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Analysis of technique and patient survival over time in patients undergoing peritoneal dialysis

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Abstract

Purpose This study used national claims data to investigate the technique and patient survival over time in incident peritoneal dialysis (PD) patients.

Methods Incident end-stage renal disease patients undergoing PD and older than 18 years were selected from Taiwan health insurance databases. These patients were grouped into three study periods according to year of dialysis initiation: 1997–2001, 2002–2006, and 2007–2011. The study end-points included technique failure and mortality.

Results The patients in the most recent era were older and more likely to have higher levels of comorbidity. Compared with the 1997–2001 group, the risks of technique failure were similar in the in the 2002–2006 (hazard ratio [HR] 1.10, 95 % confidence interval [CI] 0.98–1.24) and

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2007–2011 groups (HR 1.11, 95 % CI 0.98–1.26), respectively. Relative to the 1997–2001 group, the risks of mortality were higher in the 2002–2006 group (HR 1.59, 95 % CI 1.26–2.02) and similar in the 2007–2011 group (HR 1.20, 95 % CI 0.93–1.55). Using icodextrin and automated peritoneal dialysis (APD) were associated with lower risks of technique failure (HR 0.62 and 0.86, 95 % CI 0.56–0.68 and 0.77–0.95, respectively) and mortality (HR 0.55 and 0.81, 95 % CI 0.45–0.66 and 0.67–0.99, respectively).

Conclusions Despite increase in disease burden in the most recent era, the outcomes remained relatively stable. The use of APD and icodextrin appears to have significantly ameliorated the impact of the increase in comorbidity burden.

Keywords End-stage renal disease · Icodextrin · Mortality · Peritoneal dialysis · Technique survival

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Introduction

The incidence and prevalence of end-stage renal disease (ESRD) in Taiwan are the second highest and the highest, in the world, respectively [1]. Moreover, the prevalence of ESRD continues to increase in Taiwan and worldwide [1]. The increasing costs of renal replacement therapy cause significant financial stress on governments. Compared to hemodialysis (HD), peritoneal dialysis (PD) is more costeffective, with the annualized costs for PD therapy that are approximately 60-70 % of costs for HD [2]. Regarding outcomes, PD is associated with an early survival advantage of up to 2-3 years after dialysis but with comparable or lower survival outcomes thereafter, compared with HD [3, 4]. Mehrotra et al. [5] found that survival in PD patients improved and there was no significant difference in survival between incident PD and HD patients in dialysis initiation years of 2002-2004. Recent studies from Canada have demonstrated similar survival between HD and PD after considering selection bias and the use of central venous catheters [6, 7]. However, patients on PD have a higher risk of technique failure than patients on HD [4], which has led some to question the feasibility of PD as a renal replacement therapy. A recent US study has demonstrated that both patient and technique survival in patients on PD improved [8].

In Taiwan, only 10.3 % of prevalent ESRD patients undergoing long-term dialysis receive PD [1]. If the patient survival and technique rate for PD in Taiwan were to improve, more patients could be encouraged to use the treatment as a renal replacement therapy. Thus, this study investigated the technique and patient survival over time in incident PD patients using National Health Insurance (NHI) claims data of Taiwan.

Methods

Data source

Data in this study were extracted from a NHI research database. The NHI program covers approximately 99 % of the population of Taiwan. In accordance with the Personal Information Protection Act, patient identification in the database is scrambled. Diseases were identified according to the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM). This retrospective observational study complied with the guidelines of the Declaration of Helsinki and was approved by the Research Ethics Committee of China Medical University (CMU-REC-101-012). Since this study involved retrospective review of existing data, formal consent is not required for

this type of study. All data were de-identified and analyzed anonymously.

Study participants

We selected patients newly diagnosed with ESRD, aged \geq 18 years, and who underwent PD for more than 90 days in 1997–2011. Ninety days after dialysis initiation was defined as the index date. Patients who received kidney transplantation or HD before the index date were excluded. All study subjects were grouped into three study periods according to the year of dialysis initiation: 1997–2001, 2002–2006, and 2007–2011.

End-points

The study end-points included 5-year technique failure and mortality. Transfer to HD was defined as technique failure. Death, renal transplantation, renal function recovery and survival at the end of the study period (December 31, 2011) were censored for technique survival analysis. Transfer to HD, renal transplantation, renal function recovery and survival at the end of the study period (December 31, 2011) were censored for patient survival analysis.

