Health economic evaluation of peritoneal dialysis based on cost-effectiveness in Japan: a preliminary study

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Tomoyuki Takura¹
Makoto Hiramatsu²
Hidetomo Nakamoto³
Takahiro Kuragano⁴
Jun Minakuchi⁵
Hironori Ishida⁶
Masaaki Nakayama⁷
Susumu Takahashi⁸
Hideki Kawanishi⁹

¹Department of Health Economy and Society Policy, Graduate School of Medicine, The University of Tokyo, Tokyo, Japan; ²Outpatient Center Hospital, Okayama Saiseikai General Hospital, Okayama City, Okayama, Japan; ³General Intrarenal Medicine, Saitama Medical University, Saitama, Japan; ⁴Internal Medicine (Nephrology and Dialysis), Hyogo College of Medicine, Nishinomiya City, Hyogo, Japan; ⁵Nephrology (Endocrinology), Kawashima Hospital, Tokushima City, Tokushima, Japan; ⁶Urology, Kitasaito Hospital, Asahikawa City, Hokaido, Japan; ⁷Kidney Center, St. Luke's International Hospital, Tokyo, Japan; ⁸Head Office, International Kidney Evaluation Association Japan, Tokyo, Japan; ⁹Artificial Organs and Surgery, Tsuchiya General Hospital, Hiroshima City, Hiroshima, Japan

Background: In Japan, the medical expenditures associated with dialysis have garnered considerable interest; however, a cost-effectiveness evaluation of peritoneal dialysis (PD) is yet to be evaluated. In particular, the health economics of the “PD first” concept, which can be advantageous for clinical practice and healthcare systems, must be evaluated.

Methods: This multicenter study investigated the cost-effectiveness of PD. The major effectiveness indicator was quality-adjusted life year (QALY), with a preference-based utility value based on renal function, and the cost indicator was the amount billed for a medical service at each medical institution for qualifying illnesses. In comparison with hemodialysis (HD), a baseline analysis of PD therapy was conducted using a cost-utility analysis (CUA). Continuous ambulatory PD (CAPD) and automated PD (APD) were compared based on the incremental cost-utility ratio (ICUR) and propensity score (PS) with a limited number of cases.

Results: The mean duration since the start of PD was 35.0±14.4 months. The overall CUA for PD (179 patients) was USD 55,019/QALY, which was more cost effective (USD/monthly utility) compared with that for HD for 12–24 months (4,367 vs. 4,852; $p<0.05$). The CUA reported significantly better results in the glomerulonephritis group than in the other diseases, and the baseline CUA was significantly age sensitive. The utility score was higher in the APD group (mean age, 70.1±3.5 years) than in the CAPD group (mean age, 70.6±4.2 years; 0.987 vs. 0.860; $p<0.05$, 9 patients). Compared with CAPD, APD had an overall ICUR of USD 126,034/QALY.

Conclusion: The cost-effectiveness of PD was potentially good in the elderly and in patients on dialysis for <24 months. Therefore, the prevalence of PD may influence the public health insurance system, particularly when applying the “PD first” concept.

Keywords: diabetic nephropathy, cost-utility analysis, quality-adjusted life year, medical service reimbursement, automated peritoneal dialysis, propensity score

Introduction

Peritoneal dialysis (PD) had been shown to have clinical superiority over hemodialysis (HD) in several areas, including the minimal strain on the cardiovascular system and maintenance of residual renal function (RRF; i.e., urine volume).¹ The “PD first” concept accounts for these advantages and is the basis for recommending PD therapy.² In other words, a therapy that has advantages on the quality of life (QOL), patient prognosis, and reduced medical cost burden potentially forms the basis of a comprehensive medical treatment for renal failure. Under these circumstances, there were 37,983 renal replacement therapies in patients who underwent

Correspondence: Tomoyuki Takura
Department of Health Economy and Society Policy, Graduate School of Medicine, The University of Tokyo, Tokyo, Japan
Tel +81 35 800 9523
Fax +81 35 800 9156
Email ttakura@m.u-tokyo.ac.jp

HD, 1,946 in those who underwent PD, and 1,648 in those who underwent transplantation during 2016 in Japan.

The continuous growth of the elderly population has resulted in an increase in the number of elderly patients with end-stage renal disease (ESRD) in Japan. Although the use of PD for elderly patients has been garnering attention with regard to its QOL-related advantages, its disadvantages, such as susceptibility to malnutrition, have also been highlighted. In addition, although the requirements for few bag changes and small volume contribute to the low medical cost, instructing patients on the PD technique requires both time and effort. In Japan, the medical cost associated with dialysis, at a growth rate of 48% in the last 10 years, was estimated to be approximately USD 15 billion, which is 3.8% of the 2014 national health expenditure.³ A recent study in foreign countries has reported that the cost of PD is lower than that of HD, and the 12-month mortality in new PD cases is lower than that among patients on HD.⁴ However, another study has demonstrated a significantly higher 12-month mortality rate among patients with PD compared with that among patients with HD, depending on age and presence of comorbidities.⁵ Furthermore, in Taiwan, PD was found to be more cost effective than HD, based on the major determinants of dialysis modality costs and associated complications.⁶ In contrast, in Japan, the public reimbursement is higher for PD than for HD.⁷

Given the above data, the appropriate widespread utilization of PD would require an extensive evaluation of its socioeconomic significance, while understanding that changes in medical technology are also required. Although a modicum of medical economics-based evidence for PD does exist, economic assessment and identification of the factors that influence automated PD (APD) machines, which are being increasingly introduced in the clinical setting, have yet to be sufficiently examined.^{8,9} In particular, in Japan, although the long-term follow-up results, such as the vital prognosis of dialysis therapy, were reported to be better than those in most other countries,¹⁰ the cost-effectiveness of PD is yet to be evaluated. Renal failure progression is considered to affect the health activities and medical expenses of individuals and the health problems (life expectancy) and economic burden (medical budget) of society. In addition, renal failure treatment may affect comorbidities, such as circulatory diseases. For the proper care of patients with renal failure, reducing the disease burden while effectively utilizing limited medical resources remains an essential issue.

