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Current Practice and Outcomes of Peritoneal Dialysis in the Nippon Medical School Musashi Kosugi Hospital

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Introduction: Various innovations for preventing complications and improving a patient's quality of life have been implemented for peritoneal dialysis (PD), which was established in Japan approximately 35 years ago and introduced at our hospital in 1999. Herein, we investigate the outcomes of patients undergoing PD to identify approaches for improving their long-term prognosis.

Methods: This retrospective study included 114 patients who underwent PD between September 1999 and August 2017 and included various parameters such as patient survival rate, technical survival rate, cause(s) of PD withdrawal, incidence of peritonitis, dialysis duration, and change in residual renal function (RRF). Furthermore, factors associated with PD withdrawal and duration, as well as risk factors for peritonitis, were examined.

Results: Mean (± standard deviation) PD duration was 35.62 (±29.88) months in all patients and 37.16 (±34.09) months in 58 patients who withdrew from treatment. Five-year continuance and survival rates were 40.41% and 55.74%, respectively (p=0.0061). However, in patients aged ≥65 years, the continuance and survival rates were not significantly different (p=0.1250). Furthermore, the continuance and survival rates in diabetic patients were not significantly different from those of non-diabetic patients (p= 0.1334 and 0.7140, respectively). Comparison of changes in RRF in young and elderly patients revealed that it was not significantly sustained in elderly patients (p=0.0259). The Cox proportional hazards model revealed that age (p=0.0455) and total cholesterol levels (p=0.0494) were independent risk factors for PD withdrawal, and multiple regression analysis showed that the presence of peritonitis (p=0.0063) and low-density lipoprotein cholesterol (LDL-C) levels (p=0.0087) were significant factors for PD duration. Peritonitis incidence was 0.077 times per patient per year, and multivariate analysis identified PD duration (p=0.0009) and LDL-C levels (p=0.0054) as independent risk factors for peritonitis.

Conclusion: The findings of this study revealed that assessment of the nutritional status of the patient and prevention of peritonitis are important for continuation of PD. PD is a safe treatment option that can maintain the quality of life in elderly patients. In a rapidly aging society, the need for PD-based medical care is expected to increase. (J Nippon Med Sch 2018; 85: 102–109)

Key words: peritoneal dialysis, prognosis, peritonitis, peritoneal dialysis withdrawal, residual renal function

Introduction

An insurance plan to cover peritoneal dialysis (PD) for patients with chronic renal failure (CRF) that was introduced in 1984 has enabled long-term survival of many patients with end-stage renal failure. While the number of patients with CRF on dialysis has been increasing, with 324,986 people predicted to require dialysis by the end of 2015, no significant change has been observed in the number of patients undergoing PD (9,322) over the past several years; furthermore, the number of patients

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receiving hemodialysis (HD) combination therapy has been steadily increasing[1,2]. In patients undergoing PD, a plethora of complications, such as encapsulating peritoneal sclerosis (EPS), are accompanied by decreased bowel movement, bowel obstruction, peritoneal dysfunction, and ultrafiltration failure. EPS is thought to be caused by peritoneal adhesion and hyperplasia due to long-term dialysate use and is a major problem in long-term PD treatment[3]. Nonetheless, important advances including improvements in connecting devices and the automated PD (APD) device, a new dialysate that includes bicarbonate as a buffer, and various other innovations have aided in the prevention of complications and improvements in quality of life (QOL)[4,5]. In this study, we evaluate the current state and outcomes of PD that have been administered over the past 20 years at the Nippon Medical School Musashi Kosugi Hospital. We summarize treatment results and discuss potential approaches to improve the long-term prognosis of patients on PD.

