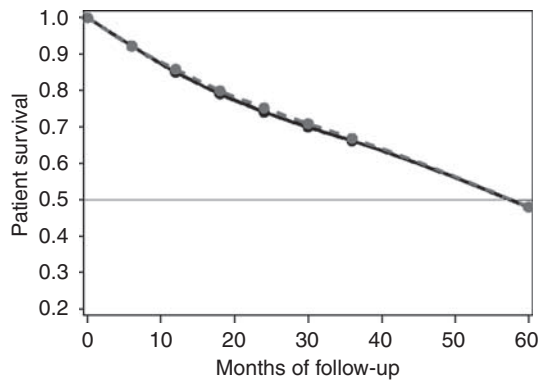


Figure 3 | Adjusted, intent-to-treat patient survival among patients undergoing continuous ambulatory peritoneal dialysis and automated peritoneal dialysis in the United States between 1996 and 2004. Survival curves are based on the assumption of non-proportional hazards and are adjusted for cohort period, demographics, clinical, laboratory, and baseline facility characteristics. An overall adjusted hazard ratio based on a proportional hazard model is included. With CAPD patients as the reference group, the hazard ratio for death for APD patients was 1.03 (0.99, 1.06).

DISCUSSION

This study provides several valuable pieces of new information about the outcomes of PD patients in the United States. First, there have been substantial reductions in the adjusted risk for death and technique failure among incident PD patients since 1996. Second, the outcomes of CAPD and APD patients are remarkably similar and the improvement in PD outcomes cannot be attributed to a greater use of APD. Third, centers with a higher PD utilization had a significantly lower risk of technique failure and marginally lower risk of death.

In this study, we examined the adjusted risk for death in incident PD patients in three 3-year cohorts, starting in 1996. The risk for death and technique failure among incident PD patients in 2002–2004 was 45 and 38%, respectively, lower than that in 1996–1998. To our knowledge, this study provides one of the most comprehensive evidence of the improvement in PD outcomes to date. We have reported earlier an improvement in the 1-year adjusted risk for death or transfer to maintenance hemodialysis among incident PD patients;¹ this study extends those findings and shows an improvement in the long-term outcomes as well. Mujais and Story⁸ also reported a small reduction in unadjusted 1-year mortality among 40,869 PD patients in the United States. However, the study was limited to patients who used supplies from Baxter Healthcare, included patients transferred from maintenance hemodialysis (and thus, included both incident and prevalent patients), was limited to a 4-year period (2000–2003), and did not include any multivariate analyses for change in outcome over time.⁸

To our knowledge, this is the first study that has documented a progressive and substantial reduction in technique failure among incident PD patients in the United States. An increased technique success implies that fewer PD

patients needed to transfer to maintenance hemodialysis—an event that is both expensive and often associated with patient morbidity. It follows, then, that the cost-savings with the use of PD are likely to have increased over the study period; however, this remains speculative.

During the period examined, a larger proportion of patients were treated with APD, and we sought to determine whether the improvement in PD outcomes was a result of greater APD use. However, we were unable to show any significant differences in the risk for either death or technique failure among CAPD and APD patients. Furthermore, there was no significant interaction between modality and cohort period showing that there were similar improvements in outcomes with both modalities.

With the increasing use of APD in the United States and elsewhere, and some single-center studies raising concern about the therapy (lower daily sodium removal, faster loss of residual renal function), it is critically important to compare the outcomes of CAPD and APD patients. Two randomized, controlled trials have been undertaken to date and have shown similar outcomes with the two modalities.^{11,12} However, only 139 subjects were enrolled in the two trials put together; hence, these studies were under-powered to detect any differences in risk for death or technique failure. In the last 2 years, three observational studies have compared the effect of PD modality on patient outcomes—one each including centers in the United States that use Baxter supplies ($n = 40,869$), from the Australia New Zealand Registry (ANZDATA) ($n = 4128$), and a single-center study from Mexico ($n = 237$).^{8–10} One of these studies showed lower risk for death (Mexico), and two of these showed a lower technique failure (the United States and Mexico). We, on the other hand, were unable to show any difference in the risk for either death or technique failure between CAPD and APD subjects.

