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LONG-TERM CLINICAL OUTCOMES OF PERITONEAL DIALYSIS PATIENTS: SINGLE CENTER EXPERIENCE FROM KOREA

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Of a large body of literature reporting clinical outcomes for patients maintained on peritoneal dialysis (PD), most publications have focused on relatively short-term results. Few reports have focused on long-term survival in PD patients. Here, we present our experience with long-term patient outcomes and further analyses of the trends in demographics and clinical outcomes of 2301 end-stage renal disease (ESRD) patients treated with continuous ambulatory PD (CAPD) during a 25-year period (1981 – 2005) at our institute. Outcomes were analyzed for 1656 patients, excluding those younger than 15 years of age at initiation of CAPD, those having less than 3 months' follow-up, or those who had been on hemodialysis or who received a kidney graft before starting CAPD.

In the study patients, technique survival at 5 and 10 years was 71.9% and 48.1% respectively. Patient survival was 69.8% and 51.8%. Mean age at the start of PD (50.4 ± 13.9 years vs. 44.2 ± 13.9 years, $p < 0.01$), ESRD incidence as a result of diabetic nephropathy (30.5% vs. 19.5%, $p < 0.01$), and incidence of cardiovascular comorbidities (26.6% vs. 20.5%, $p < 0.01$) were all significantly greater in patients who started PD during the second half of the study period (1993 – 2005) as compared with the first half (1981 – 1992). A multivariate analysis adjusting for these changes in demographics and comorbid conditions revealed that PD therapy starting in 1993 – 2005 was associated with a significant reduction in technique failure [hazard ratio (HR): 0.65; $p < 0.01$] and mortality (HR: 0.68; $p < 0.01$) as compared with the earlier period. However, in subgroup analyses, technique survival was not observed to be significantly improved in patients with diabetes.

In summary, technique and patient survival have significantly improved despite increases in patient age, cardiovascular comorbidity, and ESRD caused by diabetes. Although diabetes, older age, and cardiovascular comorbidities are not factors that are easily modifiable to improve PD outcomes, results at our institution are encouraging in an era of declining PD utilization.

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KEY WORDS: Continuous ambulatory peritoneal dialysis; patient survival; technique survival.

Continuous ambulatory peritoneal dialysis (CAPD) is an established treatment modality in patients with end-stage renal disease (ESRD), and approximately 150 000 patients are being maintained on CAPD worldwide (1). However, the decline of CAPD as compared with hemodialysis (HD) has become evident, even though many reports indicate that survival rates with peritoneal dialysis (PD) are better than those with HD during the first 2 – 3 years after dialysis initiation (2,3). In Korea, CAPD was introduced in the early 1980s, and the technique has been widely used in many centers. Currently, more than 8000 Korean patients are maintained on CAPD. Some publications have reported the outcome of CAPD in Korea (4,5), but reports of long-term CAPD results are scarce. Recently, we reported long-term outcomes for CAPD at our institute (6). Although ours was a single-center study, our extensive and dedicated clinical experience showed remarkable results. Here, we briefly discuss our long-term clinical experience, particularly with regard to survival rates and trends in the improvement of clinical outcomes over 25 years.

PATIENTS AND METHODS

During 1981 – 2005, we initiated PD in a total of 2301 patients at our institute. After excluding patients that had been younger than 15 years of age at initiation of CAPD, that had had fewer than 3 months' follow-up, and that had been on HD or received a kidney graft

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before the start of CAPD, we analyzed data relating to 1656 patients. Patients who recovered kidney function or who started CAPD for other reasons (such as acute renal failure or congestive heart failure) were also excluded.

Of the 1656 CAPD patients in the study, 912 (55.1%) were men. Mean age of the patient population at the start of CAPD was 48.9 ± 14.1 years, and mean PD duration was 46.0 ± 40.4 months (range: 3 – 226 months). Diabetes was the most common cause of ESRD (27.8%), followed by chronic glomerulonephritis (16.5%), and hypertension (13.0%).