Therefore, we performed a prospective observational study on the health economics for PD, especially APD, as a spreading medical technology in recent years in Japan. However, the stratification analysis of APD did not go beyond the scope of a case series study.

Materials and methods

Patients and interventions

This analysis was a multicenter, prospective, observational (cohort) study designed to compare two medical treatment modalities (PD vs. HD). In addition, we assessed continuous ambulatory PD (CAPD) and automated PD (APD) as the medical technologies for PD. PD uses the peritoneal membrane as a filter to clear wastes and extra fluid from the body and to return electrolyte levels to normal; to fill and drain the abdomen, APD requires the use of a cycler machine, to which the patient is connected when going to bed, and the process occurs automatically overnight.

This study was conducted under the direction of the Council on the Clinical Economic Assessment of Renal Failure, with the consent of the administrative bodies and the other responsible parties at the participating medical institutions. The authors have no support or funding to declare. This study was approved by the institutional review board of Saiseikai Kumamoto Hospital (approval number 312) and was conducted according to the Helsinki Declaration and the Ethical Guidelines for epidemiological research by the Japanese government.¹¹ In this study, management of patient data confidentiality was thorough, and patient written informed consent was waived for the following reasons: there was no invasion to the patients for observational research, existing data necessary for the treatment and billing were utilized, it was considered as consent by the answer to QOL questionnaire.

We included 179 patients (53.0% men) who reported symptoms of renal failure and underwent PD between October 2010 and October 2014. Patients with a weekly standardized total peritoneal urea clearance per urea distribution volume (single pool Kt/V) of >1.7 and those >20 and <90 years were included. A history of physical disabilities or complications was not the basis for exclusion, although patients with dementia and other conditions, e.g., respiratory failure associated with circulatory failure and advanced blood disorders prone to bleeding, that prevented consent for study participation and those with serious pathological conditions, such as cancer, were excluded.

In addition, we included 25 patients (36.0% men) who underwent conventional HD, mainly four hours per session, three times weekly. Study candidates were >20 years of age and received HD for at least six months. Moreover, few patients aged >90 years were excluded from the analysis. The eligibility criteria were as follows: (1) creatinine level <20.0 mg/dL (men), (2) pre-hemodialysis blood urea nitrogen (BUN) level <100 mg/dL, and (3) $\text{spKt/V} > 1.2$. In peculiar samples (cases of early introduction because of diabetes and aging), eGFR of $< 8.0 \text{ mL/min/1.73m}^2$ was also used as a supplementary condition for selection. Anemia and chronic kidney disease—mineral and bone disorder were treated according to the Japanese Society for Dialysis Therapy guidelines.

Study design

This study was analyzed from a social perspective. Clinical and cost data were prospectively collected during an observation period of at least six months, and all assessment indices were measured for each PD intervention. In addition to basic patient characteristics, findings from the urine and blood analyses and renal histology within one month before and after PD introduction were included in the clinical data. We selected the health-related QOL as the main effectiveness index; specifically, we applied the preference-based utility values. The selected cost index was the amount paid by the national health insurance system to the medical institution. In other words, the cost data included the entire amount billed for medical service reimbursement that was associated with qualifying illnesses at the medical institutions.

The final consideration of the medical economics of the relevant therapies was based on the results of three analytical issues: 1) baseline cost-effectiveness standard, including a comparative analysis between PD and HD; 2) primary factors that influenced cost-effectiveness; and, based on the results of the second issue, 3) comparison of the cost-effectiveness between CAPD and APD. Specifically, our study aimed to evaluate the socioeconomics of PD from a medical insurance perspective.

Analytical methods

The medical technologies were evaluated using a baseline cost-utility analysis (CUA) and were compared using the incremental cost-utility ratio (ICUR). The computation period for the utility analyses was ≥ 1 year based on the pathological characteristics of the chronic phase of the

disease and the frequency of therapy. Additionally, monthly analyses were performed.

The selected effectiveness index was quality-adjusted life year (QALY), which was based on the QOL and life expectancy, and was calculated using the EuroQoL-5 Dimension (EQ-5D), a measurement sheet for utility that is preferentially based on generic applicability to the pathological characteristics and medical technologies.