Socioeconomic status, hospital level, comorbidity, and treatment

The variables of socioeconomic status included urbanization level and monthly income (<145,840, 15,840-25,000 and >25,000 New Taiwan Dollars). Urbanization level was classified four levels: Level 1 was the highest urban living areas, and the Level 4 was the lowest. Monthly income was classified according to paid insurance fee rectified by Taiwan NHI Bureau. Because the ethnic background of the study population was quite homogenous, the ethnicity was not considered to be an independent variable. Potential comorbidities included coronary artery disease (CAD, ICD-9-CM 410-413, 414.01-414.05, 414.8, and 414.9), congestive heart failure (CHF, ICD-9-CM 428, 398.91, 402.x1), cancer (ICD-9-CM 140-208), hyperlipidemia (ICD-9-CM 272), hypertension (ICD-9-CM 401-405), diabetes (ICD-9-CM 250), stroke (ICD-9-CM 430-438), chronic hepatitis (ICD-9-CM 571, 572.2, 572.3, 572.8, 573.1, 573.2, 573.3, 573.8, 573.9) and chronic obstructive pulmonary disease (ICD-9-CM 491, 492, 496). All comorbidities were defined before the index date. Treatment variables contained automated peritoneal dialysis (APD), icodextrin (Extraneal; Baxter Healthcare Corporation), or amino acid dialysate (Nutrineal; Baxter Healthcare Corporation). Patients who received treatment \geq 30 days before the end-point were defined as users of the treatment [9, 10].

Statistical analysis

Differences in the categorical variables among the three study periods were examined using the Chi-square test, and differences in the continuous variables were analyzed using one-way analysis of variance (ANOVA). The incidence of technique failure and mortality per 1000 person-years was calculated for each study period. Cox proportional hazards regression, accounting for center clustering effects based on the sandwich estimators, was used to estimate the hazard ratios (HRs) of technique failure and death. Model 1 was adjusted for age, gender, and statistically significant variables in the crude model. Model 2 was adjusted for variables in model 1 and the treatment with a statistically significant effect in the crude model. The interaction between independent variables was tested in model 2. Scaled Schoenfeld residuals were used to test the association between the technique failure or mortality and follow-up time. The results showed that the assumption was not violated. Kaplan-Meier analysis was used to plot the technique survival and patient survival curves in the three study periods. All analyses were performed using SAS 9.4 software (SAS Institute, Cary, NC) and a two-tailed p value of <0.05 was considered statistically significant.

Results

Characteristics among different study periods

A total of 6904 incident ESRD patients who underwent PD were included in this study, with 1310 (20 %) patients in the 1997–2001 group, 2183 (31.6 %) patients in the 2002–2006 group, and 3411 (49.4 %) patients in the 2007–2011 group. The mean age increased from 50.1 years (1997–2001) to 55.4 years (2007–2011) (Table 1). The proportion of women decreased from 59.4 % (1997–2001) to 51.3 % (2007–2011). Patients in the 2002–2006 group were more likely to live in higher urban areas than patients in other study periods. The proportion of patients with higher income increased from 18.9 % in the 1997–2001 group to 22.1 % in the 2007–2011 group. Patients in the 2007–2011 group exhibited a higher prevalence of comorbidity and were more likely to receive APD or icodextrin treatment than those in the other two study periods (Tables 1).

Incidence and risk factors for technique failure

In total, 562, 960, and 959 PD patients had technique failure and the incidence was 153.32, 149.42, and 162.59 per 1000 person-years in the 1997–2001, 2002–2006, and 2007–2011 groups, respectively (data not shown).

