Title

Recent analysis of status and outcomes of peritoneal dialysis in the Tokai area of Japan: the second

report of the Tokai peritoneal dialysis registry

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Abstract

Background　　　　Early withdrawal within 3years after starting peritoneal dialysis (PD) and PD-related peritonitis have been major obstacles preventing increases in the population of PD patients. To address these problems, we implemented education programs for medical staff. This study analyzed the recent status and outcomes of PD therapy, focusing on findings such as the incidence and prognosis of peritonitis as of 5years after our last study.

Methods　　　　We investigated background, laboratory data and status of PD therapy, reasons for withdrawal from PD and incidental statements on peritonitis from 2010 to 2012 (R2), and compared findings with those from our last study of 2005 to 2007 (R1).

Results　　　　Early PD therapy withdrawal in R2 clearly improved to 44.5%, compared with 50.9% in R1. Peritonitis incidence improved slightly from once per 42.8months/patient in R1 to once per 47.3months/patient in R2. Notably, PD-related peritonitis as a cause of mortality improved markedly in R2, but outcomes of PD-related peritonitis did not change significantly between R1 and R2. In contrast, social problems increased as a reason for withdrawal from PD therapy.

Conclusion　　　　Our efforts at education might have been useful for improving early withdrawal from PD and deaths attributable to PD-related peritonitis. However, since improvements to incidence of PD-related peritonitis were limited by education, further improvement in PD-related peritonitis incidence requires development of new sterilized connecting systems during PD bag exchanges to decrease

PD-related peritonitis opportunities. Construction of medical support systems to address social problems

is required to maintain long-term PD therapy.

Introduction

Peritoneal dialysis (PD) is a useful renal replacement therapy for end-stage renal failure

(ESRD) and is also recognized as a home medical care. In recent decades, only about 3% of all Japanese

patients with ESRD have received PD therapy[1, 2]. To analyze the reasons and thus facilitate reduced

use of PD in our local area, we have started a registry of PD patients to clarify problems associated with

PD therapy in the Tokai area from 2005. Our previous study using data from this registry for the period

from 2005 to 2007 (R1) reported that early withdrawals (defined as withdrawal within3 years of starting

PD) comprised >50% of all withdrawals and that continuation of long-term PD therapy was mainly

prevented by peritonitis[3]. Indeed, the most common reason for technical failure was neither

under-dialysis/ultrafiltration failure nor encapsulating peritoneal sclerosis (EPS)/pre-EPS. Associated with

PD-related peritonitis, one problem was the high proportion (>30%) of negative results from bacterial

culture studies in peritonitis. Empirical therapy for peritonitis might also be problematic, as reported in a

study from the United Kingdom[4, 5]. For these reasons, we have implemented several annual PD

education programs and opportunities for discussion to improve the management of PD therapy by

physicians and healthcare professionals such as nurses, medical engineers, pharmacists and nutritionists

(Supplementary Table 1).

The present study again used the Tokai registry of PD patients, to identify changes in problems

associated with PD therapy using data collected from 2010 to 2012 (R2), compared with those from R1[3],

with a particular focus on causes of early withdrawal and the incidence and outcomes of PD-related

peritonitis.

Methods

Preparation to construct the database

Data for this cohort study were examined retrospectively. In the present study, patients who

received PD therapy between 2010 and the end of 2012 were analyzed as the R2 cohort which were

obtained from 15 institutions in the Tokai area of Japan (Table 1). For the reference population, we used

data from patients receiving PD therapy between 2005 and the end of 2007 as the R1 cohort[3]. The

registration process to construct the database and analyze data was approved by the ethics committees of

each participating institution (#309-3).

Collection of R2 data from PD patients was performed once a year from January 1, 2010 to

December 13, 2012. The profile of our database system is shown in Table 2. Peritonitis was diagnosed

according to the 2010 guidelines of the International Society for Peritoneal Dialysis (ISPD)[6].

First, we investigated the basic status and characteristics of all registered PD patients. We also

summarized basic characteristics and reasons for withdrawal from PD therapy. Furthermore, we focused

on outcomes and reasons for withdrawal due to technical failure in R2, compared with R1. Technical

failure was defined as withdrawal from PD at the participating institution, excluding for reasons of renal

transplantation or movement to another hospital to continue PD therapy.

Comparison of basic and laboratory statuses, control of anemia, residual renal function (RRF), and status related to chronic kidney disease (CKD)-mineral and bone disorder (MBD) between R1 and R2

We estimated nutrition-related data, laboratory status, anemia, urine volume (UV), cardiothoracic ratio (CTR), RRF, and data and drugs related to CKD-MBD in R2 (Table 2), and compared R1 and R2 for each year up to 8 years after starting PD therapy. In addition to erythropoiesis-stimulating agents (ESAs) such as erythropoietin (epoetin-alfa/beta) and darbepoetin-alfa included in R1 as agents to improve anemia in CKD, epoetin-beta pegol was included as a new ESA in R2. Doses of different ESAs were adjusted to erythropoietin-equivalents (200U of erythropoietin was considered equivalent to 1μg of darbepoetin-alfa or 0.93μg of epoetin-beta pegol, based on data provided by Kuwahara *et al.*[7].