Patients and Methods

We conducted a retrospective analysis of 114 patients who were initiated on PD between September 1999 and August 2017 at the Nippon Medical School Musashi Kosugi Hospital. Data were collected from patient medical records to examine various parameters such as renal function, age, primary disease at PD initiation, planned afferent presence, presence of diabetes mellitus (DM) and peritonitis, patient survival rate, technical survival rate, cause(s) of PD withdrawal, dialysis duration, incidence of peritonitis, and change in residual renal function (RRF). Data on the following parameters were also collected: albumin (Alb; g/dL), total cholesterol (T-Cho; mg/dL), low-density lipoprotein-cholesterol (LDL-C; mg/dL), triglyceride (TG; mg/dL), estimated glomerular filtration ratio (eGFR; mL/min/1.73 m^2), calcium (mg/dL), phosphorus (mg/dL), intact parathyroid hormone (iPTH; pg/mL), hemoglobin (Hb; g/dL), and C-reactive protein (CRP; mg/dL). Further, factors that influenced PD withdrawal and PD duration as well as risk factors for peritonitis were also examined.

All laboratory values were presented as means ± standard deviations (SD). Continuous variables were compared using Student's *t* test or one-way analysis of variance (ANOVA), and survival analysis was performed on longitudinal data to address its multiplicity. Tukey's multiple comparison test was used as the *post hoc* test, and Fisher's exact test was used for various inter-group comparisons. The Mantel-Cox log-rank test was used for comparison of survival curves. *P* values <0.05 were considered as statistically significant for all analyses performed. All statistical analyses were performed using Prism® software version 6 (GraphPad Software, La Jolla, CA, USA). The Cox proportional hazards model, multiple linear regression test, and logistic regression analyses were performed using JMP® software version 12 (SAS Institute, Cary, NC, USA).

Results

The study population of 114 patients, including 14 patients from other hospitals, comprised 82 males and 32 females. Forty-six patients were ambulatory, four of whom received HD in combination with PD. Mean age at PD initiation was 64.0±18.0 years, and 21 patients (18.4%) required induction under emergent conditions.

Primary diseases were diabetic nephropathy, nephrosclerosis, chronic glomerulonephritis, autosomal dominant polycystic kidney disease, and liver cirrhosis in 42 (36.8%), 41 (35.9%), 21 (18.4%), 4 (3.5%), and 3 (2.6%) patients, respectively. Treatment regimens were continuous ambulatory PD (CAPD) and APD in 17 (14.9%) and 97 (85.1%) patients, respectively. Mean dialysate dose was 4,997±2,224 mL, serum creatinine level at initiation was 6.682±3.086 mg/dL, and eGFR was 8.178±3.655 mL/min/1.73 m^2 (**Table 1**). Laboratory values and other parameters were compared after the study patients were classified as those who were initiated on PD during the first ten years of the study period (before 2010) and those who were started during the last eight years (2010 onward). Our analysis revealed that serum creatinine levels at PD initiation were lower in the earlier group than in the latter group (unpaired *t* test, p=0.0552) and that there was no significant difference in eGFR between the two groups (unpaired *t* test, p=0.3397). Although there was a statistically insignificant increase in the total number of patients newly undergoing PD at the study hospital, there was a significant increase in the number of elderly patients who were initiated on PD during the study period (unpaired *t* test, p=0.0035).

Mean dialysis duration was 35.62±29.88 months, and 24 patients continued dialysis for more than 5 years. Five-year continuance rate was 40.41%, with a half-life of approximately 51 months, and five-year survival rate was 55.74%, with a half-life of approximately 75 months. The log-rank test revealed a significant difference between the continuance and survival rates (p=0.0061; **Fig. 1**). However, these rates were not significantly different when compared in diabetic and non-diabetic patients