Compared with patients in the 1997–2001 group, patients in the 2002-2006 and 2007-2011 groups exhibited 0.98and 1.04-fold risks, respectively, in crude model (95 % confidence interval [CI]: 0.88-1.09 and 0.93-1.17, respectively), comparable risks in model 1 (HR 0.92, 95 % CI 0.82-1.02 and HR 0.89, 95 % CI 0.79-1.00, respectively), and also comparable risks in model 2 (HR 1.10, 95 % CI 0.98-1.24 and HR: 1.11, 95 % CI 0.98-1.26, respectively) Table 2. At the 5-year follow-up, the adjusted technique survival rate in the 2007-2011 group was the highest than those in the 1997-2001 and 2002-2006 groups in model 1 (45.96 vs. 41.36 and 44.69 %; Fig. 1a), but was nonsignificantly lower in model 2 (42.95 vs. 46.56 and 43.31 %; Fig. 1b). In model 2, the risk increased with age (HR 1.01, 95 % CI 1.01-1.01). Men exhibited a higher risk than women (HR 1.35, 95 % CI 1.25-1.47). Diabetes was associated with the highest risk (HR 1.70, 95 % CI 1.54-1.87), and followed by CHF (HR 1.29, 95 % CI 1.13-1.48), and CAD (HR 1.13, 95 % CI 1.00-1.27). Icodextrin users and APD user had a lower risk than nonusers (HR 0.62 and 0.86, 95 % CI 0.56-0.68 and 0.77-0.95, respectively). The interaction effects between both icodextrin use and study periods, and APD use and study periods were significant (p for interaction <0.0001) (Table 3). The association between the risk of technique failure and APD use was significant in the 1997-2001 period (HR 0.19, 95 % CI 0.10-0.36). Icodextrin users had a lower risk of technique failure in all study periods. A sensitivity analysis for technique survival considering the competing risk of death was further performed (Table S1 and S2). The results showed that there was no significantly difference in the risk of technique failure among patients in three study periods. The interaction effects were also significant between both APD use and study periods, and icodextrin use and study periods. The results were similar to Table 3 (Table S2). The risks of the first peritonitis event were similar across the varying time periods (data not shown).

Incidence and risk factors for death

The death numbers were 115, 312, and 295 in the 1997–2001, 2002–2006, and 2007–2011 groups, respectively. Mortality increased from 31.37 per 1000 person-years (1997–2001), 48.56 per 1000 person-years (2002–2006), to 50.02 per 1000 person-years (2007–2011) (data not shown). Compared with the patients in the 1997–2001 group, those in the 2002–2006 and 2007–2011 groups exhibited 26 % higher (95 % CI 1.01–1.58), and 10 % (95 % CI 0.70–1.16) lower risks for death in model 1 (Table 4). In model 2, patients in the 2007–2011 group

Table 1Demographiccharacteristics among incidentperitoneal dialysis patients inthree study periods

	Period			p value
	1997–2001 N = 1310 %	2002–2006 N = 2183 %	2007–2011 N = 3411 %	
Age (year)				<0.0001
18–39	29.3	20.9	15.7	
40–59	41.3	47.5	47.1	
60+	29.4	31.6	37.1	
Mean (SD) [#]	50.1 (15.5)	52.5 (15.3)	55.4 (14.9)	< 0.0001
Gender				< 0.0001
Women	59.4	56.8	51.3	
Men	40.6	43.2	48.8	
Urbanization level [§]				0.004
1	31.5	33.8	29.4	
2	29.6	31.4	31.4	
3	17.4	15.2	16.0	
4	21.5	19.7	23.2	
Monthly income, NTD				0.01
<15840	47.8	50.2	46.3	
15,840-25,000	32.4	29.5	31.7	
>25,000	18.9	20.3	22.1	
Comorbidity				
CAD	12.4	14.6	15.6	0.02
CHF	6.56	8.89	10.5	0.0001
Cancer	2.13	2.52	4.95	< 0.0001
Hyperlipidemia	13.7	20.5	30.1	< 0.0001
Hypertension	60.8	70.7	80.1	< 0.0001
Chronic hepatitis	4.43	4.99	5.89	0.09
COPD	2.75	3.34	3.11	0.62
Stroke	5.11	5.54	6.04	0.44
Diabetes	26.0	31.2	42.6	< 0.0001
Treatment				
APD	4.73	24.8	35.2	< 0.0001
Icodextrin	2.75	36.9	45.7	< 0.0001
Nutrineal	6.87	10.8	2.79	< 0.0001
Mean follow-up duration (years)	2.80 (1.82)	2.94 (1.81)	1.73 (1.26)	< 0.0001

NTD New Taiwan dollar, *CAD* coronary artery disease, *CHF* congestive heart failure, *COPD* chronic obstructive pulmonary disease, *APD* automated peritoneal dialysis

Chi-square test and # ANOVA test

[§] Level 1 was the highest urban living areas, and the Level 4 was the lowest

had a similar risk compared to those in the 1997–2001 group (HR 1.20, 95 % CI 0.93–1.55). The survival rates for the 1997–2001, 2002–2006 and 2007–2011 group at 5-year follow-up were 77.99, 74.39 and 78.89 % in model 1 (Fig. 1c), and 80.21, 73.65 and 77.15 % in model 2 (Fig. 1d). In model 2, diabetes was associated the

highest risk (HR 2.64, 95 % CI 2.21–3.16), and followed by COPD (HR 1.44, 95 % CI 1.03–2.01), stroke (HR 1.44, 95 % CI 1.12–1.87), and chronic hepatitis (HR 1.40, 95 % CI 1.02–1.92). Icodextrin users and APD users had 45 and 19 % lower risk than nonusers (95 % CI 0.45–0.66 and 0.67–0.99).