To control for CKD-MBD, lanthanum carbonate as a new phosphate binder and cinacalcet hydrochloride as a calcium-sensing receptor binder were newly available in R2. Doses of lanthanum carbonate and cinacalcet hydrochloride were thus shown in R2 only.

Analysis of reasons for withdrawal from PD due to technical failure in R1 and R2

Subset analyses were conducted for 357 patients withdrawn from PD due to technical failure.

First, we compared R1 and R2 in terms of background data and reasons for withdrawal from PD as

technical failure, including incidence of withdrawal due to PD-related peritonitis (n=63) or social

problems (n=35). Second, using univariate logistic regression modeling, we analyzed whether each of

these reasons for withdrawal was significantly associated with any of the following factors: R1 or R2;

presence of diabetes mellitus (DM); sex; age <65years or ≥65years; use of a sterilizing device during

PD-bag exchanges; type of sterilizing device (no device (manual), ultraviolet ray sterilization device or

sterile tubing welder device); use of automated PD (APD) or non-APD; use of the classical insertion

technique (non-embedding) or the Moncrief-Popovich technique (embedding)[8] as the method for PD

catheter placement; and duration until the patient was finally withdrawn from PD therapy.

To perform further analysis with multivariate logistic regression modeling, we chose factors for

which values of p<0.25 were obtained from univariate analysis as independent variables. In the present

study, "social problems" were defined as difficulties in self-performance related to PD therapies such as

blindness, discomfort in movement of the extremities and dementia (including mild cognitive

impairment). Poor self-management due to behaviors of patients themselves, such as lack of control in

water intake, diet restriction or skipping PD-bag changes or dissatisfaction with PD therapy, had been

categorized as a social problem in our previous report[3], but was excluded in the "social problems"

category both in R1 and R2 in the present study. In the present study, PD patients who withdrew due to

"social problems" might have been able to continue PD therapy with medical assistance from their family

and/or medical staff, such as with assisted PD[9,10]. Dissatisfaction and poor self-management due to

patient behaviors were instead included under the new category of "dissatisfaction, etc.".

Incidence of PD-related peritonitis and analysis of culture-negative results, duration of PD until

first occurrence of peritonitis and prognosis of incidental peritonitis in R1 and R2

We analyzed episodes of PD-related peritonitis in R1 and in R2 patients during 3years of

observation in each registration period. We compared duration of PD until incidence of peritonitis

between R1 and R2. Then, to assess clinical outcomes of peritonitis, we compared recovery rate from the

306 episodes of peritonitis in R2 against that from the 264 episodes of peritonitis in R1. We also

compared duration of PD until withdrawal due to PD-related peritonitis between R1 and R2.

Statistical analysis

Comparisons of continuous variables between the two cohorts were performed using unpaired

t-tests for annual laboratory data. To compare groups in the subset of withdrawn patients, the

Mann-Whitney U test was applied for continuous variables and Fisher's exact test for categorical

variables. We also analyzed whether "PD-related peritonitis" or "social problems" as the reason for

withdrawal was associated with registries using cross-tabulation and Fisher's exact test. To explore

patient background factors associated with withdrawal due to "PD-related peritonitis" or "social problems", univariate logistic regression analysis was used. For further analysis of withdrawal caused by "social problems", multivariate logistic regression analysis was performed using those independent variables showing values of p<0.25 in univariate analyses. For episodes of peritonitis extracted from R1 and R2, PD history until the incidence of peritonitis and PD history until withdrawal were compared using the Mann-Whitney U test, while recovery from peritonitis was compared using Fisher's exact test.

All values are shown as mean ± standard deviation (SD). Values of p<0.05 were considered significant. Analyses were performed using IBM SPSS Statistics version 22.0 (IBM, Armonk, NY) and R version 3.0.2 (R Foundation for Statistical Computing, Vienna, Austria).

Results

Comparison of background and basal characteristics of all registered PD patients between R1 and R2

Total number of PD patients, mean age, sex and pathology underlying ESRD for R1 and R2 are shown in Table 3. Briefly, compared with the 561 patients in R1, the total registered number of PD patients increased to 676. The ratio of males to females increased slightly from 64.2% in R1 to 68.6% in R2, and mean age in R2 was approximately 61.5years, 1.5years older than that in R1. Ratios of DM as a cause of ESRD were similar between in R1 and R2.

Concerning methods of PD catheter placement, embedding was more common in R2 (51.0%) than in R1 (33.7%)[3]. Use of a sterile connecting device to change PD fluid was much more frequent in R2 (72.7%) than in R1 (61.9%) (Table 3).