There are several strengths of this study that significantly increase the robustness of our findings. First, we included all incident patients in the United States over the 9-year period. This makes it the largest study to date that has looked into this question ($n = 66,381$). Second, comparisons of CAPD and APD outcomes are often hampered on how to deal with patients who transfer between these two modalities. Some investigators have tried to overcome this limitation by ITT analysis (Baxter), whereas others have assigned patients to APD as long as they had been treated with the therapy for at least one period (ANZDATA).^{8,9} Furthermore, generally, studies have assumed that the outcomes are proportional over time. We believe we have overcome each of the above limitations in that both ITT and time-dependent as-treated analyses were performed and non-proportional hazards models were used to study relative risk for APD patients, compared with those for CAPD patients, in six 6-month intervals. Finally, the hazards were estimated after comprehensive multivariate adjustment. Whereas the study from Mexico reported only the results of the univariate analysis, the Baxter Healthcare study used only limited multivariate

Table 4 | Summary of overall, intention-to-treat, non-proportional hazard regression for technique survival in incident chronic peritoneal dialysis patients between 1996 and 2004 (CAPD, n = 42,803; APD, n = 23,345)

Variable	Reference	Hazard ratio (95% confidence interval)	Overall P-value
<i>Cohort period</i>	1996–1998		< 0.0001
1999–2001		0.90 (0.87, 0.93)	
2002–2004		0.62 (0.59, 0.64)	
<i>Interval × modality (months)</i>	CAPD		0.11
0–6		0.98 (0.92, 1.04)	
6–12		1.05 (0.98, 1.13)	
12–18		1.05 (0.97, 1.13)	
18–24		1.05 (0.96, 1.15)	
24–30		0.99 (0.91, 1.09)	
30–36		0.93 (0.83, 1.03)	
36–161		0.93 (0.84, 1.02)	
<i>Age, years</i>	18–44 years		< 0.0001
45–64		1.03 (0.99, 1.07)	
65+		1.14 (1.10, 1.19)	
<i>Male gender</i>	Female	1.05 (1.01, 1.08)	0.004
<i>Race</i>	White		< 0.0001
Asian		0.70 (0.65, 0.76)	
Black		1.16 (1.12, 1.20)	
Other/unknown		0.97 (0.89, 1.06)	
<i>Cause of ESRD</i>	Diabetes		< 0.0001
Hypertension		0.88 (0.83, 0.93)	
Glomerulonephritis		0.83 (0.78, 0.88)	
Other		0.87 (0.82, 0.92)	
Cardiac arrest or dysrhythmia	No	0.95 (0.88, 1.02)	0.17
Cerebrovascular disease	No	1.12 (1.05, 1.19)	0.0003
Congestive heart failure	No	1.01 (0.97, 1.05)	0.58
Ischemic heart disease or myocardial infarction	No	0.98 (0.94, 1.02)	0.28
Peripheral vascular disease	No	1.03 (0.98, 1.09)	0.19
Limited activities of daily living	No	1.12 (0.97, 1.30)	0.13
Chronic obstructive pulmonary disease	No	1.04 (0.96, 1.12)	0.39
Current smokers	No	1.15 (1.09, 1.22)	< 0.0001
Diabetes (primary or secondary)	No	1.03 (0.98, 1.08)	0.23
Malignant neoplasm	No	1.08 (1.00, 1.17)	0.04
<i>Body mass index quintiles (kg/m²)</i>	< 21.88 kg/m ²		< 0.0001
21.88–24.61		1.03 (0.98, 1.08)	
24.61–27.43		1.06 (1.01, 1.11)	
27.43–31.37		1.15 (1.10, 1.21)	
> 31.37		1.37 (1.30, 1.44)	
Data missing		1.02 (0.96, 1.08)	
<i>Hemoglobin quintiles (g per 100 ml)</i>	< 8.9 g per 100 ml		< 0.0001
8.9–9.9		0.97 (0.93, 1.02)	
9.9–10.7		0.94 (0.89, 0.98)	
10.7–11.7		0.90 (0.86, 0.95)	
> 11.7		0.88 (0.84, 0.93)	
Data missing		0.95 (0.90, 1.00)	
<i>Serum albumin quintiles (g per 100 ml)</i>	< 2.9 g per 100 ml		< 0.0001
2.9–3.4		0.89 (0.85, 0.94)	
3.4–3.7		0.86 (0.81, 0.91)	
3.7–4.0		0.81 (0.76, 0.85)	
> 4.0		0.77 (0.73, 0.81)	
Data missing		0.88 (0.83, 0.92)	
<i>Blood urea nitrogen quintiles (mg per 100 ml)</i>	< 59 mg per 100 ml		0.39
59–73		0.99 (0.94, 1.04)	
73–87		0.96 (0.91, 1.00)	
87–105		0.98 (0.93, 1.03)	
> 105		0.96 (0.91, 1.01)	
Data missing		0.95 (0.89, 1.01)	