APD

Icodextrin

Nutrineal

Table 2 Hazard ratios (HRs) and 95 % confidence intervals (CIs) for technique failure calculated using Cox proportional hazards regression accounting for center clustering effects based on sandwich estimators

Variable	Crude HR (95 % CI)	Model 1 HR (95 % CI)	Model 2 HR (95 % CI)
variable	Crude HK (95 % CI)	Model 1 HR (95 % CI)	Model 2 HR (95 % CI)
Period			
1997–2001	Reference	Reference	Reference
2002-2006	0.98 (0.88-1.09)	0.92 (0.82-1.02)	1.10 (0.98–1.24)
2007-2011	1.04 (0.93–1.17)	0.89 (0.79–1.00)	1.11 (0.98–1.26)
Age (per 1-year increase)	1.02 (1.01-1.02)*	1.01 (1.01–1.01)***	1.01 (1.01–1.01)***
Gender			
Women	Reference	Reference	Reference
Men	1.40 (1.30–1.52)***	1.34 (1.23–1.45)***	1.35 (1.25–1.47)***
Urbanization level [§]			
1	Reference		
2	1.04 (0.93–1.16)		
3	1.08 (0.94–1.22)		
4	1.03 (0.91–1.17)		
Monthly income, NTD			
<15840	1.26 (1.14–1.41)***	1.11 (0.99–1.24)	1.12 (1.00–1.25)*
15840-25,000	1.15 (1.02–1.30)*	1.12 (0.99–1.26)	1.11 (0.99–1.25)
>25,000	Reference	Reference	Reference
Comorbidity (yes vs. no)			
CAD	1.55 (1.39–1.72)***	1.11 (0.99–1.25)	1.13 (1.00–1.27)*
CHF	1.67 (1.47–1.89)***	1.27 (1.10–1.46)***	1.29 (1.13–1.48)***
Cancer	1.26 (1.03–1.54)*	1.19 (0.97–1.46)	1.20 (0.98–1.48)
Hyperlipidemia	1.32 (1.20–1.44)***	1.06 (0.96–1.17)	1.09 (0.99–1.20)
Hypertension	1.23 (1.12–1.34)***	0.99 (0.90-1.10)	1.02 (0.92–1.12)
Chronic hepatitis	1.12 (0.94–1.34)		
COPD	1.37 (1.10–1.71)**	1.15 (0.92–1.43)	1.16 (0.93–1.46)
Stroke	1.54 (1.30–1.81)***	1.12 (0.94–1.33)	1.08 (0.91-1.29)
Diabetes	1.85 (1.70-2.01)***	1.55 (1.41-1.70)***	1.70 (1.54–1.87)***
Treatment (yes vs. no)			

Model 1: adjusted for study period, continuous age, gender, monthly income, CAD, CHF, cancer, hyperlipidemia, hypertension, COPD, stroke, and diabetes

Model 2: further adjustment of APD use, and icodextrin use in model 1

NTD New Taiwan dollar, CAD coronary artery disease, CHF congestive heart failure, COPD chronic obstructive pulmonary disease, APD automated peritoneal dialysis

* p < 0.05; ** p < 0.01; *** p < 0.001

[§] Level 1 was the highest urban living areas, and the Level 4 was the lowest

0.84 (0.76-0.93)***

0.74 (0.68-0.81)***

0.95 (0.82-1.10)

Discussion

The present study revealed comparable technique and patient survival over time in spite of PD delivered to patients with higher levels of comorbidity and older age in the most recent era. Icodextrin and APD use was associated with lower risk of technique failure and mortality.

Mehrotal et al. analyzed the data from the United States Renal Data System and found that, compared with those in 1996–1998, the adjusted hazard ratio (HR) for technique failure or death of incident PD patients in 2002-2004 were 0.62 (95 % CI 0.59–0.64) and 0.55 (95 % CI 0.53–0.57), respectively [8]. In addition, there was no significant difference in risk of technique failure or death between continuous ambulatory PD (CAPD) and APD. Thus, the improved outcomes could not be attributed to a greater use of APD. Using the data from the Canadian Organ Replacement Register, Perl et al. [6] demonstrated that, compared with a 1995-2000 cohort, the risk of PD technique survival was lower among incident patients in 2001-2005 (adjusted