Withdrawal was observed in 228 of the 676 PD patients (33.7%) in R2, compared with 174 of the 561 PD patients (31.0%) in R1. Early withdrawal was seen in 44.7% of withdrawals in R2, clearly less than the 50.9% in R1 (Fig. 1a). Of note, death showed a marked decrease as an outcome of withdrawal, from 39.7% in R1 to 25.3% in R2. In contrast, renal transplantation increased slightly from 6.9% in R1 to 8.3% in R2 (Fig. 1b). Detailed causes of death in R1 and R2 are shown in Figure 2a.

As reasons for withdrawal of patients from PD for transfer to HD, PD-related peritonitis (excluding cases with gastrointestinal perforation or necrotizing appendicitis) tended to decrease from 24.7% in R1 to 23.2% in R2 (Fig. 2b). In contrast, withdrawal due to "social problems" clearly increased from 9.0% in R1 to 19.0% in R2 (Fig. 2b). Details of the cause of death and transfer to HD in R2 are shown in Fig. 2.

Laboratory status, UV and PD status in R2 and R1

Compared with R1, BMI and CTR were no different in R2, whereas serum albumin levels were slightly but significantly decreased (Fig. 3). Serum levels of total cholesterol showed no change between R1 and R2, except in year 1 (Fig. 3c). Neither systolic nor diastolic blood pressures changed significantly

between R1 and R2, except in years 4 and 5 (Fig. 3d-e). As a marker of inflammation, serum C-reactive

protein levels did not change significantly between R1 and R2 (Fig. 3g). In R2, hemoglobin (Hb) and

hematocrit (Hct) were well-preserved compared with R1, because ESA doses were significantly increased

compared with R1, except in years 6, 7 and 8 (Fig. 3h-j). Blood urea nitrogen and serum potassium levels

showed little difference between R1 and R2, except in years 1, 5 and 8 (Fig. 4a,c). Although serum

creatinine levels increased significantly year by year, R2 levels did not differ significantly compared with

R1 (Fig. 4b). In R2, frequency of diuretic use was significantly higher than that in R1 over all 8 years and

UV remained significantly more than in R1 until year 4 (Fig. 4d,h). The results suggested that

preservation of RRF was better in R2. Therefore, in years 1 and 2 after starting PD therapy, ultrafiltration

volume was significantly less in R2 than in R1 (Fig. 4e), and daily PD fluid volume was less in R2 than in

R1 (Fig. 4g). Although dialysate-to-plasma creatinine concentration ratio (D/P Cre) as a peritoneal

function showed no significant change at less than 6 years, D/P Cre values were significantly less in R2

for years 7 and 8 (Fig. 4f).

Analysis of calcium metabolism and treatment with activated vitamin D and phosphate binders

At more than 3 years after starting PD therapy, significant decreases in serum levels of calcium

and phosphate were observed in R2 compared with R1, except for years 3, 6 and 7 in serum phosphate

levels (Fig. 5a-b). Serum intact parathyroid hormone (iPTH) levels tended to show lower decreases in R2

than in R1 (Fig. 5c). Dose of activated vitamin D in R2 showed little change compared with R1 except for

years 3 and 6 (Fig. 5d). In terms of the use of phosphate binders, dose of calcium carbonate in R2 was

significantly decreased in years 1, 3 and 8, compared with R1 (Fig. 5e). In contrast, dose of sevelamer

hydrochloride in R2 was decreased from year 2 until year 5 compared to R1 (Fig. 5f). In R2, lanthanum

started to be used as a new phosphate binder and cinacalcet started to be used as a calcium-sensing

receptor binder (Fig. 5g-h).

Comparison of basic characteristics and factors influencing peritonitis and social problems in

patients withdrawn from PD between R1 and R2

We also analyzed withdrawals caused by technical failure and related factors. When we

compared background characteristics of withdrawn patients in R1 and R2, no significant associations

were seen for history of PD therapy, age, sex, DM, or use of an APD system in the induction period

(Supplementary Table 2). In contrast, use of an APD system at the time of both induction and withdrawal,

embedding as the insertion technique and use of a sterilizing device were significantly higher in R2,

compared with R1 (Supplementary Table 2).

Next, when we investigated the frequency of "PD-related peritonitis" or "social problems"

among the 357 cases of withdrawal caused by technical failure (from all 401 cases of withdrawal),

frequency of peritonitis did not differ between R1 and R2 (p=0.755), but frequency of "social problems"

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was higher in R2 than in R1 (p=0.010). Under logistic regression analysis for "PD-related peritonitis" as a reason for withdrawal, no significant factors other than duration of PD before withdrawal were identified (Supplementary Table 3). On the other hand, under logistic regression analysis for social problems as a reason for withdrawal, R2 showed a significantly higher correlation than R1 (p=0.010), age ≥65 years showed a significantly higher correlation than age <65 years (p=0.044) and DM showed a significantly higher correlation than non-DM (p=0.027), and a 1-month longer duration of PD was expected to decrease the occurrence of withdrawal caused by social problems (p=0.005) (Supplementary Table 4). As further analysis, under multivariate analysis for R1 vs. R2, age <65 years vs. ≥65 years, non-DM vs. DM, and duration of PD until withdrawal, only R2 and shorter duration of PD until withdrawal were significantly associated with social problems as a reason for withdrawal (p=0.010 each) (Supplementary Table 4).