Table 4 continued on following page

Table 4 | Continued

Variable	Reference	Hazard ratio (95% confidence interval)	Overall P-value
Glomerular filtration rate quintiles (ml/min per 1.73 m ²)	<5.65 ml/min per 1.73 m ²		0.01
5.65–7.18		1.01 (0.97, 1.06)	
7.18–8.84		1.04 (0.99, 1.09)	
8.84–11.41		1.06 (1.01, 1.11)	
> 11.41		1.07 (1.01, 1.13)	
Data missing		0.88 (0.78, 1.01)	
Type of center	For profit		0.10
Not for profit		0.97 (0.94, 1.00)	
Unknown		0.81 (0.60, 1.10)	
Period prevalent HD patient census (count)	1–35		<0.0001
36–59		1.04 (0.96, 1.12)	
60–90		1.04 (0.96, 1.11)	
> 90		1.10 (1.02, 1.17)	
Facility count = 0		0.84 (0.77, 0.92)	
Period prevalent PD patient census (count)	1–5		<0.0001
6–12		0.91 (0.84, 0.98)	
13–24		0.80 (0.75, 0.86)	
> 24		0.72 (0.67, 0.77)	

APD, automated peritoneal dialysis; CAPD, continuous ambulatory peritoneal dialysis; ESRD, end-stage renal disease; HD, hemodialysis; ITT, intention to treat; PD, peritoneal dialysis.

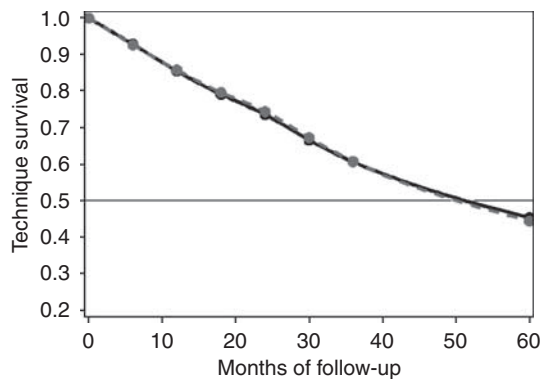


Figure 4 | Adjusted, intent-to-treat technique survival among patients undergoing continuous ambulatory peritoneal dialysis and automated peritoneal dialysis in the United States between 1996 and 2004. Technique survival curves are based on the assumption of non-proportional hazards and are adjusted for demographics, clinical, laboratory, and baseline facility characteristics. An overall adjusted hazard ratio based on a proportional hazard model is included. With CAPD patients as the reference group, the hazard ratio for technique failure for APD patients was 1.00 (0.97, 1.03).

adjustment (age, gender, diabetes, patient type, and center census).^{8,10} In addition to adjusting the data for a large number of demographic, clinical, and laboratory variables, facility characteristics were included in the multivariate models.