0.86 (0.77-0.95)**

0.62 (0.56-0.68)***

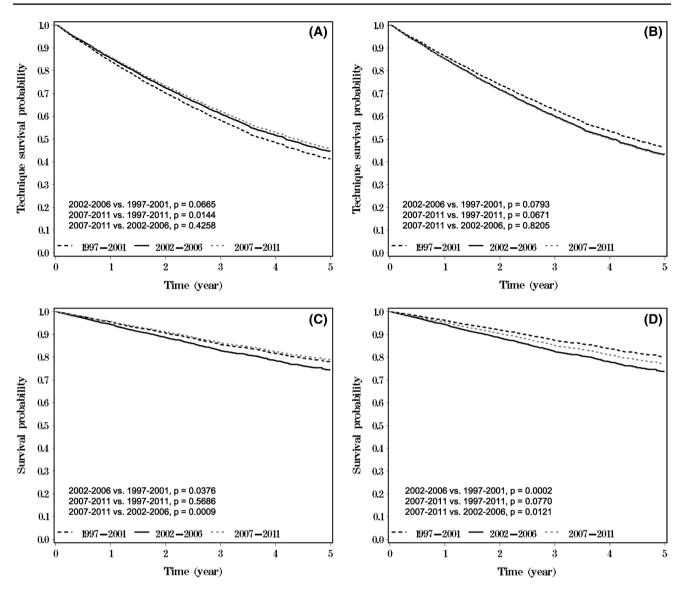


Fig. 1 Technique and patient survival curves among three study periods plotted using Kaplan–Meier analysis **a** for technique survival after adjustment for continuous age, gender, monthly income, and comorbidity including CAD, CHF, cancer, hyperlipidemia, hypertension, COPD, stroke, and diabetes, **b** for technique survival after adjustment for continuous age, gender, monthly income, and comorbidity including CAD, CHF, cancer, hyperlipidemia, hypertension, COPD, stroke, and diabetes, APD use, and icodextrin use,

c for patient survival after adjustment for continuous age, gender, urbanization level, monthly income, and comorbidity including CAD, CHF, cancer, hyperlipidemia, hypertension, chronic hepatitis, COPD, stroke, and diabetes, **d** for patient survival after adjustment for continuous age, gender, urbanization level, monthly income, and comorbidity including CAD, CHF, cancer, hyperlipidemia, hypertension, chronic hepatitis, COPD, stroke, and diabetes, APD use, and icodextrin use

HR 0.75, 95 % CI 0.62–0.92), but similar among those in 2006–2009. In addition, compared with the 1995–2000 cohort, the adjusted HR for mortality was lower among incident patients in 2001–2005 (adjusted HR 0.73, 95 % CI 0.66–0.80) and 2006–2009 (adjusted HR 0.57, 95 % CI 0.50–0.64) [6]. The use of APD, but not the use of icodextrin, was adjusted for analysis in the both above mentioned studies. The present study revealed that, compared with the

1997–2001 cohort, the risk of PD technique failure was similar in the 2002–2006 (adjusted HR 1.10, 95 % CI 0.98–1.24) and 2007–2011 (adjusted HR 1.11, 95 % CI 0.98–1.26) cohorts. In addition, compared with the 1997–2001 cohort, the risk of mortality was similar among the incident PD patients in 2007–2011 (HR 1.20, 95 % CI 0.93–1.55), but higher among those in 2002–2006 (HR 1.59, 95 % CI 1.26–2.02). Different from previous studies, the present

 Table 3
 Association between
the risk of technique failure and treatment calculated using Cox proportional hazards regression accounting for center clustering effects based on sandwich estimators stratified by study periods

	Period: 1997-2001	Period: 2002-2006	Period: 2007-2011	P for interaction
	HR (99.75 % CI)	HR (99.75 % CI)	HR (95 % CI)	
APD				< 0.0001
No	Reference	Reference	Reference	
Yes	0.19 (0.10-0.36)***	0.94 (0.80–1.11)	0.89 (0.77-1.03)	
Icodextrin				< 0.0001
No	Reference	Reference	Reference	
Yes	0.21 (0.11-0.41)***	0.45 (0.39-0.53)***	0.83 (0.72–0.96)*	

Adjusted for continuous age, sex, monthly income, coronary artery disease, congestive heart failure, cancer, hyperlipidemia, hypertension, chronic obstructive pulmonary disease, stroke, and diabetes * *p* < 0.05; *** *p* < 0.001

study adjusted the effect of both APD and icodextrin and revealed comparable outcomes over time.