Frequency of peritonitis and culture-negative peritonitis were decreased in R2, compared with R1

Incidence of PD-related peritonitis occurrence improved to once per 47.3 months/patient in R2, compared to once per 42.8 months/patient in R1[3] although PD-related peritonitis still represented one of the major reasons for withdrawal (Fig. 2b). In R2, incidence of PD-related peritonitis varied among the 15 institutions, with a minimum incidence of once per 219.5 patient/months and a maximum of once per 16.2 patient/months. Most cases of infectious peritonitis were caused by a single microorganism. Only 4.0% of

all peritonitis episodes involved multiple-organism infection. Among multiple-organism infections, 33.3% were caused by endogenous reasons such as gastrointestinal perforation, including perforated appendicitis. Microorganisms causing PD-related peritonitis in R2 were mainly Gram-positive *cocci* (47.6%), principally involving *Staphylococcus* sp. (46.7%) and *Streptococcus* sp. (19.2%). Details of identified microorganisms are shown in Table 4. Although 7 of 154 patients died due to peritonitis in R1, only 1 patient died due to peritonitis (by *Enterococcus faecalis*) in R2. Culture negative-results of bacterial cultures decreased to 27.0% in R2, compared to 31.8% in R1 (Fig. 6).

Analyses of peritonitis episodes: patient characteristics, duration of PD until first episode of peritonitis, recovery from peritonitis, and duration of PD until withdrawal due to peritonitis in R1 and R2

Backgrounds and characteristics did not differ significantly between patients with peritonitis in R1 and R2 (Supplementary Table 5). In the comparison of duration of PD until peritonitis, no significant difference was evident between R1 and R2 (p=0.440, Supplementary Table 6). In episodes of PD-related peritonitis, including endogenous peritonitis caused by gastrointestinal perforation, recovery rate from peritonitis as an outcome did not differ significantly between R1 and R2 (p=0.903, Supplementary Table 7). Concerning withdrawal from PD caused by PD-related peritonitis, duration of PD until withdrawal again did not differ significantly between R1 and R2 (p=0.549, Supplementary Table 8).

Discussion

In the management of CKD patients, education for patients is considered important for patients both with dialysis and without dialysis (pre-dialysis) to improve their prognosis[11-12]. Several reports have suggested that education for PD patients might be effective to improve the prognosis of PD therapy and prevent peritonitis[13-16]. A previous report identified differing levels of patient education between different institutions as one problem[15]. Our efforts were aimed at improving the prognosis of PD therapy through the sharing of information of PD care for patients among healthcare staff in our local area. Five years after our last study[3], we investigated outcomes, laboratory status and incidence of peritonitis with PD therapy in the Tokai area in R2, compared with our last study (R1).

First, in R2 compared with R1, points of improvement were early withdrawal from PD therapy and withdrawal due to death. Renal transplantation was also slightly increased as an outcome of withdrawal from PD therapy. In terms of PD-related peritonitis, both incidence of peritonitis and frequency of peritonitis related death were improved in R2, compared with R1. However, frequency of peritonitis as a reason for withdrawal from PD was unchanged between R1 and R2. In addition, frequency of successful recovery from peritonitis did not differ between R1 and R2. In R2, frequency of culture-negative peritonitis was clearly decreased, but still higher than recommended in the 2010 ISPD guideline[6]. Of note, ~~increased~~ frequency of social problems increased substantially as a reason for

withdrawal. As individual characteristics of social problems as a reason for withdrawal, DM as a basic

disease underlying ESRD and old age (≥65 years) became significant risk factors for withdrawal from PD

therapy. Interestingly, occurrence of social problems as a reason for withdrawal correlated inversely with

duration of PD until withdrawal. With PD-related peritonitis as a reason for withdrawal, increased

duration of PD was associated with lower frequency of peritonitis.

Second, concerning changes in laboratory data, both Hb and Hct levels were clearly preserved

in R2 compared with R1 because of the use of higher doses of ESAs in R2, in accordance with the 2008

guidelines of the Japanese Society for Dialysis Therapy[17]. In R2, availability of epoetin beta pegol as a

new ESA might be another reason for improvements in anemic state. Preservation of RRF is known to

improve mortality, even if patients with CKD develop ESRD[11]. Therefore, we also focused on patient

status related to RRF. Concerning RRF, urinary volume was seen to be better preserved in R2 until year 4

after starting PD therapy. Unfortunately, we could not evaluate residual creatinine clearance and Kt/V

(urea clearance) as two parameters used to measure the adequacy of dialysis and RRF between R1 and R2

because of the small number of data collected in R1. However, compared with R1, increased use of

diuretics was also considered to have contributed to the maintenance of UV in R2. In contrast, total dwell

volume of PD fluid was decreased in R2. In particular, in R2, a high ultrafiltration volume might not be

required within 3 years after starting PD therapy because of the good preservation of UV in R2 compared

with R1. Levels of D/P Cre were not significantly changed between R1 and R2, except in years 7 and 8.