Over the last few years, studies from Canada, the Netherlands, and the United States have shown the importance of cumulative physician experience, and center

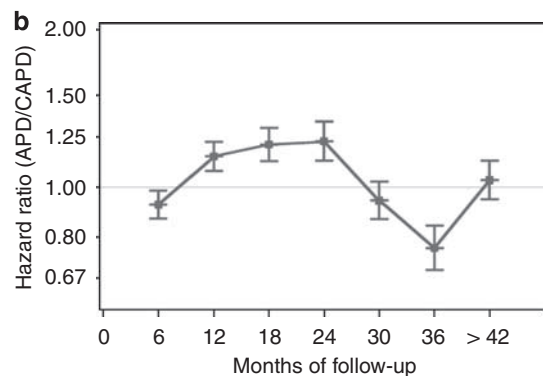
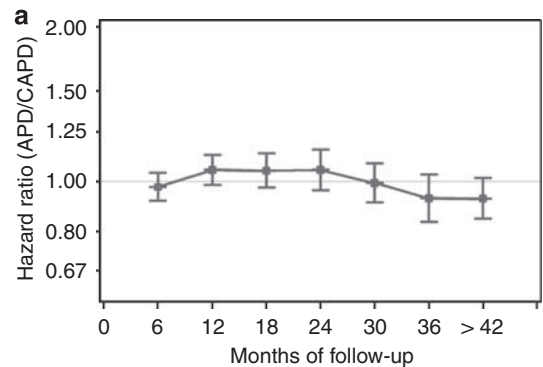


Figure 5 | Adjusted hazard ratio for technique survival, using non-proportional hazards, among patients undergoing automated peritoneal dialysis compared with those undergoing continuous ambulatory peritoneal dialysis between 1996 and 2004. (a) Intent-to-treat and (b) as-treated analysis. Data are adjusted for cohort period, demographics, clinical, laboratory, and baseline facility characteristics.

census on outcomes of PD patients.^{8,13,14} This study further expands our knowledge of the center census effect on outcomes. First, the proportion of PD patients in a dialysis unit in the United States that are treated with APD is, to a large extent, determined by the dialysis facility where they are treated. Indeed, among 41,265 incident CAPD patients with facility-linked census data, the average APD census count constituted 41% of the average PD census count, compared with 68% for units where the 22,574 incident APD patients with facility-linked census data were treated ($P < 0.001$, Table 1). Thus, the dialysis facility is an important determinant of selection of the PD modality. Second, we were able to identify a trend toward lower mortality in larger centers, although, when compared jointly across all center size categories, this trend did not reach statistical significance. Third, we identified a significant decreasing trend in technique failure with increasing numbers of PD patients. In addition to larger cumulative experience, dialysis facilities with a larger PD patient census are likely to have resolved 'system' and infrastructure issues (such as availability of nurses on call, procedures for catheter placement and care, protocols to reduce infectious risk), which serve to reduce the risk for transfer to maintenance hemodialysis. Adjusting data for facility characteristics further strengthens the robustness of our conclusion that CAPD and APD patients have similar outcomes.

Despite its strength, this study is not without limitations. First, there may be some risk for ascertainment bias vis-à-vis PD modality. We used the definition traditionally used to determine the initial PD modality (implying the modality with which the patient was being treated on day 90 of end-stage renal disease). Using this definition, 40% of incident patients were initially treated with APD between 2002 and 2004. In contrast, almost 60% of patients using Baxter Healthcare supplies were reported to being treated with APD.⁸ However, the interval between the date of onset of ESRD and the ascertainment of PD modality was not reported. Moreover, the USRDS data used herein is likely to be more reliable with regard to the date of onset of ESRD, treatment with non-PD modalities, and, thus, ascertainment of the initial PD modality. Second, there may be selection bias such that high transporters may more likely be assigned to APD than to CAPD, and data on peritoneal transport type are not available in the USRDS. High transporters have been reported earlier to have a higher risk for death and technique failure.¹⁵ This, in turn, may have biased the data toward the null hypothesis. However, there are several reasons why this is unlikely to be the case. The use of APD obviates the higher risk for death or technique failure seen in high transporters treated with CAPD.¹⁵ Consistent with these findings, despite adjustment for peritoneal transport rate in the ANZDATA analyses, there was no demonstrable difference in the risk for death or technique failure in CAPD and APD patients.⁹ As discussed earlier, dialysis facility was a strong determinant of the proportion of patients treated with APD. The difference in APD use by dialysis facilities is more likely to be a result of