Table 1 Patient characteristics

total, n	114
Female, n (%)	35 (30.7)
Age (years)	64.63±16.77
BMI (kg/m^2)	23.99±2.537
PD duration (months)	35.52±29.96
Period until PD withdrawal (months)	37.16±34.09
Dialysate volume (mL/day)	4,997±2,224
APD, n (%)	97 (85.1)
D/P ratio	0.8250±0.1136
D/D_0 ratio	0.2786±0.1046
Weekly KT/V_{urea}	1.720±0.4344
Emergency induction, n (%)	21 (18.4)
Current outpatient, n (%)	46 (40.4)
Other hospital visiting, n (%)	14 (12.3)
Hemodialysis combination, n (%)	4 (3.5)
Primary disease	
DM, n (%)	42 (36.8)
Nephrosclerosis, n (%)	41 (36.0)
CGN, n (%)	21 (18.4)
PKD, n (%)	4 (3.5)
Liver cirrhosis, n (%)	3 (2.6)
Others, n (%)	3 (2.6)

BMI, body mass index; PD, peritoneal dialysis; APD, automated peritoneal dialysis; DM, diabetes mellitus; CGN, chronic glomerulonephritis; PKD, polycystic kidney disease

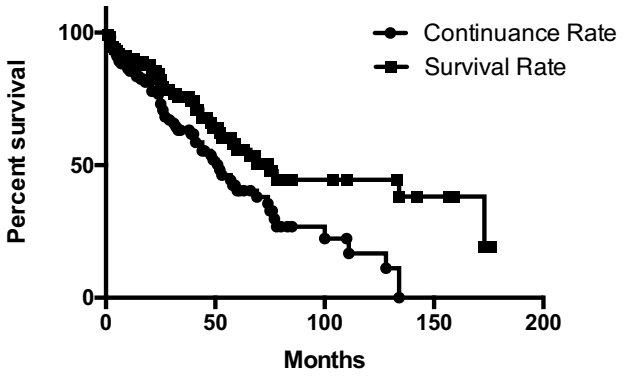

Fig. 1 Comparison of survival curves derived from continuance and survival rates. The Mantel-Cox log-rank test, p=0.0061.

(log-rank test, p=0.1334 and 0.7140, respectively; **Fig. 2**). Further comparison of the continuance and survival rates among the young and the elderly patients demonstrated that they were significantly different in patients aged ≤65 years (log-rank test, p=0.0489) but not in those aged >65 years (log-rank test, p=0.1250) (**Fig. 3**).

At the study hospital, 38 patients, 69.1% of the PD withdrawal patients, continued PD until death, termed "last PD", a desirable outcome for the elderly. Among the outcomes, ten patients were transferred to long-term care hospitals that could perform PD, and six elderly patients received PD by on-site medical treatment at home.

Based on the Japanese Society for Dialysis Therapy (JSDT) PD guidelines (2009), RRF was defined as ≥100 mL urine flow over 24 h. Among the patients with preserved RRF, 42.44% continued PD for ≥5 years. Comparison of changes in RRF between the young and elderly patients revealed that the change in RRF in elderly patients was not significantly sustained (log-rank test, p=0.0259; **Fig. 4**).

Of the 114 study patients, 58 discontinued PD due to several reasons including death (n=38; 69.1%), technical issues during the procedure (n=9; 16.4%), long-term nature of the PD treatment (n=6; 10.9%), and kidney transplantation (n=2; 3.6%). We examined factors that were associated with PD withdrawal using the Cox proportional hazards model, with age, planned induction, DM, peritonitis, Alb, T-Cho, LDL-C, TG, eGFR, Ca, P, iPTH, Hb, and CRP as variables, and identified six candidate factors: age, T-Cho, LDL-C, Hb, CRP, and iPTH (**Table 2**). Subsequently, age and T-Cho were independent risk factors for PD withdrawal (**Table 2**).

Simple linear regression analysis revealed six significant factors (age, presence of peritonitis, Alb, LDL-C, Ca, and CRP) that were associated with PD duration, whereas multiple regression analysis revealed peritonitis (p=0.0063) and LDL (p=0.0087) as significant factors that were associated with PD duration. Further, peritonitis was identified as the most important factor associated with PD duration (**Table 3**).

At the study institution, 11 patients with APD and 3 patients with CAPD developed PD-related infections. Hernia occurred in five patients with each treatment style. The incidence rates of PD-related infections and hernia between the APD and CAPD groups were also compared using Fisher's exact test, which revealed that there was no significant difference in PD-related infections between the two groups (p=0.4364), whereas the incidence of hernia was significantly lower in the APD group (p=0.0065).