Levels of D/P Cre are reportedly well-preserved when biocompatible PD fluids are used[18]. Because conventional acidic PD fluids had been used for at least a few years in most PD patients with data for years 7 and 8 in R1, D/P Cre values might have been higher in R1 than in R2.

In relation to CKD-MBD, lanthanum carbonate was added as a new phosphate binder, and the calcium-sensing channel blocker cinacalcet hydrochloride became available from the end of 2010. Therefore, levels of both serum calcium and serum phosphate might have been better controlled in R2 than in R1. As a result, elevation of serum iPTH levels might be slightly suppressed in R2, compared with those in R1.

In terms of PD-related peritonitis in this study, the number of deaths due to PD-related peritonitis was markedly decreased in R2 compared to R1 because management for PD-related peritonitis such as usage of antibiotics and decisions regarding PD-catheter removal might be adjusted according to the ISPD guideline[6] in the Tokai area. Microorganisms causing peritonitis were Gram-positive in over 47% of cases in R2, suggesting that contamination during PD bag exchanges might still be an important problem. Culture-negative peritonitis was clearly improved in R2, but was still over the 20% level recommended by the ISPD guideline for culture-negative peritonitis[6]. We therefore need to continue efforts to decrease negative results from bacterial examinations attributable to inadequate collection procedures for bacterial examinations. New techniques such as measurement of bacterial and fungal mRNA fragments[19] and evaluation of immune fingerprints[20] might facilitate diagnosis of

culture-negative infections. Further development of such techniques might be required to decrease culture-negative peritonitis.

We made a concerted effort to provide education programs related to PD therapy and facilitate the sharing of information associated with global standards between medical staff at our own and other institutions, and also improved education for PD patients, especially in the management of peritonitis. In R2, the number of PD patients increased in several institutions, compared with the R1 study. The larger number of PD patients might have contributed to the decrease in early withdrawal of PD patients through what we call "center effects"[21,22], sufficient increases in numbers of PD patients might not have been seen in each institution in our study. As a result, we did not see a statistical improvement in the frequency of withdrawals from PD because of PD-related peritonitis in R2, even though the frequency of deaths associated with PD-related peritonitis was clearly improved and the incidence of peritonitis was slightly decreased. However, as a limitation to evaluating educational effects in multi-institutional cohorts, optimizing decision-making processes and evaluating outcomes has been reported as difficult[15]. In further studies, analysis of multi-center effects also might be expected.

In conclusion, although our efforts might be considered to have slightly improved the incidence of peritonitis and death as a reason for withdrawal of PD in the Tokai area, improving the incidence of peritonitis as a reason for withdrawal from PD therapy was difficult. Current sterilizing device systems for PD-bag changes have not dramatically suppressed the incidence of peritonitis as a reason for

withdrawal from PD therapy. Our study also showed an increase in social problems as a reason for withdrawal from PD compared with the R1 study. We now face an aging society not only in Japan, but also worldwide. With an increasing number of elderly patients, we also have to construct social support networks for disabled patients receiving PD therapy in Japan. The present results strongly suggest a need for new systems for PD bag exchanges to improve the prognosis of PD therapy[23].

Conflict of Interest

Acknowledgements

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FIGURE LEGENDS

Fig. 1   Duration of peritoneal dialysis (PD) therapy until withdrawal from PD patients and reasons for withdrawal in R1 and R2

Set of graphs a show duration of PD until withdrawal from PD therapy in R1 and R2. Set of graphs b show prognosis after withdrawal from PD therapy in R1 and R2.

Fig. 2   Reasons for death or transfer to hemodialysis in R1 and R2

Graph a shows reasons for death as a cause of withdrawal from PD. Graph b shows reasons for transfer to hemodialysis as a cause of withdrawal from PD. □, R1; ■, R2.

Fig. 3   Nutritional status, systemic blood pressure, cardiothoracic ratio (CTR), and C-reactive protein level, and anemia in peritoneal dialysis (PD) patients in R1 and R2

Body mass index (a), serum albumin level (b), and cholesterol level (c) are shown as markers of nutritional status. Blood pressure is shown as systolic (d) and diastolic (e). CTR (f). Serum C-reactive protein level (g) is shown as an inflammatory marker. Blood hemoglobin level (h), hematocrit (i), and use of ESA as erythropoietin-equivalents (j) are shown as markers of anemia status.

Dotted and solid lines show R1 and R2, respectively. *: $p < 0.05$; **: $p < 0.01$; ***: $p < 0.005$; ****: $p < 0.001$; *****: $p < 0.0005$; ******: $p < 0.0001$. Each value represents mean ± SD.

Fig. 4   Residual renal function, status of peritoneal dialysis (PD) and peritoneal function in PD

patients in R1 and R2

Levels of blood urea nitrogen (BUN) (a) and creatinine (b) are shown as markers of renal function. Serum

potassium level (c). Changes in daily urinary volume (d), changes in ultrafiltration volume (e) and

dialysate-to-plasma creatinine concentration ratio (D/P Cre) (f) are shown as markers of peritoneal

function. Amount of peritoneal dialysis fluid (g) is also shown. Changes in use of diuretic (h).