RESULTS

PATIENT OUTCOMES

The 1-, 3-, 5-, and 10-year technique survival rates were 94.9%, 83.7%, 71.9%, and 48.1% respectively. The main causes of technique failure were peritonitis (72.3%), ultrafiltration failure (14.0%), mechanical malfunction and leakage (7.3%), and exit-site and tunnel infection (3.4%). The 1-, 3-, 5-, and 10-year patient survival rates were 93.4%, 81.5%, 69.8%, and 51.8% respectively. Most deaths were the result of cardiovascular disease (31.8%) or infection (27.1%).

TRENDS IN DEMOGRAPHICS AND CLINICAL OUTCOMES OVER 25 YEARS

Table 1 details trends in demographics, causes of ESRD, and comorbid conditions of patients during the first (1981 – 1992) and second (1993 – 2005) halves of the study period. Mean age of patients at the start of CAPD increased from 44.2 ± 13.9 years to 50.4 ± 13.9 years. Also, the proportion of patients over 60 years of age at CAPD initiation doubled from the first to the second half of the study period. The proportion of incident PD patients whose renal failure was caused by diabetic nephropathy rose to 30.5% from 19.5% during that time (Table 1).

Table 2 shows changes in clinical outcomes between the two halves of the study period. The technique survival rate was significantly improved in patients who started PD in 1993 – 2005 as compared with the patients who started in 1981 – 1992 (Figure 1, Table 2). Technique failure caused by peritonitis declined significantly in the second half of the study period (1993 – 2005) as compared with the first half (1981 – 1992). Overall patient survival did not differ between the two periods; however, mortality attributable to cardiovascular diseases significantly increased, and mortality attributable to infection decreased (Table 2).

RISK ANALYSES FOR TECHNIQUE AND PATIENT SURVIVAL

Unadjusted univariate analysis showed no difference in mortality between patients who started CAPD in 1993 – 2005 and those who started in 1981 – 1992 (Table 3). However, a multivariate Cox proportional hazards regression model revealed that patient survival increased significantly when adjusted for age, sex, diabetes status, and cardiovascular comorbidity [Figure 1, Table 3; hazard ratio (HR): 0.68; $p < 0.001$]. In addition, male sex (HR: 1.28; $p < 0.05$), presence of diabetes (HR: 2.68; $p < 0.01$), older age (HR: 1.06; $p < 0.01$), and cardiovascular comorbidity at the start of PD (HR: 2.66; $p < 0.01$) were all significantly associated with an increased risk of death. Technique survival increased significantly from the first to the second half of the study period even after adjustment for those covariates. Only the presence of diabetes was identified as a significant risk factor for technique

TABLE 1
Trends in Demographics, Causes of End-Stage Renal Disease (ESRD), and Comorbidities Between the First and Second Halves of the Study Period

	1981–1992		1993–2005	
	(*n*)	(%)	(*n*)	(%)
Patients (*n*)	410		1246	
Sex (men:women)	242:168		670:576	
Age (years)	44.2±13.9		50.4±13.9[a]	
16–30	84	20.5	114	9.1[a]
31–45	127	31.0	324	26.0
46–60	149	36.3	499	40.1
>60	50	12.2	309	24.8[a]
Cause of ESRD				
Diabetes	80	19.5	380	30.5[a]
CGN	77	18.8	196	15.7
Hypertension	40	9.8	176	14.1[a]
PKD	11	2.6	24	1.9
Others	28	6.8	60	4.8
Unknown	174	42.4	410	32.9[a]
Comorbidities				
CVD	87	20.5	332	26.6[a]
Lung disease	3	0.7	12	1.0
Liver disease	11	2.7	29	2.3
Malignancy	7	1.7	26	2.1

[a] $p < 0.01$ compared with 1981–1992.
CGN = chronic glomerulonephritis; PKD = polycystic kidney disease; CVD = cardiovascular disease.