This study analyzed the medical expenses of chronic renal failure, including primary illnesses like diabetes and those directly related to dialysis therapy (e.g., catheterization/shunt, patient education, and treatment of related side effects, such as infections, bone disorders, dialysis amyloidosis, and arteriosclerosis). However, we excluded the hospitalization costs for major comorbidities, other cancer and trauma treatments that were not directly related, and geriatric syndromes and degenerative diseases. The cost indicator of the study was based on a direct medical expense: the amount billed to the Social Insurance Medical Fee Payment Fund of the medical institution, which includes the patient coinsurances (very low) and the patient copayments (hospital meals). The cost calculation included initial and subsequent visits, medical guidance and patient education, and treatment; medications and medical equipment, laboratory tests, and evaluation of test results; imaging and reading images; prescription and preparation of drugs; administration and injection of drugs; medical procedures; and convalescence and rehabilitation. Indirect medical expenses, such as labor productivity loss, travel expenses, and welfare (nursing care) expenses for patients and families, were excluded.

The points were assigned as units that represented the amount billed as reimbursement for medical services and were calculated as 1 point per JPY 10. The JPY to USD conversion was calculated based on the prevailing exchange rate in March 2014 (USD 1 = JPY 101.3).

Cost-effectiveness

The medical economic assessment methods for health programs included the CUA, which measures the cost per utility; a smaller value indicates a higher performance. The concept used to assess medical technology was the ICUR, which compares incremental costs with incremental utility. The ICUR was expressed as incremental cost per incremental utility, and the formula used to calculate it was as follows:¹²

$$ICUR = \frac{\text{Cost of the intervention arm (APD)} - \text{cost of the control arm (CAPD)}}{\text{Utility of the intervention arm (APD)} - \text{utility of the control arm (CAPD)}} \quad (1)$$

If the cost of the medical technologies being compared increased and if the increase in utility surpassed that of the cost, performance (i.e., cost-effectiveness) was considered to have improved.

Statistical analysis

The Welch's *t*-test was used to determine the difference between population means, and the correlation coefficient was adopted for the correlation analysis. SAS release 9.4 (SAS Institute Inc., Cary, NC, USA) was used for the statistical analyses. The standard of significance for the statistical tests was 5%, and the results were presented as mean $\pm$ standard deviation. Our analysis of sensitivity entailed a one-way sensitivity analysis of the effect and cost indices (each index underwent $\pm 50\%$ change).

We assessed the significance of the population correlation coefficient using the CUA as the response variable and clinical indices as the predictor variables. In this analysis, data for the treatment journey utilized the respective values at the time of sampling during the observation period.

The ICUR values were compared between CAPD and APD using a stratified analysis, with equivalence maintained between the two groups, and were corrected for sample size using a propensity score (PS) analysis. Specifically, after investigating the basis for covariate selection (correlation coefficient), we adjusted the description (discriminant analysis) of the PS and aligned the sample numbers using a matching technique (Greedy matching). In addition, we checked for balance by careful examination of the summary statistics for each group and finally confirmed the effect size using Wilcoxon signed rank test (Figure 1).

Results

Background of the study patients

As per our initial observation of the PD population, the mean age was 64.6 ± 13.2 years. The mean duration since the start of PD was 35.0 ± 14.4 months (range, 6–48 months; Table 1). The primary diseases related to renal failure were diabetic nephropathy (76 cases, 42.5%); glomerulonephritis (50 cases, 30.0%); and nephrosclerosis (21 cases, 11.7%). The parameters of renal function at the start of the observation period were weekly residual Kt/V 0.7 ± 0.3 ; BUN 50.7 ± 13.7 mg/dL; serum phosphorus (P) 4.7 ± 1.2 mg/dL; and hemoglobin (Hb) 10.7 ± 1.2 g/dL. The PD type was CAPD in 144 cases (80.4%) and APD in 35 cases (19.5%).

Figure 1 Method of determining the equivalence of CAPD and APD groups. To compare the cost-effectiveness of CAPD and APD, data were processed by conducting an analysis of the propensity score and a stratified analysis to ensure equivalence between the two groups.

Table I Patients' clinical characteristics

Characteristic	PD (Mean±Standard deviation)	HD (Mean±Standard deviation)	Significant difference (p-value)
Number of cases (cases)	179	25	—
Age (years)	64.6±13.2	62.8±14.0	n. s.
Males (%)	53.0	36.0	n. s.
Duration of dialysis (months)	35.0±14.4	36.1±11.6	n. s.
Primary disease (cases, %)			
Diabetic nephropathy	76; 42.5%	5; 25.0%	n. s.
Glomerulonephritis	50; 30.0%	11; 45.8%	n. s.
Nephrosclerosis	21; 11.7%	2; 8.3%	n. s.
Other	32; 17.9%	6; 20.8%	n. s.
Laboratory tests			
Residual Kt/V	0.7±0.3	—	—
BUN (mg/dL)	50.7±13.7	69.6 ±14.3	**
Alb (g/dL)	3.2±0.5	3.9±0.3	**
P (mg/dL)	4.7±1.2	5.3±1.1	n. s.
K (mEq/L)	4.1±0.6	4.9±0.5	**
Hb (g/dL)	10.7±1.2	10.2±0.8	n. s.
HDL (mg/dL)	55.1±23.6	62.6±17.2	n. s.
TG (mg/dL)	133.4±83.6	123.1±73.4	n. s.
Type of PD			
CAPD (cases, %)	144; 80.4%		
APD (cases, %)	35; 19.5%		

Notes: Welch's t-test ** $p < 0.01$, n. s.: not significant; Residual Kt/V; total weekly peritoneal urea clearance per urea distribution volume.