Dotted and solid lines show R1 and R2, respectively. *: $p < 0.05$; **: $p < 0.01$; ***: $p < 0.005$; ****: p

< 0.001; *****: $p < 0.0005$; ******: $p < 0.0001$. Each value represents mean ± SD.

Fig. 5   Calcium metabolism and doses of related agents in peritoneal dialysis patients in R1 and

R2

Levels of calcium (a), phosphate (b), intact parathyroid hormone (iPTH) (c), and active vitamin D (d),

and doses of calcium carbonate (e), and sevelamer hydrochloride (f). Doses of lanthanum carbonate (g)

and cinacalcet hydrochloride (h) are shown as agents newly available in R2.

Dotted and solid lines show R1 and R2, respectively. *: $p < 0.05$; **: $p < 0.01$; ***: $p < 0.005$; ****: p

< 0.001; *****: $p < 0.0005$; ******: $p < 0.0001$. Each value represents mean ± SD.

Fig. 6   Categories of microorganisms and culture negatives in R1 and R2

In R2 compared with R1, Gram-positive cocci were slightly increased and culture-negative results were

moderately decreased. G+C, Gram-positive cocci; G+R, Gram-positive rods; G-C, Gram-negative cocci;

G-R, Gram-negative rods; G-, unclassified Gram-negative organisms; tbc, tuberculosis; negative,

culture-negative results; unknown, no bacterial examination was performed or no data were available.

Table 1 Number of peritoneal dialysis (PD) patients in the 13 institutions from 2005 to 2007 (Registry 1) and in the 15 institutions from 2010 to 2012 (Registry 2)

The 15 institutions (12 institutions in Aichi Prefecture, 1 institution in Mie Prefecture, and 2 institutions in Gifu Prefecture) were as follows: Nagoya University Hospital, Handa City Hospital, Minami Seikyo Hospital, Yokkaichi Municipal Hospital, Anjo Kosei Hospital, Nagoya Kyoritsu Hospital, Tosei General Hospital, Chubu Rosai Hospital, Toyota Kosei Hospital, Daiyukai Daiichi Hospital, Kasugai Municipal Hospital, and Konankousei Hospital, Ogaki Kita Clinic, Ogaki Municipal Hospital (Registry 2 only) and Kainan Hospital (Registry 2 only)

Year	Number of patients			
	<24	25-49	50-99	≥100
2005	9	3	1	0
2006	7	4	2	0
2007	5	6	2	0
	(refer to Mizuno et al. Clin Exp Nephrol 2011)			
2010	8 (2)	3	4	0
2011	7 (2)	3	5	0
2012	8 (2)	2	5	0

(Number) shows newly registered institutions.

Table 2   Profile lists of the database system in the present study

Major contents	Subgroups
1. Background	a. Age
	b. Sex
	c. Renal disease causing end-stage renal disease
2. Incidence and prevalence of peritoneal dialysis (PD) patients	
3. Reasons for withdrawal from PD therapy	
4. Duration of PD therapy and differences between diabetes mellitus (DM) and non-DM patients	
5. Nutritional condition	
	a. Body mass index
	b. Serum albumin
	c. Total cholesterol level
6. Anemia state	
	a. Blood hemoglobin level
	b. Blood hematocrit
	c. Monthly ESA dose
7. Renal function	

a. Urine volume

b. Blood urea nitrogen level

c. Serum creatinine level

8. PD status

   a. PD catheter insertion technique

   b. Continuous ambulatory PD or automated PD

   c. PD with sterile connecting device to change PD fluid (PDF)*

   d. Daily PDF dose

   e. Dialysate-to-plasma creatinine concentration ratio

9. Cardiovascular status

   a. Systemic blood pressure

   b. Cardiothoracic ratio

10. Relationship to calcium metabolism

    a. Serum calcium

    b. Serum phosphate

    c. Intact parathyroid hormone

    d. Dose of phosphate binders (calcium carbonate, sevelamer hydrochloride, and/or lanthanum

       carbonate)

e.   Dose of cinacalcet hydrochloride

ESA: erythropoiesis-stimulating agent; *: no connecting device (manual), ultraviolet ray sterilization

device (UVD), or sterile tubing welder device (STWD).