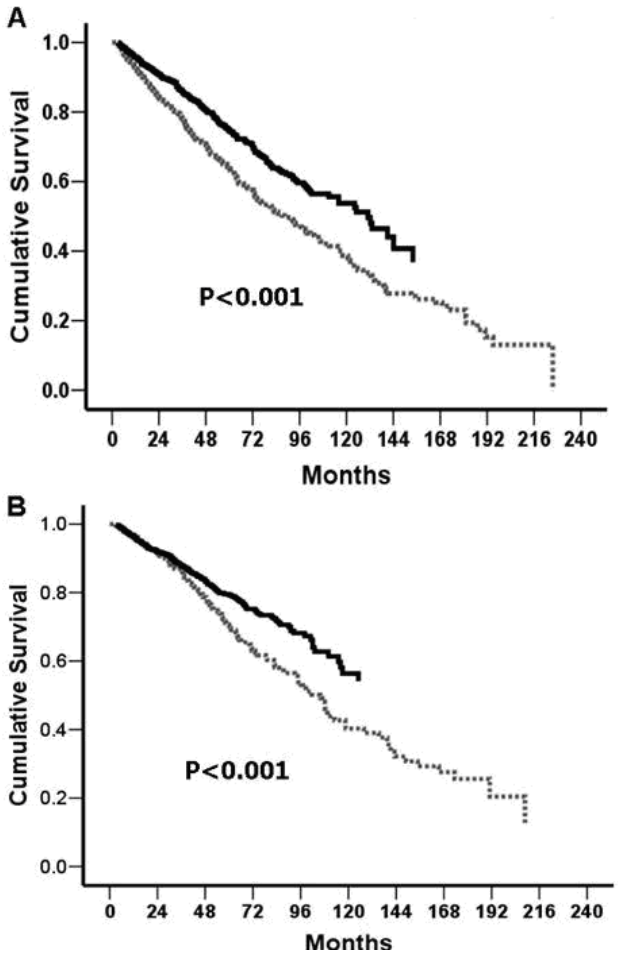

Figure 1 — (A) Technique survival and (B) patient survival for the two halves of the study period (1981 – 1992 and 1993 – 2005), adjusting for age, sex, diabetes status, and cardiovascular comorbidity. The technique and patient survival rates were both significantly better in patients who started peritoneal dialysis during 1993 – 2005 (solid line) than in patients who started peritoneal dialysis during 1981 – 1992 (dashed line).

failure in the multivariate analysis (Table 3; HR: 1.28; $p < 0.05$).

When we conducted subgroup analyses by diabetes status and age, we observed improved patient survival in both diabetic and nondiabetic patients from the 1993 – 2005 cohort as compared with parallel groups from the 1981 – 1992 cohort. However, the improved survival in the 1993 – 2005 cohort was more significant in patients younger than 55 years of age at the start of CAPD; improvement in patients older than 55 years was marginal [HR: 0.77; 95% confidence interval (CI): 0.56 to 1.05].

Technique survival improved significantly in older and younger patients alike. However, improved technique survival was not observed in patients with diabetes (Figure 2).

TABLE 2
Clinical Outcomes in the First and Second Halves of the Study Period

	1981–1992		1993–2005	
	(*n*)	(%)	(*n*)	(%)
Patients (*n*)	410		1246	
5-Year patient survival		71.5		69.1
Cause of death				
Cardiovascular	17	13.4	73	23.8[a]
Cerebrovascular	14	11.0	34	11.1
Infection	50	39.4	68	22.1[a]
Malignancy	6	4.7	14	4.5
5-Year technique survival		64.5		74.7[a]
Cause of technique failure				
Peritonitis	149	79.7	167	66.8[a]
Ultrafiltration failure	20	10.7	41	16.4
Mechanical/leakage	8	4.2	24	9.6
ESI/tunnel infection	5	2.7	10	4.0

[a] $p < 0.05$ compared with 1981–1992.
ESI = exit-site infection.