Abbreviations: BUN, blood urea nitrogen; Alb, Albumin; P, Phosphorus; K, potassium; Hb, hemoglobin; HDL, high-density lipoprotein; TG, triglyceride.

This study included 25 patients on HD, with a mean age of 62.8±14.0 years (PD vs. HD; $p > 0.05$) and a mean duration since the start of HD of 36.1±11.6 months ($p > 0.05$; Table 1). The primary diseases related to renal failure were glomerulonephritis (11 cases, 45.8%) and diabetic nephropathy (5 cases, 25.0%). The parameters of renal function at the start of the observation period were BUN 69.6±14.3 mg/dL (PD vs. HD; $p < 0.01$), K 4.1±0.6 mEq/L ($p < 0.01$), serum P 5.3±1.1 mg/dL ($p > 0.05$), and Hb 10.2±0.8 g/dL ($p > 0.05$).

Baseline cost-utility analysis

The baseline characteristics of all cases that received PD intervention for renal failure were utility score of 0.825±0.177 per month, medical cost of USD 3,615±1,435 per month, and CUA of USD 4,585±2,097 per utility (monthly conversion). When the values were converted to an annual figure, with utility adjusted to QALYs, the result was USD 55,019±25,163/QALY (Table 2). Moreover, because the baseline cost and CUA did not significantly differ between the PD and HD groups, we did not calculate the ICUR. The one-way sensitivity analysis indicated that the CUA ranged from USD 26,291/QALY to USD 105,164/QALY.

When the post-PD intervention CUA was chronologically adjusted, the CUA tended to gradually worsen with time (Figure 2), with the performance dropping markedly from 48 months onwards ($p < 0.05$). Furthermore, the baseline CUA (USD/utility, monthly conversion) for 12–24 months was significantly better in the PD group than in the HD group (4,367±2,017 vs. 4,852±1,635; $p < 0.05$). Based on annual conversion, the overall baseline CUA of the HD group was USD 58,815±18,347/QALY and was not significantly different from that of the PD group. Our analysis showed that the CUA significantly correlated with age, primary diseases, potassium (K), and high-density lipoprotein (HDL; all $p < 0.01$; Table 3). In addition, serum P and triglycerides (TG) were associated with the CUA ($p < 0.05$).

Stratified analysis by disease and age

Adjusting for primary disease, the mean baseline utility score for all patients (0.826±0.177) was higher than that for the diabetic nephropathy group (0.797±0.186) and significantly higher than that for the glomerulonephritis group (0.843±0.181; $p < 0.05$). The baseline medical cost (USD/month) was marginally lower for glomerulonephritis (3,173±1,156)

Table 2 Comparison of the PD and HD cost-effectiveness (Baseline cost-utility analysis)

Item	PD (Mean±Standard deviation)	HD (Mean±Standard deviation)	Significant difference (p-value)
Utility (EQ-5D score, monthly conversion)	0.825±0.177	0.785±0.181	*
Medical costs (medical department outpatient, US \$/month)	3,615±1,435	3,626±439	n. s.
Cost-utility analysis (US\$/QALY, annual conversion)	55,019±25,163	58,815±18,347	n. s.

Notes: Welch's t-test * $p < 0.05$, n. s.: not significant.

than for diabetic nephropathy ($3,494 \pm 1,367$). Accordingly, we analyzed the baseline CUA (USD/utility, monthly conversion) by primary disease and found that the CUA was significantly better for glomerulonephritis than for diabetic nephropathy ($3,920 \pm 1,448$ vs. $4,642 \pm 2,196$; $p < 0.05$; Figure 3).

Upon adjusting the baseline utility score by age, we found that patients in their 70s (0.866 ± 0.176) had the highest value, whereas those below 50 years of age (0.776 ± 0.195) had the lowest value. Our investigation of the baseline medical cost (USD/month) indicated that compared with the mean value in all patients ($3,622 \pm 1,430$), the value was significantly higher in patients in their 50s ($3,942 \pm 1,220$, $p < 0.05$) and was the lowest

in patients in their 60s ($3,357 \pm 1,606$; Figure 4). Analysis of the baseline CUA (USD/utility, monthly conversion) by age indicated that compared with the mean value in all patients ($4,590 \pm 2,086$), the value was significantly higher in patients in their 50s ($5,135 \pm 1,984$) but significantly lower in patients in their 70s ($4,196 \pm 1,689$; both age groups: $p < 0.05$; Figure 5).

Comparative analysis between CAPD and APD

Of the factors we believed capable of influencing the CUA (i. e., age, primary diseases, and the serum K, HDL, P, and TG), based on the results of the second issue, the CUA in the

Figure 2 Changes over the course of PD intervention and cost-effectiveness. The cost-effectiveness tended to gradually deteriorate once PD intervention was initiated (difference became marked from 36 months). Furthermore, the baseline CUA for 12–24 months was significantly better in the PD group than in the HD group. Error bars denote standard error (SE). Statistical significance of population mean difference was analyzed using Welch's t-test.