Table 3   Basic characteristics of patients on peritoneal dialysis in Registries 1 and 2

	Registry 1	Registry 2
Contents	n (%)	n (%)
Total number	561	676
Sex		
Male	360 (64.2)	464 (68.6)
Female	201 (35.8)	212 (31.4)
Age (years)	60.0 ± 13.1	61.5 ± 11.9
Cause of end-stage renal disease		
Chronic glomerulonephritis	230 (41.0)	240 (35.5)
Diabetic nephropathy	191 (34.0)	232 (34.3)
Nephrosclerosis	88 (15.7)	98 (14.5)
Polycystic kidney	9 (1.6)	17 (2.5)
Chronic pyelonephritis	4 (0.7)	1 (0.1)
Post renal failure	3 (0.5)	4 (0.6)
Interstitial nephritis	3 (0.5)	2 (0.3)
Alport syndrome	0 (0)	3 (0.4)

Fabry disease	2 (0.4)	2 (0.3)
Post-acute renal failure	2 (0.4)	8 (1.2)
Malignant hypertension	2 (0.4)	3 (0.4)
RPGN*	0 (0)	10 (1.5)
Others	9 (1.6)	17 (2.5)
Unknown	18 (3.2)	39 (5.8)

Insertion technique of PD-catheter

Non-embedding	372 (66.3)	331 (49.0)
Embedding	189 (33.7)	345 (51.0)

Connecting system for PD bags

Manual	214 (38.1)	185 (27.4)
UVD**	304 (54.2)	446 (66.0)
STWD***	43 (7.7)	45 (6.7)

*: RPGN, rapidly progressive glomerulonephritis; **: UVD, ultraviolet ray sterilization device; ***:

STWD***, sterile tubing welder device.

Table 4 Microorganisms identified from bacterial culture in peritoneal dialysis (PD)-related

peritonitis from 2010 to 2012 (R2)

Group of microorganisms	n (%)
Gram-positive cocci	115 (66.1)
Staphylococcus sp.	46 (26.4)
MSSA	26 (14.9)
MRSA	20 (11.5)
Staphylococcus epidermidis	18 (10.3)
Other CNS	10 (4.3)
Streptococcus sp.	59 (33.9)
Enterococcus sp.	6 (3.4)
Micrococcus sp.	3 (1.7)
Others	1 (0.6)
Gram-positive rods	7 (4.0)
Corynebacterium sp.	3 (1.7)
Others*	4 (2.3)
Gram-negative species	44 (25.3)

Acinetobacter sp.	8 (4.6)
Serratia sp.	7 (4.0)
Pseudomonas aeruginosa	6 (3.5)
Klebsiella sp.	5 (2.9)
Escherichia coli	4 (2.3)
Citrobacter sp.	2 (1.1)
Enterobacter sp.	2 (1.1)
Pasteurella sp.	2 (1.1)
Others**	8 (4.6)
Fungi	8 (4.6)

MSSA: methicillin-susceptible *Staphylococcus aureus*; MRSA: methicillin-resistant *Staphylococcus aureus*; CNS: coagulase-negative *Staphylococcus*; *: *Brevibacterium* in 1 case, *Listeria* in 1 case, and unspecified Gram-negative rods in 2 cases; **: *Moraxella*, *Bacteroides*, *Fusobacterium*, *Flavimonas*, *Alcaligenes*, *Sphingomonas*, *Stenotrophomonas* and *Prevotella* for 1 case each.
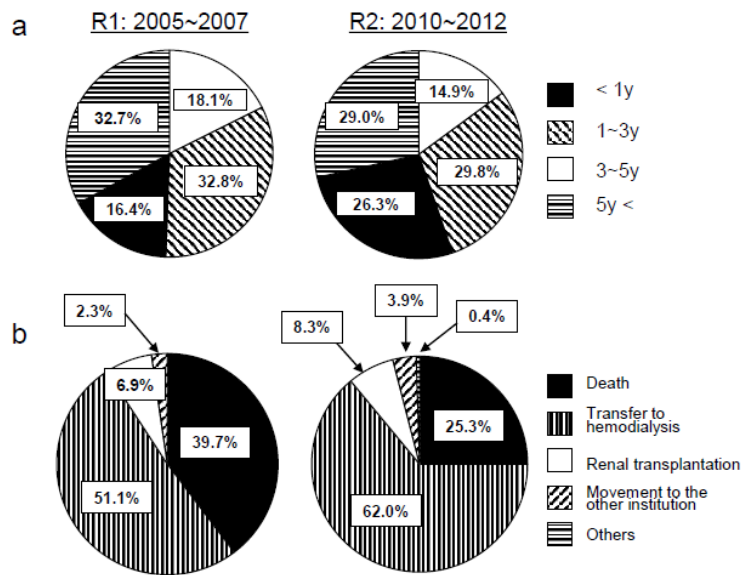
Figure 1
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a

R1: 2005~2007   R2: 2010~2012

- ■ < 1y
- ▨ 1~3y
- □ 3~5y
- ▤ 5y <

b

- ■ Death
- ▥ Transfer to hemodialysis
- □ Renal transplantation
- ▨ Movement to the other institution
- ▤ Others