DISCUSSION

Our long-term clinical experience demonstrate remarkable CAPD outcomes over the 25 years starting in 1981. Technique and patient survival rates alike were higher as compared with rates reported earlier (7–10). Moreover, the overall survival rate for PD patients at our center is comparable to that for patients maintained on HD in other Asian countries, including Japan (11).

A noteworthy finding of the present study is the significant improvement in both technique and patient survival for patients who started PD in 1993 – 2005 as compared with patients from the earlier half of the study period, despite the increasing proportions of older and diabetic patients. One reason for the improved technique survival was a decreased incidence of peritonitis: we previously reported a lower overall peritonitis rate as compared with rates in other countries. Moreover, peritonitis rates have been declining since the early 1990s at our center (6). Many studies have showed that the Y-set and double-bag systems have contributed greatly to the reduction in the peritonitis rate (12,13). Those two connection methodologies were provided starting in the early 1990s and were used for all PD patients at our institute starting in the mid-1990s. We observed a significant fall in the rate of gram-positive peritonitis from that time forward (6). Accordingly, technique failure declined significantly during 1993 – 2005 because of declines in peritonitis

and improvements in PD connection systems (Tables 2 and 3).

In addition, our study revealed that patient survival at our center was greater than that previously reported for other centers and countries. The reason for the superior patient survival rate at our center is not yet fully understood. The relatively younger age of patients at CAPD initiation and the lower proportion of diabetic patients can account for only part of our center's superior outcome, age and diabetes having generally been established to be the most important and significant determinants of survival outcome in CAPD patients. However, the mean age of new ESRD patients initiating CAPD and the proportion of diabetic ESRD patients increased significantly during the second half of the study period reported here (Table 1). Even considering those changes, a multivariate analysis nevertheless showed a significant improvement in patient survival in the 1993 – 2005 cohort as compared with the 1981 – 1992 cohort—an outcome not very different from that in the unadjusted model (Table 3).

Interestingly, a number of studies reported a survival advantage for Asian ESRD patients over Caucasian patients (11,14,15). Relevant to those findings are the results of the Dialysis Outcomes and Practice Patterns Study, which indicated that the relative risk for death is significantly higher for HD patients in both Europe and the United States as compared with HD patients in Japan (16). Just as Japanese PD patients achieve excellent results, with 5- and 10-year patient survival rates being 67.4% and 48.6% respectively (11), patients at our center show equally remarkable results. But to truly determine if patient survival on PD is better in Asian patients than in patients from Western countries, further exploration is required.

To further elucidate which patients had the best outcomes in the two halves of our study period, we conducted subgroup analyses according to diabetes status and patient age (Figure 2). Patient survival was improved in the second half of the study period regardless of diabetes status and age. Although survival was not significantly better in older patients (those over 55 years of age), it came close ($p = 0.076$). In addition, technique survival was significantly better in younger and older patients alike. However, improved technique survival was observed only in nondiabetic patients, in whom 5-year technique survival significantly improved to 76.4% in 1993 – 2005 from 64.7% in 1981 – 1992. In contrast, in diabetic patients, survival was not statistically different between the two periods (58.8% in 1981 – 1992 vs. 64.6% in 1993 – 2005, $p = 0.28$).

An improvement in patient and technique survival for CAPD patients with diabetes is a future challenge. Prolonged use of conventional glucose PD solutions may accelerate changes in peritoneal membrane structure and function in patients with diabetes,

TABLE 3
Technique and Patient Survival by Multivariate Cox Proportional Hazards Model