Table 3 Correlation analysis of factors influencing the cost-effectiveness

Item	Correlation analysis	
	Population correlation coefficient (ρ)	p-value
Age	-0.158	**
Duration of PD (months)	0.030	0.499
Disease (code)	0.193	**
Residual Kt/V	-0.058	0.199
BUN	0.043	0.345
Alb	0.062	0.379
Ca	0.074	0.209
P	0.172	*
K	-0.144	**
PTH	-0.099	0.050
Hb	0.080	0.070
HDL	-0.130	**
LDL	0.073	0.222
TG	-0.098	*

Notes: Welch's t-test * $p < 0.05$, ** $p < 0.01$; When we assessed the significance of the population correlation coefficient using the CUA as the response variable and clinical indices as the predictor variables, we found a strong correlation between cost-effectiveness and age, disease, P, K, HDL, and TG.

population that comprised patients with diabetic nephropathy in their 60s and 70s was calculated and compared between CAPD and APD. Using a PS analysis, we ultimately compared nine cases from each group (APD: 70.1 ± 3.5 years vs. CAPD: 70.6 ± 4.2 years; $p > 0.05$; Table 4). The CAPD and APD groups had no significant differences in the duration on

dialysis (18.5 ± 16.5 months and 18.6 ± 31.7 months, respectively) and residual Kt/V (0.8 ± 0.2 and 0.9 ± 0.5 , respectively).

The utility score was higher in the APD group than in the CAPD group (0.987 ± 0.039 vs. 0.860 ± 0.164 ; $p < 0.05$). However, the medical cost (USD/month) was significantly higher in the APD group than in the CAPD group ($4,591 \pm 1,494$ vs. $3,275 \pm 1,204$; $p < 0.01$). The baseline CUA (USD/QALY) was significantly better in the CAPD group than in the APD group ($49,023 \pm 66,773$ vs. $59,830 \pm 19,376$; $p < 0.05$).

Compared with the CAPD group, the APD group had an ICUR of USD 126,034/QALY, when converted into an annual figure. Furthermore, the annual ICUR was USD 74,598/QALY at 12–24 months following an intervention (Table 4). In addition, the baseline CUA (USD/QALY) was significantly better in the overall CAPD group ($n=144$) than in the overall APD group ($n=35$; $52,774 \pm 24,339$ vs. $64,254 \pm 26,725$; $p < 0.05$).

Discussion

The effectiveness index (utility) of PD was statistically superior to that of HD ($p < 0.05$), but there was no difference in the cost index. In addition, the CUA for PD was slightly better than that for HD although there was no statistical difference. Although there were restrictions on the observation period (≥ 6 months), our study results suggested that the baseline cost-effectiveness of PD was satisfactory and that the primary disease, renal function,

Figure 3 A cost-utility analysis by primary disease. Adjusting the baseline CUA by disease revealed that glomerulonephritis had a significantly better CUA than nephropathy. Error bars denote SE. Statistical significance of population mean difference was analyzed using Welch's t-test.

Figure 4 A medical cost analysis by age. The medical costs for patients in their 50s were significantly higher than those in their 60s and 70s. In general, medical costs for the elderly tended to be lower than those for middle-aged patients (indices in the figure: 5th percentile, first quartile; median, 3rd and 95th percentile; outliers of maximum and minimum). Statistical significance of population mean difference was analyzed using Welch's t-test.

Figure 5 A cost-utility analysis by age. The baseline CUA was adjusted by age group and showed a tendency for a significantly higher CUA for patients in their 70s than for those in their 50s. Error bars denote SE. Statistical significance of population mean difference was analyzed using Welch's t-test.

Table 4 Comparison of the CAPD and APD cost-effectiveness and incremental cost-utility ratio

Item (Disease: Diabetic nephropathy, Age: 60–70 years)		APD (Mean±Standard deviation)	CAPD (Mean±Standard deviation)	Significant difference (p-value)
Number of cases	(cases)	9	9	—
Age	(years)	70.1±3.5	70.6±4.2	n. s.
Males	(%)	66.7	55.6	n. s.
Dialysis duration	(months)	18.6±31.7	18.5±16.5	n. s.
Test values				
Residual Kt/V		0.9±0.5	0.8±0.2	n. s.
BUN (mg/dL)		44.0±12.7	49.7±13.3	n. s.
Alb (g/dL)		3.4±0.2	3.0±0.6	n. s.
P (mg/dL)		4.9±0.9	4.7±1.2	n. s.
K (mEq/L)		4.3±0.4	4.2±0.5	n. s.
HDL (mg/dL)		50.6±9.3	69.1±37.2	n. s.
TG (mg/dL)		96.4±62.9	165.6±124.0	*
Utility (EQ-5D score, monthly conversion)		0.987±0.039	0.860±0.164	*
Medical costs (medical department outpatient, US\$/month)		4,591±1,494	3,275±1,204	**
Cost-utility analysis (US\$/QALY, annual conversion)		59,830±19,376	49,023±66,773	*
Incremental cost-utility ratio (ICUR: CAPD vs. APD calculation) (US\$/QALY, annual conversion)				
		126,034 (12–24 months after intervention: 74,598)		

Notes: Welch's t-test * $p < 0.05$, ** $p < 0.01$, n. s.: not significant.

and other factors influenced the medical economics. The results also suggested that the cost-effectiveness of PD was potentially good in the elderly and patients with less than 24 months on dialysis. In addition, comparison of the ICUR between CAPD and APD suggested that, in the early stage of initiation, APD may be a superior PD technique, and the major determinants were utilities. However, the number of patients in the APD and HD groups was very small, so it was difficult to draw conclusions. The findings of cost-effectiveness might be related to the high utility level with home medical care, and the possible reasons for the low long-term performance were the factors related to encapsulating peritoneal sclerosis.