Our multivariate analysis demonstrated that icodextrin use was associated with lower risk of technique failure (HR 0.62, 95 % CI 0.56-0.68) and mortality (HR 0.55: 95 %, CI 0.45–0.66). Icodextrin has been reimbursed by the NHI since December 2004. According to NHI regulations, icodextrin can be prescribed to be taken once daily by patients with diabetes and glycated hemoglobin >7.0 %, requiring 2.5 or 4.25 % dextrose solution in more than half of daily exchanges, or with high or high-average peritoneal membrane transport. Han et al. [11] indicated that long-term icodextrin use was associated with lower risks of all-cause mortality (HR, 0.69) and technique failure (HR, 0.60). Our recent study demonstrated that icodextrin use reduced technique failure and improved patient survival in both diabetic and nondiabetic PD patients [10]. The benefits of icodextrin use include enhancing peritoneal ultrafiltration, particularly in patients undergoing long-term PD [12], increasing clearance of small solutes [13], preserving peritoneal membrane [14], and favorable metabolic effects [15]. Thus, increased utilization and availability of icodextrin might account for the comparable both technique and patient survival in patients on PD over time despite of the increase in disease burden for the most recent periods.

Another crucial finding is that APD use was associated with lower risk of technique failure (HR 0.86, 95 % CI 0.77-0.95) and mortality (HR 0.81, 95 % CI 0.67-0.99) in multivariate analysis. Whether APD improves the outcomes among patients on PD, compared with those on CAPD, is still unknown [16]. The only prospective trial conducted on this topic found no difference in patient or technique survival between patients on APD and CAPD [17]. However, the study was limited by a small sample size. An observational study from Australia and New Zealand demonstrated that APD was associated with a lower risk of death in patients with high peritoneal membrane transport (adjusted HR 0.56, 95 % CI 0.35-0.87) and higher risk of death in patients with low peritoneal membrane transport (adjusted HR 2.19, 95 % CI 1.02-4.70) [18]. An observational study from Taiwan revealed that APD was associated with improved patient and technique survival among patients aged younger than 65 years [19]. According to NHI regulations, APD can be prescribed without restriction since 2008, irrespective of the transport type. Increased utilization and availability of APD in Taiwan might also account for comparable technique and patient survival in patients on PD over time despite of higher disease burden in the most recent period. Other possible reasons for comparable outcome over time include enhanced measures for the prevention of PD-related infection, technique advances, and increased experience of PD among nurses and nephrologists [20–22].

The strengths of this study include its larger sample size and long follow-up time. However, the present study has several limitations. First, the database used provided limited information on socio-demographic characteristics. For example, no data on body mass index, or smoking history was available. Second, no laboratory information, such as hemoglobin, albumin, residual renal function, peritoneal membrane transport status, or adequacy data, was available. Thus, these variables could not be adjusted for in the analyses. However, the indication of dialysis was audited under the NHI program, and thus the residual renal function at the start of dialysis might not change over time. The NHI program also audited the quality of dialysis to ensure adequacy. Third, icodextrin or APD prescription was decided by medical staff, and there was a selection bias. However, we adjusted several variables by using Cox proportional hazards regression to reduce the selection bias. Furthermore, the causes of technique failure and death were not provided by the database.

In conclusion, despite the increase in disease burden in the most recent era, the outcomes remained relatively stable. APD and icodextrin were more widely used in the most recent period. APD and icodextrin use was associated with lower risk of technique failure and mortality. The use of APD and icodextrin appears to have significantly

Table 4 Hazard ratios (HRs) and 95 % confidence intervals (CIs) for patient death calculated using Cox proportional hazards regression accounting for center clustering effects based on sandwich estimators