Peritonitis incidence at the study institution was 7.7 cases per 100 patients, which was lower than the admissible incidence rate specified in the International Peritoneal Dialysis guidelines. Multivariate analysis using the stepwise method revealed PD duration and LDL as independent risk factors for peritonitis and PD duration as the most important risk factor for peritonitis (p=0.0009; **Table 4**).

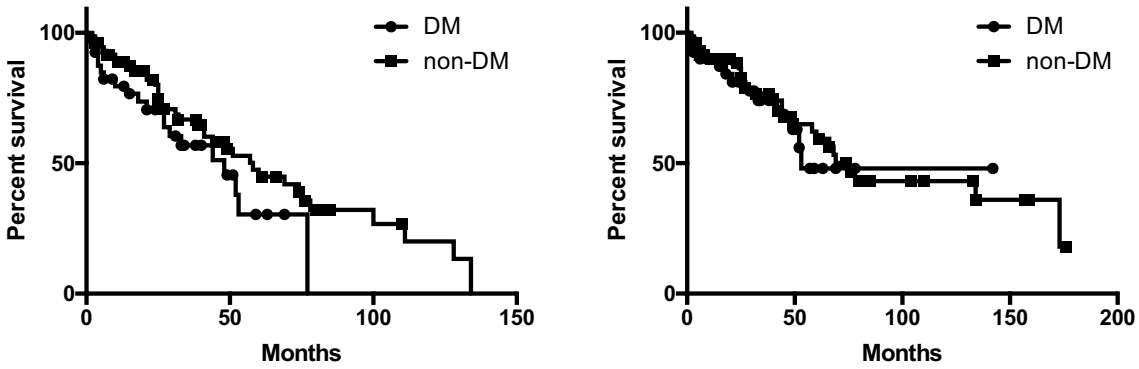

Fig. 2 Comparison of continuance and survival rate curves. Left: Continuance rates of patients with and without DM. The Mantel-Cox log-rank test, p=0.1334. Right: Survival rates of patients with and without DM. The Mantel-Cox log-rank test, p=0.7140. DM: diabetes mellitus

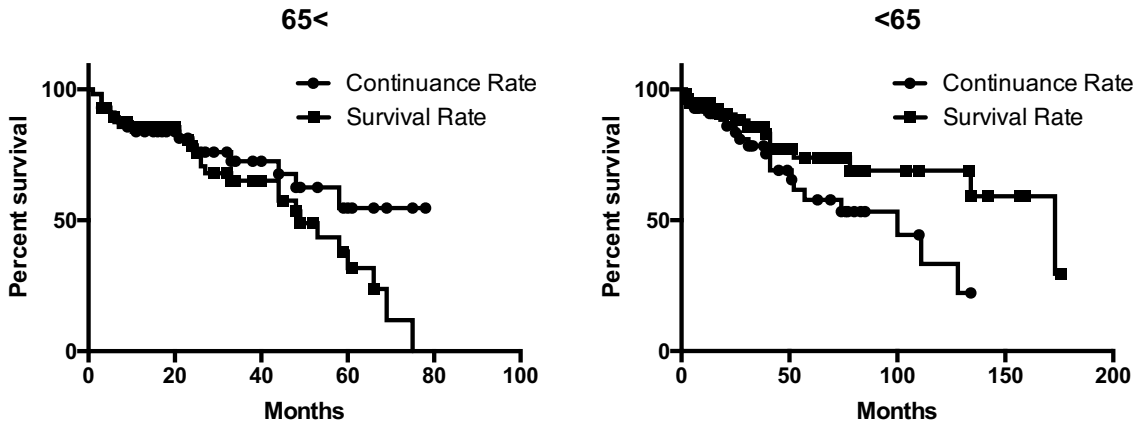

Fig. 3 Comparison of survival curves derived from continuance and survival rates. Left: patients aged ≥65 years. The Mantel-Cox log-rank test, p=0.1250. Right: patients aged<65 years. The Mantel-Cox log-rank test, p=0.0489.