Conversely, age and dialysis duration were equivalent between the PD and HD groups, but the present study was unable to consider all factors. In general, patients who choose PD tend to be younger, with fewer complications and family support. Therefore, the EQ-5D scores of the groups must be cautiously interpreted. Moreover, the HD group had a relatively low rate of diabetic nephropathy, which affected the sample size of APD in the ICUR. Although there was no statistically significant difference

in gender composition between the two groups, the HD group had a high proportion of females. This trend could affect the therapeutic effect analysis. That is, females were more likely than males to initiate HD with a catheter and lose both primary and post-interventional patencies in the first year. Future studies should perform careful comparison of the various renal failure therapies among patients with comparable clinical characteristics and conduct an analysis that includes the combined use of HD.

A research identified several classic factors, such as low HDL cholesterol, as risk factors in HD patients.¹³ In recent years, abnormalities in serum K and P metabolism have been identified as cardiovascular mortality risk factors in patients on dialysis.¹⁴ The present study also identified serum P, K, HDL, and TG as factors that influenced the cost-effectiveness. Future research focused on this topic is essential for interpreting these results, but the main reasons for these factors may be related to the cost of medications and hospitalizations, such as those for anemia, hyperphosphatemia treatment, and secondary hyperparathyroidism treatment. For example, in the AURORA study¹⁵ and 4D study,¹⁶ the initiation of

rosuvastatin and atorvastatin treatment had no significant effect on the primary clinical endpoint in patients undergoing HD. Based on these data, we recognized that the adequate management of dialysis using relevant indices was extremely important in improving the socioeconomic burden of ESRD therapy.

A previous study¹⁷ showed that the etiology of chronic kidney disease (CKD) had a major influence on the cost-effectiveness of HD treatment; in particular, diabetic nephropathy, which is one of the most common etiologies of CKD, resulted to lower cost-effectiveness, when compared with that for glomerulonephritis. The present study showed similar results. The difference in the cost-effectiveness between the two diseases was nearly the same for PD treatment in the present study and for HD treatment in previous studies, which showed that the diabetic nephropathy group, compared with the glomerulonephritis group, had approximately 20% lower performance. In addition, the initiation of renal replacement therapy for diabetic nephropathy was somewhat more likely to indicate that HD initiation was better in terms of mortality outcomes;^{18–23} conversely, some reports indicated that PD initiation was better.^{24,25} Thus, further research on the relationship between the primary disease and the chosen therapy is necessary.

The cost-effectiveness of PD was relatively good in the elderly group when patients aged >90 years were excluded; this was likely due to increased utility and decreased medical costs. The decrease in the medical costs in elderly patients might be related to low dose of the PD fluid, compared with that in younger patients. The possible reasons for the high utility level were factors related to lifestyle, in addition to medical factors. In the present study, we did not perform a detailed analysis of these issues because of limited available data, although we considered these as important issues for a future study. In the future, it would be desirable to gather further evidence on the influence of disease characteristics on socioeconomics.

The maintenance of the RRF after the initiation of dialysis is considered to vary widely among patients, depending on the underlying disease, drugs administered, and dialysate used. A recent study estimated the speed of RRF decline to be approximately $-1.5 \text{ mL/min/1.73 m}^2/\text{year}$.^{26–30} Although a Japanese population was not targeted, a related study indicated that the mean duration of PD was 30 months.³¹ In this case, after reaching the objectives of optimal dialysis [i.e., dialyzer clearance of urea, dialysis time/volume (spKt/V) urea of 1.7 per week],

uremic toxin management can be achieved by PD alone in approximately three years.

Using this information, we calculated and compared the ICUR between CAPD and APD and found relatively excellent results within 24 months of the commencement of APD, with CUA for diabetic nephropathy of USD 59,830/QALY and ICUR for 12–24 months of USD 74,598/QALY. Incidentally, the social consensus in Japan has settled on paying approximately USD 66,140 per QALY.³² Moreover, as an approach to ICUR based on the discussion thus far, we estimated the reducing bias using PS. However, the PS analysis in this study had limitations, such as sampling bias toward the APD group and the lack of reflection of the social covariates.

The baseline utility itself was high, because APD is often indicated for patients who are relatively active. Therefore, even if the cost of the related apparatus increases, cost-effectiveness can be maintained. In other words, the selection of APD for a fixed period after initiating intervention would be generally appropriate, from a medical economics perspective. However, the results of ICUR indicated that the cost-effectiveness of overall APD was not superior to that of CAPD. Because the present study focused on a small population that cannot be considered representative of the general population, future large-scale studies that evaluate this issue will be required.

Therefore, the prevalence of PD may influence the public health insurance system, particularly when applying the “PD first” approach. However, a discussion from the viewpoint of reducing the load of social security is needed, because the public reimbursement has been reported to be higher for PD than for HD in Japan.⁷ Notably, this study showed roughly equal results for PD and HD.

The rule of rescue, which states that more resources should be used to save the lives of patients suffering from fatal diseases,³³ often appears in debates about the distribution of medical resources and in conjunction with the fair inning rule, which states that the weight of ensuring QALY should be placed on the future generation and disadvantaged individuals.³⁴ In general, these rules can be applied to ESRD, which was the subject of the present study. Accordingly, we assumed that the social consensus on the consumption of medical resources will increase for ESRD. Accordingly, based on our results and the issues discussed above, the baseline cost-effectiveness of PD was good.