Variables	Crude HR (95 % CI)	Model 1 HR (95 % CI)	Model 2 HR (95 % CI)
Period			
1997–2001	Reference	Reference	Reference
2002-2006	1.58 (1.26–1.98)***	1.26 (1.01-1.58)*	1.59 (1.26-2.02)***
2007-2011	1.37 (1.07–1.75)*	0.90 (0.70-1.16)	1.20 (0.93-1.55)
Age (per 1-year increase)	1.08 (1.08-1.09)*	1.08 (1.07-1.09)***	1.08 (1.07-1.08)***
Gender			
Women	Reference	Reference	Reference
Men	1.12 (0.97-1.30)	1.11 (0.95–1.30)	1.14 (0.98–1.33)
Urbanization level§			
1	Reference	Reference	Reference
2	1.00 (0.82–1.22)	1.08 (0.87–1.34)	1.07 (0.86–1.33)
3	1.21 (0.95–1.55)	1.31 (1.01–1.69)*	1.27 (0.98-1.64)
4	1.41 (1.13–1.77)**	1.28 (1.00-1.63)*	1.27 (0.99–1.62)
Monthly income, NTD			
<15,840	2.66 (2.06-3.44)***	1.05 (0.80-1.38)	1.07 (0.82–1.41)
15,840-25,000	2.15 (1.63-2.83)***	1.22 (0.91–1.63)	1.21 (0.91–1.62)
>25,000	Reference	Reference	Reference
Comorbidity (yes vs. no)			
CAD	2.72 (2.30-3.22)***	1.19 (0.99–1.44)	1.20 (0.99–1.45)
CHF	2.96 (2.45-3.56)***	1.23 (0.99–1.53)	1.27 (1.02–1.57)
Cancer	1.73 (1.26–2.37)***	1.18 (0.86–1.64)	1.20 (0.86–1.66)
Hyperlipidemia	1.59 (1.36–1.87)***	1.11 (0.94–1.33)	1.16 (0.97–1.38)
Hypertension	1.72 (1.42-2.08)***	0.91 (0.74–1.11)	0.93 (0.76–1.13)
Chronic hepatitis	1.46 (1.08–1.98)*	1.40 (1.02–1.93)*	1.40 (1.02–1.92)*
COPD	2.88 (2.14-3.87)***	1.44 (1.03–2.00)*	1.44 (1.03–2.01)*
Stroke	3.24 (2.60-4.04)***	1.48 (1.14–1.91)**	1.44 (1.12–1.87)***
Diabetes	3.51 (2.99–4.11)***	2.37 (1.99–2.81)***	2.64 (2.21-3.16)***
Treatment (yes vs. no)			
APD	0.76 (0.63-0.92)**		0.81 (0.67-0.99)*
Icodextrin	0.71 (0.60-0.84)***		0.55 (0.45-0.66)***
Nutrineal	1.21 (0.93-1.59)		

Model 1, adjusted for study period, continuous age, gender, urbanization level, monthly income, CAD, CHF, cancer, hyperlipidemia, hypertension, chronic hepatitis, COPD, stroke, and diabetes

Model 2, further adjustment of APD use and icodextrin use in model 1

NTD New Taiwan dollar, CAD coronary artery disease, CHF congestive heart failure, COPD chronic obstructive pulmonary disease, APD automated peritoneal dialysis

* *p* < 0.05; ** *p* < 0.01; *** *p* < 0.001

[§] Level 1 was the highest urban living areas, and the Level 4 was the lowest

ameliorated the impact of the increase in comorbidity burden. These finding may encourage more patients to use PD as a renal replacement therapy.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

Informed consent For this type of study formal consent is not required.

References

- U.S. Renal Data System, USRDS 2014 annual data report: atlas of chronic kidney and end-stage renal disease in the United States, National Institute of Health, National Institute of Diabetes and Digestive and Kidney Diseases, Bethesda, MD
- Lee H, Manns B, Taub K, Ghali WA, Dean S, Johnson D, Donaldson C (2002) 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(3):611–622. doi:10.1053/ ajkd.2002.34924
- 3. U.S. Renal Data System, USRDS 2007 Annual data report: atlas of chronic kidney and end-stage renal disease in the United States, National Institute of Health, National Institute of Diabetes and Digestive and Kidney Diseases, Bethesda, MD
- Yeates K, Zhu N, Vonesh E, Trpeski L, Blake P, Fenton S (2012) Hemodialysis and peritoneal dialysis are associated with similar outcomes for end-stage renal disease treatment in Canada. Nephrol Dial Transplant 27(9):3568–3575. doi:10.1093/ndt/gfr674
- Mehrotra R, Chiu YW, Kalantar-Zadeh K, Bargman J, Vonesh E (2011) Similar outcomes with hemodialysis and peritoneal dialysis in patients with end-stage renal disease. Arch Intern Med 171(2):110–118. doi:10.1001/archinternmed.2010.352
- Perl J, Wald R, Bargman JM, Na Y, Jassal SV, Jain AK, Moist L, Nessim SJ (2012) Changes in patient and technique survival over time among incident peritoneal dialysis patients in Canada. Clin J Am Soc Nephrol 7(7):1145–1154. doi:10.2215/CJN.01480212
- Perl J, Wald R, McFarlane P, Bargman JM, Vonesh E, Na Y, Jassal SV, Moist L (2011) Hemodialysis vascular access modifies the association between dialysis modality and survival. J Am Soc Nephrol 22(6):1113–1121. doi:10.1681/ASN.2010111155
- Mehrotra R, Chiu YW, Kalantar-Zadeh K, Vonesh E (2009) The outcomes of continuous ambulatory and automated peritoneal dialysis are similar. Kidney Int 76(1):97–107. doi:10.1038/ ki.2009.94