provider preference rather than a systematic difference in patients' peritoneal transport type. Thus, it appears unlikely that selection bias may have affected our results. Third, APD is a heterogeneous therapy and the prescription may vary by the duration and the number of exchanges of nighttime cycling and the number of daytime exchanges. This information was unavailable and we cannot be certain whether varying the APD prescription has an effect on patient outcomes. Finally, we cannot exclude residual confounding, as the reporting of coexisting illnesses on the Medical Evidence form 2728 is often incomplete.¹⁶ However, recent studies suggest that a more comprehensive adjustment for coexisting illnesses when performing survival studies in dialysis patients does not appear to alter the hazard ratios.¹⁷ Moreover, the error is likely to be random and probably equally likely for CAPD and APD patients. These considerations suggest that despite the limitation of data on coexisting diseases, our findings of similar outcomes with CAPD and APD are likely to be robust.

In conclusion, in this study, we show a continued and substantial reduction in the risk of death and technique failure for PD patients. Patients treated with CAPD and APD have similar outcomes, which have improved similarly over the same time period. Thus, improvement of the PD outcomes over the studied period cannot be attributed to a greater use of APD. Reduced infectious risk, or more selective assignment of patients to the therapy over time, or better prescription management may account for the improved PD outcomes.

MATERIALS AND METHODS

Data source

The study protocol was reviewed and approved as exempt by the Institutional Review Board at Los Angeles Biomedical Research Center. The data for all incident patients over a 9-year period (1996 through 2004) were obtained from the Patient and MEDEVID files of the USRDS. The data were linked to the RXHIST60 file to assign treatment modality and to the Facility File to ascertain selected characteristics of the dialysis unit.

Definitions

As is the convention, the dialysis modality 90 days after the first service date and continuous treatment for at least 60 days ('60-d rule') was considered to be the initial modality.¹⁸ Information on the presence/absence of various coexisting illnesses and the initial laboratory results was obtained from the Medical Evidence Form 2728. The unit affiliation was defined as the dialysis facility where the patient was being treated on day 90 of end-stage renal disease. Each patient's data was linked with the facility data from the same year as the one in which the patient was deemed to be incident. The patient census in the facility file refers to the point-prevalent count of patients undergoing treatment with each modality on 31 December of the survey year. However, for the purposes of this analysis, we enumerated a period-prevalent count obtained by adding to the point-prevalent facility count those incident patients who started the year in the facility but whose follow-up ended before 31 December of the given survey year (as determined by the patient-level data). For this analysis, only patients in whom the modality on

day 90 was either CAPD or APD were included; patients undergoing treatment with 'other' PD were excluded. Patients from facilities with missing census data or whose census total was 0 for a given survey year were excluded from all analyses that adjust for facility-level characteristics (2542 of the 66,381 incident CPD patients or 3.8%).