Finally, the following limitations of the study must be considered. First, there were limited numbers of cases in

the HD and APD groups. Second, the patient background, particularly in the HD group, was not well described. Furthermore, caretaker burnout and welfare-related cares were excluded.

Conclusion

In this prospective observational study on the health economics of PD, we show that the cost-effectiveness of PD is potentially good in the elderly and in patients on dialysis for <24 months, although the number of HD groups assessed was limited. Therefore, the prevalence of PD use may affect the public health insurance system, particularly when applying the “PD first” concept.

Ethics approval

This study was conducted according to the Ethical Guidelines for Epidemiological Research by the Japanese Government.

Data sharing statement

The datasets analyzed during the current study will be made available by the corresponding author upon reasonable request.

Abbreviations

Alb, Albumin; APD, automated peritoneal dialysis; BUN, blood urea nitrogen; CAPD, continuous ambulatory PD; CUA, COST-utility analysis; EQ-5D, EuroQoL-5 dimension; ESRD, end-stage renal disease; Hb, hemoglobin; HD, hemodialysis; HDL, high-density lipoprotein; ICUR, incremental cost-utility ratio; K, potassium; P, phosphorus PD, peritoneal dialysis; PS, propensity score; QALY, quality-adjusted life year; QOL, quality of life; RRF, residual renal function; SD, standard deviation; SE, standard error; TG, triglyceride.

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Author contributions

All authors contributed to data analysis, drafting and revising the article, gave final approval of the version to be published, and agree to be accountable for all aspects of the work.

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References

1. Lameire N, Van Biesen W, Vanholder R. The role of peritoneal dialysis as first modality in an integrative approach to patients with end-stage renal disease. *Perit Dial Int*. 2000;20(Suppl 2): S134–141.
2. Blake PG. Integrated end-stage renal disease care: the role of peritoneal dialysis. *Nephrol Dial Transplant*. 2001;16(Suppl 5):61–66. doi:10.1093/ndt/16.suppl_5.61
3. Takura T. Concept of applying health economics to dialysis therapy. *J Jpn Soc Dialysis Ther*. 2012;45(2):101–105. doi:10.4009/jsdt.45.101
4. Treharne C, Liu FX, Arici M, Crowe L, Farooqui U. Peritoneal dialysis and in-centre haemodialysis: a cost-utility analysis from a UK payer perspective. *Appl Health Econ Health Policy*. 2014;12(4):409–420. doi:10.1007/s40258-014-0108-7
5. McDonald SP, Marshall MR, Johnson DW, Polkinghorne KR. Relationship between dialysis modality and mortality. *J Am Soc Nephrol*. 2009;20(1):155–163. doi:10.1681/ASN.2008121233
6. Chang YT, Hwang JS, Hung SY, et al. Cost-effectiveness of hemodialysis and peritoneal dialysis: a national cohort study with 14 years follow-up and matched for comorbidities and propensity score. *Sci Rep*. 2016;27(6):30266. doi:10.1038/srep30266
7. Karopadi AN, Mason G, Rettore E, Ronco C. The role of economies of scale in the cost of dialysis across the world: a macroeconomic perspective. *Nephrol Dial Transplant*. 2014;29(4):885–892. doi:10.1093/ndt/gft528
8. Klarenbach S, Tonelli M, Pauly R, et al. Economic evaluation of frequent home nocturnal hemodialysis based on a randomized controlled trial. *J Am Soc Nephrol*. 2014;25(3):587–594. doi:10.1681/ASN.2013040360
9. Howard K, Salkeld G, White S, et al. The cost-effectiveness of increasing kidney transplantation and home-based dialysis. *Nephrology (Carlton)*. 2009;14(1):123–132. doi:10.1111/nep.2009.14.issue-1
10. Goodkin DA, Bragg-Gresham JL, Koenig KG, et al. Association of comorbid conditions and mortality in hemodialysis patients in Europe, Japan, and the United States in the Dialysis Outcomes and Practice Patterns Study (DOPPS). *J Am Soc Nephrol*. 2003;14(12):3270–3277. doi:10.1097/01.asn.0000078024.50060.c6
11. The ethical guidelines for epidemiological research by the Japanese Government: Ministry of Education, Culture, Sports, Science and Technology Ministry of Health, Labour and Welfare; 2008. Available from: http://www.lifescience.mext.go.jp/files/pdf/n796_01.pdf. Accessed December 28, 2015.
12. Asche CV. *Applying Comparative Effectiveness Data to Medical Decision Making: Easily Accessible Overview of Comparative Effectiveness*. 1st ed. Switzerland: ADIS; 2016:1–113.
13. Melamed ML, Eustace JA, Plantinga LC, et al. Third-generation parathyroid hormone assays and all-cause mortality in incident dialysis patients: the CHOICE study. *Nephrol Dial Transplant*. 2008;23(5):1650–1658. doi:10.1093/ndt/gfn212
14. De Boer IH, Gorodetskaya I, Young B, Hsu CY, Chertow GM. The severity of secondary hyperparathyroidism in chronic renal insufficiency is GFR-dependent, race-dependent, and associated with cardiovascular disease. *J Am Soc Nephrol*. 2002;13(11):2762–2769. doi:10.1097/01.ASN.0000034202.91413.EB
15. Fellström BC, Jardine AG, Schmieder RE, et al. Rosuvastatin and cardiovascular events in patients undergoing hemodialysis. *N Engl J Med*. 2009;360(14):1395–1407. doi:10.1056/NEJMoa0810177