Covariates	Unadjusted		Adjusted[a]	
	HR	95% CI	HR	95% CI
Technique survival				
Age (per 1-year increase)	1.00	0.99 to 1.00	0.99	0.98 to 1.01
Sex (women vs. men)	0.91	0.75 to 1.10	0.93	0.77 to 1.12
With diabetes (vs. without diabetes)	1.14	0.89 to 1.44	1.28	1.01 to 1.65[b]
CVD comorbidity (vs. no CVD comorbidity)	0.99	0.56 to 1.76	0.96	0.54 to 1.72
PD starting in 1993–2005 (vs. in 1981–1992)	0.66	0.54 to 0.80[c]	0.65	0.53 to 0.79[b]
Patient survival				
Age (per 1-year increase)	1.07	1.06 to 1.08[c]	1.06	1.05 to 1.07[c]
Sex (women vs. men)	0.77	0.64 to 0.93[c]	0.78	0.65 to 0.95[c]
With diabetes (vs. without diabetes)	4.15	3.42 to 5.05[c]	2.68	2.16 to 3.31[c]
CVD comorbidity (vs. no CVD comorbidity)	4.82	3.63 to 6.42[c]	2.66	1.99 to 3.56[c]
PD starting in 1993–2005 (vs. in 1981–1992)	0.93	0.75 to 1.15	0.68	0.55 to 0.86[c]

[a] Adjusted for age, sex, diabetes, and cardiovascular comorbidity.
[b] $p < 0.05$.
[c] $p < 0.001$.
HR = hazard ratio; CI = confidence interval; CVD = cardiovascular disease; PD = peritoneal dialysis.

causing an increased incidence of peritonitis and ultrafiltration failure. In this regard, the new bio-compatible PD solutions containing lower levels of glucose degradation products and the new non glucose, icodextrin-based solutions are highly promising. Use of these newer solutions may prevent or delay alterations in peritoneal membrane structure and function in diabetic patients during long-term PD (17–19).

The present study is limited by the exclusion of certain important factors that could influence clinical outcomes, including details of comorbid conditions, residual renal function, nutritional status, and peritoneal transport characteristics, among others. A significant number of patients who had undergone previous HD or transplantation before initiating PD were excluded from the analysis. In addition, our study was not a multicenter study, and therefore a center-specific effect (20) cannot be excluded. However, we believe that ours is one of the largest cohort studies of CAPD patients. To our knowledge, 25 years is the longest period of experience reported in the literature. The size and breadth of the present study are clear strengths.

CONCLUSIONS

We found that patient and technique survival rates at our center were higher than those previously reported for other countries. Both rates improved significantly over 25 years. Although diabetes, old age, and cardiovascular comorbidities are factors that are not easily modifiable to improve PD outcomes, our results are encouraging in an era of declining PD utilization.

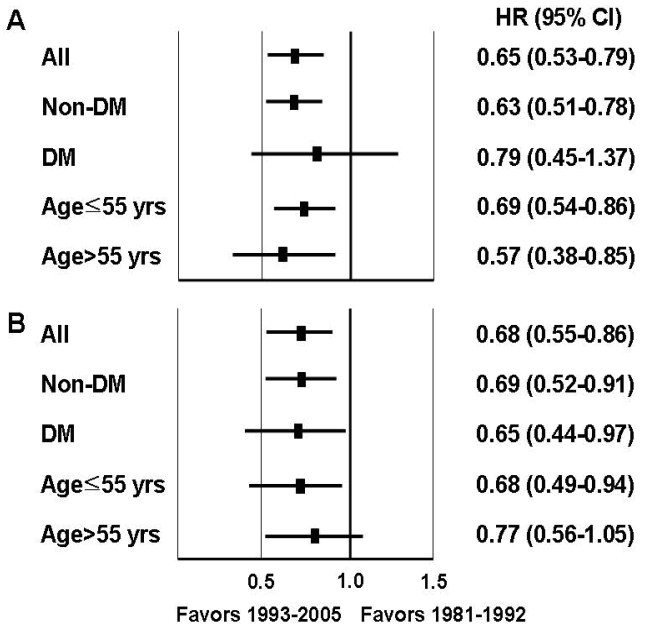

Figure 2 — Multivariate Cox proportional hazards model for technique failure and mortality in patients who started continuous ambulatory peritoneal dialysis during 1993 – 2005 as compared with patients who started during 1981 – 1992, according to diabetes (DM) status and age. (A) Technique survival. (B) Patient survival. HR = hazard ratio; CI = confidence interval.

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