Statistical analyses

Baseline characteristics of CAPD and APD patients were compared using Pearson χ^2 tests for categorical variables and the Student *t*-test for continuous variables. Patients were followed till the time of transfer to maintenance hemodialysis, home hemodialysis, 'other' PD, transplant, or death, whichever happened first, or till the time of last follow-up (30 September 2006). Proportional and non-proportional hazards models using a piecewise exponential survival model (or the interval Poisson regression model) were used to compare case-mix adjusted mortality and technique failure rates between CAPD and APD at successive 6-month intervals through the first 36 months.^{19–21} Average or time-independent hazard ratios of death and technique failure for APD compared with CAPD patients were estimated using a proportional hazards model, whereas time-dependent relative risks and adjusted patient survival curves were estimated with a non-proportional hazards model. Hazard ratios and corresponding 95% CIs were adjusted for case-mix differences in cohorts, age, gender, race, cause of end-stage renal disease, individual comorbidities, baseline body mass index, estimated glomerular filtration rate, baseline laboratory values (hemoglobin, blood urea nitrogen, and albumin), type of dialysis facility (for-profit, non-profit, other), and dialysis facility census (period-prevalent numbers of hemodialysis and PD patients). To avoid imputing missing values with respect to patient-level data and making unnecessary parametric assumptions (e.g., assuming age has a linear effect on the log-risk of death), age, body mass index, estimated glomerular filtration rate, and all three laboratory variables were analyzed as discrete categorical variables.^{22,23} Missing laboratory values were categorized as not available within the various analyses, a strategy that has been used successfully in earlier studies to avoid excluding patients with missing values (<http://www.nature.com/ki/journal/v66/n6/full/4494902a.html>).^{22,23} All analyses were carried out using the SAS statistical software package (version 9.2, SAS Inc., Cary, NC, USA); in particular, the GENMOD procedure was used to fit the data using a piecewise exponential survival model (both proportional hazards and non-proportional hazards) as implemented by the interval Poisson regression. Additional analyses based on the Cox proportional hazards model were also run, but, as has been shown earlier, the results were nearly identical with those obtained under the piecewise exponential survival model (data not shown).¹⁹ The piecewise exponential survival model was chosen for its flexibility in providing adjusted population-averaged survival curve estimates.

The primary analysis was carried out using an ITT approach in which death or technique failure was assigned to a patient's initial treatment modality regardless of a change in therapy during the course of follow-up. A time-dependent as-treated analysis was also performed, in which the event of interest (i.e., death or technique failure) was assigned to the modality the patient was on at the time of the event or in those cases where patients switched from CAPD to APD or vice versa, within 60 days after the switch in therapy. In this latter case, any event (i.e., death or transfer to maintenance hemodialysis) that occurred within 60 days after a therapy change was attributed to the prior treatment modality. To confirm results

comparing APD and CAPD patient and technique survival, as well as confirm trends in patient outcomes over the three cohort periods for all 66,381 patients, a second set of analyses was performed excluding adjustments for facility-level characteristics. The results were nearly identical with those reported here (data not shown).

Model goodness of fit was assessed by both a likelihood ratio test and quasi-likelihood ratio test, in which higher order ITT models containing select interactions with treatment modality (i.e., cohort by modality, age by modality, and diabetes by modality) were compared with the ITT models reported on in this manuscript. These higher order models were compared against the models without interactions so as to rule out earlier identified interaction effects that are known to be present in mortality comparisons between PD and hemodialysis.²⁴ For both mortality and technique failure, the likelihood ratio and quasi-likelihood ratio tests were not significant ($P > 0.32$ in all cases), indicating the models used in this manuscript provide a reasonable fit to the observed rate of events. Finally, adjusted population-averaged survival curves were computed using the direct adjusted survival curve approach described by Zhang *et al.*²⁴ From these, median life expectancies were computed using life table methodology.²⁵

DISCLOSURE

Rajnish Mehrotra and/or Kamyar Kalantar-Zadeh have received research support from Amgen, Baxter Healthcare, and Shire; honoraria from Baxter Healthcare Corporation and Shire; and/or served as a consultant for Novartis. Edward Vonesh is a consultant for Baxter Healthcare Corporation.

ACKNOWLEDGMENTS

The data used in this study were supplied by the USRDS and the findings do not represent the opinion of the US government or the USRDS. The study was supported by a research grant from Baxter Healthcare. Rajnish Mehrotra is supported by a grant from the National Institutes of Health (RR18298), the American Heart Association, and DaVita Inc. The authors thank Eileen Eriksen for management of data obtained from the USRDS.