16. Wanner C, Krane V, März W, et al. Atorvastatin in patients with type 2 diabetes mellitus undergoing hemodialysis. *N Engl J Med.* **2005**;353(3):238–248. doi:10.1056/NEJMoa043545
17. Takura T, Nakanishi T, Kawanishi H, et al. Cost-effectiveness of maintenance hemodialysis in Japan. *Ther Apher Dial.* **2015**;19(5):441–449. doi:10.1111/1744-9987.12314
18. Kim HJ, Park JT, Han SH, et al. The pattern of choosing dialysis modality and related mortality outcomes in Korea: a national population-based study. *Korean J Intern Med.* **2017**;32(4):699–710. doi:10.3904/kjim.2017.141
19. Tamayo Isla RA, Ameh OI, Mapiye D, et al. Baseline predictors of mortality among predominantly rural-dwelling end-stage renal disease patients on chronic dialysis therapies in Limpopo, South Africa. *PLoS One.* **2016**;11(6):e0156642. doi:10.1371/journal.pone.0156642
20. Nesrallah GE, Li L, Suri RS. Comparative effectiveness of home dialysis therapies: a matched cohort study. *Can J Kidney Health Dis.* **2016**;3:19. doi:10.1186/s40697-016-0105-x
21. Marshall MR, Polkinghorne KR, Kerr PG, Hawley CM, Agar JW, McDonald SP. Intensive hemodialysis and mortality risk in Australian and New Zealand populations. *Am J Kidney Dis.* **2016**;67(4):617–628. doi:10.1053/j.ajkd.2015.09.025
22. Wang IK, Liang WM, Lin CL, et al. Impact of dialysis modality on the survival of patients with end-stage renal disease and prior stroke. *Int Urol Nephrol.* **2016**;48(1):139–147. doi:10.1007/s11255-015-1157-z
23. Marshall MR, Walker RC, Polkinghorne KR, Lynn KL. Survival on home dialysis in New Zealand. *PLoS One.* **2014**;9(5):e96847. doi:10.1371/journal.pone.0096847
24. Lee MJ, Kwon YE, Park KS, et al. Glycemic control modifies difference in mortality risk between hemodialysis and peritoneal dialysis in incident dialysis patients with diabetes results from a nationwide prospective cohort in Korea. *Medicine (Baltimore).* **2016**;95(11):e3118. doi:10.1097/MD.0000000000004864
25. Heaf JG, Wehberg S. Relative survival of peritoneal dialysis and haemodialysis patients: effect of cohort and mode of dialysis initiation. *PLoS One.* **2014**;9(3):e90119. doi:10.1371/journal.pone.0090119
26. Fan SL, Pile T, Punzalan S, Raftery MJ, Yaqoob MM. Randomized controlled study of biocompatible peritoneal dialysis solutions: effect on residual renal function. *Kidney Int.* **2008**;73(2):200–206. doi:10.1038/sj.ki.5002574
27. Szeto CC, Chow KM, Lam CW, et al. Clinical biocompatibility of a neutral peritoneal dialysis solution with minimal glucose-degradation products—a 1-year randomized control trial. *Nephrol Dial Transplant.* **2007**;22(2):552–559. doi:10.1093/ndt/gfl559
28. Haag-Weber M, Krämer R, Haake R, et al. Low-GDP fluid (Gambrosol trio) attenuates decline of residual renal function in PD patients: a prospective randomized study. *Nephrol Dial Transplant.* **2010**;25(7):2288–2296. doi:10.1093/ndt/gfq044
29. Kim SG, Kim S, Hwang YH, et al. Could solutions low in glucose degradation products preserve residual renal function in incident peritoneal dialysis patients? A 1-year multicenter prospective randomized controlled trial (Balnet Study). *Perit Dial Int.* **2008**;28(Suppl 3):S117–122.
30. Jansen MA, Hart AA, Korevaar JC, Dekker FW, Boeschoten EW, Krediet RT. Predictors of the rate of decline of residual renal function in incident dialysis patients. *Kidney Int.* **2002**;62(3):1046–1053. doi:10.1046/j.1523-1755.2002.00505.x
31. Bajo MA, Priez-Lozano ML, Albar-Vizcaino P, et al. Low-GDP peritoneal dialysis solution ('balance') has less impact in vitro and ex vivo on epithelial-to-mesenchymal transition (EMT) of mesothelial cells than a standard fluid. *Nephrol Dial Transplant.* **2011**;26(1):282–291. doi:10.1093/ndt/gfq709
32. Ohkusa Y, Sugawara T. Research for willingness to pay for one QALY gain. *Med Soc.* **2006**;16(2):157–165.
33. McKie J, Richardson J. The rule of rescue. *Soc Sci Med.* **2003**;56(12):2407–2419. doi:10.1016/S0277-9536(02)00244-7
34. Williams A. Intergenerational equity: an exploration of the 'fair innings' argument. *Health Econ.* **1997**;6(2):117–132. doi:10.1002/(ISSN)1099-1050

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