- Badve SV, Hawley CM, McDonald SP, Mudge DW, Rosman JB, Brown FG, Johnson DW (2008) Automated and continuous ambulatory peritoneal dialysis have similar outcomes. Kidney Int 73(4):480–488. doi:10.1038/sj.ki.5002705
- Wang IK, Li YF, Chen JH, Liang CC, Liu YL, Lin HH, Chang CT, Tsai WC, Yen TH, Huang CC (2015) Icodextrin decreases technique failure and improves patient survival in peritoneal dialysis patients. Nephrology (Carlton) 20(3):161–167. doi:10.1111/ nep.12375
- Han SH, Ahn SV, Yun JY, Tranaeus A, Han DS (2012) Effects of icodextrin on patient survival and technique success in patients undergoing peritoneal dialysis. Nephrol Dial Transplant 27(5):2044–2050. doi:10.1093/ndt/gfr580
- Davies SJ, Woodrow G, Donovan K, Plum J, Williams P, Johansson AC, Bosselmann HP, Heimburger O, Simonsen O, Davenport A, Tranaeus A, Divino Filho JC (2003) Icodextrin improves the fluid status of peritoneal dialysis patients: results of a double-blind randomized controlled trial. J Am Soc Nephrol 14(9):2338–2344
- Davies SJ, Brown EA, Frandsen NE, Rodrigues AS, Rodriguez-Carmona A, Vychytil A, Macnamara E, Ekstrand A, Tranaeus A, Filho JC (2005) Longitudinal membrane function in functionally anuric patients treated with APD: data from EAPOS on the effects of glucose and icodextrin prescription. Kidney Int 67(4):1609–1615. doi:10.1111/j.1523-1755.2005.00243.x
- Garcia-Lopez E, Lindholm B, Davies S (2012) An update on peritoneal dialysis solutions. Nat Rev Nephrol 8(4):224–233. doi:10.1038/nrneph.2012.13
- Bredie SJ, Bosch FH, Demacker PN, Stalenhoef AF, van Leusen R (2001) Effects of peritoneal dialysis with an overnight icodextrin dwell on parameters of glucose and lipid metabolism. Perit Dial Int 21(3):275–281
- Bieber SD, Burkart J, Golper TA, Teitelbaum I, Mehrotra R (2014) Comparative outcomes between continuous ambulatory and automated peritoneal dialysis: a narrative review. Am J Kidney Dis 63(6):1027–1037. doi:10.1053/j.ajkd.2013.11.025
- 17. de Fijter CW, Oe LP, Nauta JJ, van der Meulen J, Verbrugh HA, Verhoef J, Donker AJ (1994) Clinical efficacy and morbidity associated with continuous cyclic compared with continuous ambulatory peritoneal dialysis. Ann Intern Med 120(4):264–271
- Johnson DW, Hawley CM, McDonald SP, Brown FG, Rosman JB, Wiggins KJ, Bannister KM, Badve SV (2010) Superior survival of high transporters treated with automated versus continuous ambulatory peritoneal dialysis. Nephrol Dial Transplant 25(6):1973–1979. doi:10.1093/ndt/gfp780
- Sun CY, Lee CC, Lin YY, Wu MS (2011) In younger dialysis patients, automated peritoneal dialysis is associated with better long-term patient and technique survival than is continuous ambulatory peritoneal dialysis. Perit Dial Int 31(3):301–307. doi:10.3747/pdi.2010.00072
- Chaudhary K, Sangha H, Khanna R (2011) Peritoneal dialysis first: rationale. Clin J Am Soc Nephrol 6(2):447–456. doi:10.2215/CJN.07920910
- Nessim SJ, Bargman JM, Austin PC, Story K, Jassal SV (2009) Impact of age on peritonitis risk in peritoneal dialysis patients: an era effect. Clin J Am Soc Nephrol 4(1):135–141. doi:10.2215/ CJN.02060508
- 22. Whaley-Connell A, Pavey BS, Satalowich R, Prowant BF, Misra M, Twardowski ZJ, Nolph KD, Khanna R (2005) Rates of continuous ambulatory peritoneal dialysis-associated peritonitis at the University of Missouri. Adv Perit Dial 21:72–75