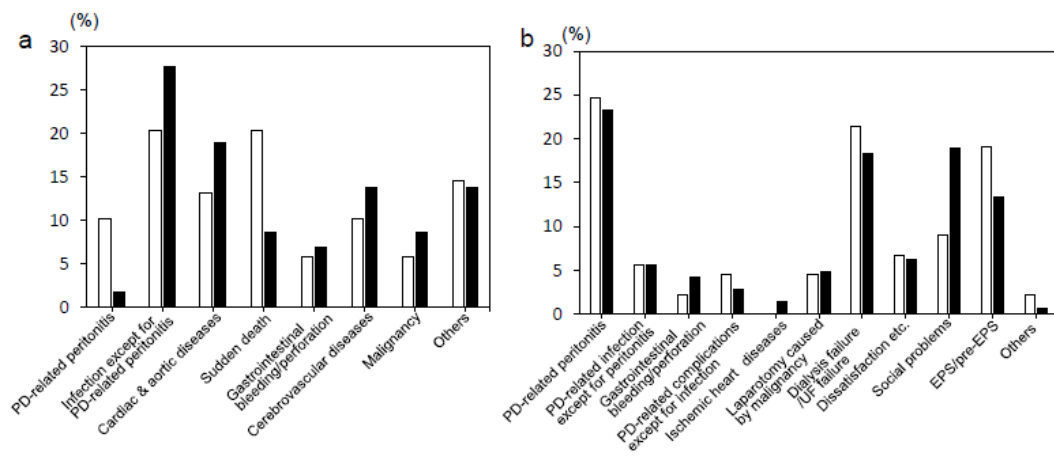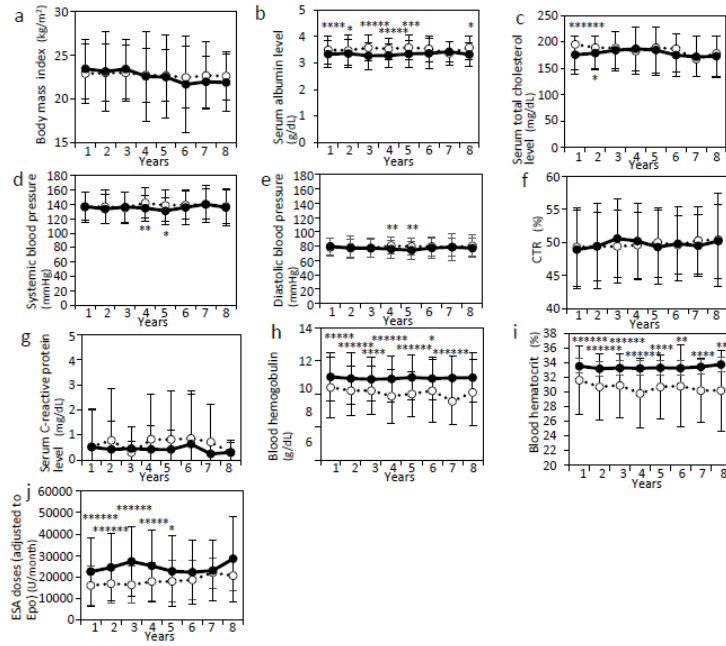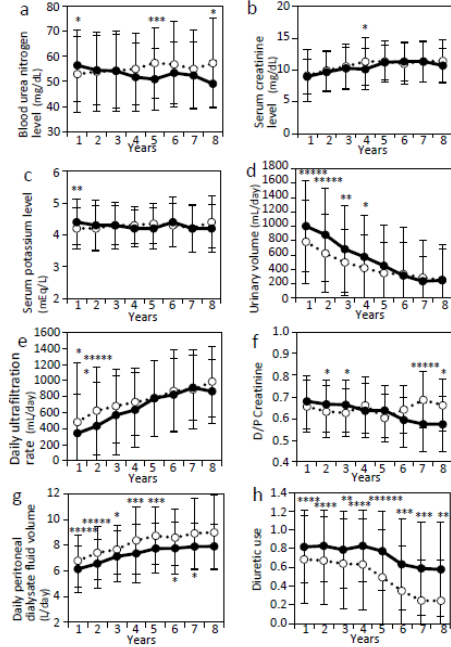## Figure 2
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a
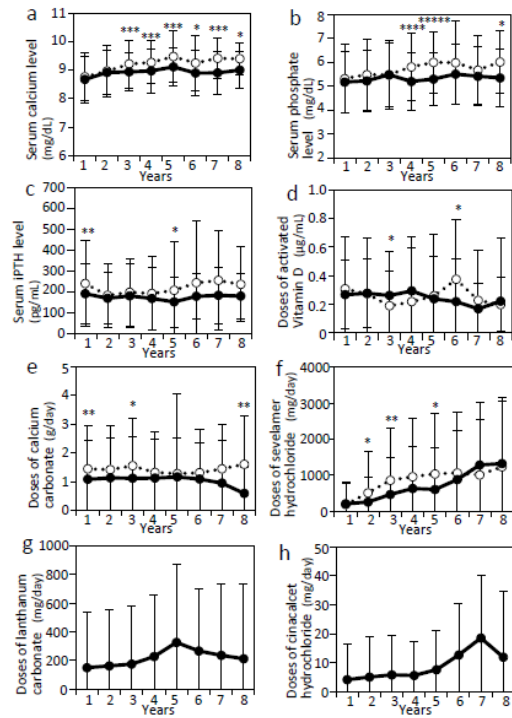

b

37

Figure 3

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Figure 4

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Figure 5

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Figure 6

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