REFERENCES

- Mehrotra R, Kermah D, Fried L *et al.* Chronic peritoneal dialysis in the United States: declining despite utilization improving outcomes. *J Am Soc Nephrol* 2007; **18**: 2781–2788.
- Bender FH, Bernardini J, Piraino B. Prevention of infectious complications in peritoneal dialysis: best demonstrated practices. *Kidney Int Suppl* 2006; Suppl 103: S44–S54.
- Mehrotra R. Changing patterns of peritoneal dialysis utilization in the United States. *Perit Dial Int* 2007; **27**(Suppl 2): S51–S52.
- National Kidney Foundation. NKF-DOQI clinical practice guidelines for peritoneal dialysis adequacy. *Am J Kidney Dis* 1997; **30**: S69–S133.
- Rabindranath KS, Adams J, Ali TZ *et al.* Automated vs continuous ambulatory peritoneal dialysis: a systematic review of randomized controlled trials. *Nephrol Dial Transplant* 2007; **22**: 2991–2998.
- Mehrotra R. Long term outcomes in automated peritoneal dialysis: similar or better than continuous ambulatory peritoneal dialysis? *Perit Dial Int* 2009; **29**(Suppl 2): S111–S114.
- Westra WM, Kopple JD, Krediet RT *et al.* Dietary protein requirements and dialysate protein losses in chronic peritoneal dialysis patients. *Perit Dial Int* 2007; **27**: 192–195.
- Mujais S, Story K. Peritoneal dialysis in the US: evaluation of outcomes in contemporary cohorts. *Kidney Int Suppl* 2006; Suppl 103: S21–S26.
- Badve SV, Hawley CM, McDonald SP *et al.* Automated and continuous ambulatory peritoneal dialysis have similar outcomes. *Kidney Int* 2008; **73**: 480–488.
- Sanchez AR, Madonia C, Rascon-Pacheco RA. Improved patient/technique survival and peritonitis rates in patients treated with automated peritoneal dialysis when compared to continuous ambulatory peritoneal dialysis in a Mexican PD center. *Kidney Int Suppl* 2008; Suppl 108: S76–S80.

11. de Fijter CW, Oe LP, Nauta JJ *et al.* Clinical efficacy and morbidity associated with continuous cyclic compared with continuous ambulatory peritoneal dialysis. *Ann Intern Med* 1994; **120**: 264–271.
12. Bro S, Bjorner JB, Tofte-Jensen P *et al.* A prospective, randomized multicenter study comparing APD and CAPD treatment. *Perit Dial Int* 1999; **19**: 526–533.
13. Schaubel DE, Blake PG, Fenton SS. Effect of renal center characteristics on mortality and technique failure on peritoneal dialysis. *Kidney Int* 2001; **60**: 1517–1524.
14. Huisman RM, Nieuwenhuizen MG, Th de Charro F. Patient-related and centre-related factors influencing technique survival of peritoneal dialysis in The Netherlands. *Nephrol Dial Transplant* 2002; **17**: 1655–1660.
15. Brimble KS, Walker M, Margetts PJ *et al.* Meta-analysis: peritoneal membrane transport, mortality, and technique failure in peritoneal dialysis. *J Am Soc Nephrol* 2006; **17**: 2591–2598.
16. Longenecker JC, Coresh J, Klag MJ *et al.* Validation of comorbid conditions on the end-stage renal disease medical evidence report: the CHOICE study. Choices for Healthy Outcomes in Caring for ESRD. *J Am Soc Nephrol* 2000; **11**: 520–529.
17. van Manen JG, van Dijk PC, Stel VS *et al.* Confounding effect of comorbidity in survival studies in patients on renal replacement therapy. *Nephrol Dial Transplant* 2007; **22**: 187–195.
18. United States Renal Data System. *US Department of Public Health and Human Services, Public Health Service, National Institutes of Health*, NIH Publication: Bethesda, 2007.
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*. SAS Institute Inc.: Cary, NC, 1995.
22. Snyder JJ, Foley RN, Gilbertson DT *et al.* Body size and outcomes on peritoneal dialysis in the United States. *Kidney Int* 2003; **64**: 1838–1844.
23. 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.
24. 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. *Comput Methods Programs Biomed* 2007; **88**: 95–101.
25. Lee ET. *Statistical Methods for Survival Data Analysis*. Lifetime Learning Publications: Belmont, CA, 1980.