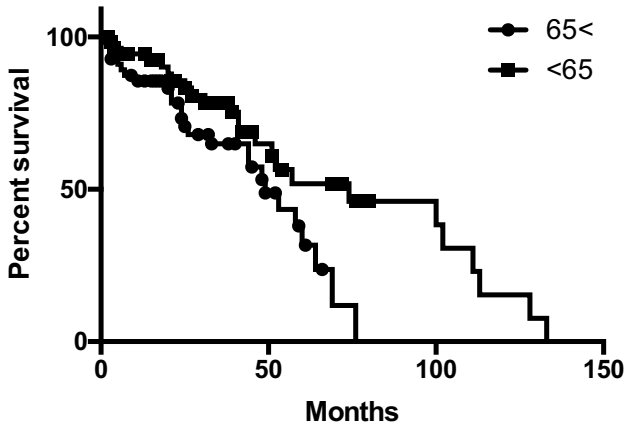

Fig. 4 Comparison of survival curves derived from RRF. The Mantel-Cox log-rank test, p=0.0259. RRF: residual renal function

Discussion

An investigation by the JSDT in 2014 revealed that 2,008 of 4,446 patients undergoing PD used APD (45.2%)[1], which was much lower than the proportion of PD patients using APD in the current study (85.1%). There are several factors contributing to the higher rate of APD use at the study institution. First, APD is superior to CAPD as it is expected to improve patient QOL in addition to improving dialysis efficiency and reducing the burden on caregivers. In addition, APD has several medical advantages including shorter dialysate storage time that is associated with a reduction in glucose absorption via the peritoneum, lower risk of infection due to a reduction in the number of times the patient touches the catheter, and lower hernia incidence as dialysis is performed in the supine position with no increase in abdominal pressure. During hospitalization, certified nurses and other staff members educate all patients and their families on APD procedures.

A comparison of serum creatinine levels and eGFR between the first ten years (before 2010) and the last eight years (2010 onward) of the study revealed that serum

Table 2 Cox proportional hazards analysis for PD withdrawal

Variables	Hazard ratio	95% CI	*p* value
Age (year)	1.025954	1.000508–1.052482	0.0455
TC (mg/dL)	0.976304	0.951105–0.999941	0.0494
LDL-C (mg/dL)	1.013039	0.985468–1.04317	0.3650
Hb (g/dL)	0.945725	0.726825–1.221809	0.6711
CRP (mg/dL)	1.164219	0.950072–1.377987	0.1312
iPTH (pg/mL)	0.999313	0.996798–1.001526	0.5603

PD, peritoneal dialysis; TC, total cholesterol; LDL-C, low-density lipoprotein cholesterol; Hb, hemoglobin; CRP, C-reactive protein; iPTH, intact parathyroid hormone

Table 3 Multiple linear regression analysis for PD duration

Variables	Unstandardized coefficient (B)	Standardized coefficient (Beta)	95% CI	*p* value
Age	–0.43952	–0.178238	–0.465901–0.1094245	0.2214
Peritonitis	10.118577	8.753466	2.544055–2.544055	0.0063
Alb	18.156214	6.1233544	–2.771303–15.018011	0.1747
LDL-C	0.2237216	0.2043656	0.052943–0.3557881	0.0087
Ca	8.727914	4.9173553	–1.494179–11.328889	0.1310
CRP	–3.852723	–1.571001	–4.583721–1.4417183	0.3029

PD, peritoneal dialysis; Alb, albumin; LDL-C, low-density lipoprotein cholesterol; CRP, C-reactive protein; CI, confidence interval

Table 4 Logistic regression for peritonitis

Variables	Univariate analysis		Multivariate analysis	
	Odds ratio (95% CI)	*p* value	Odds ratio (95% CI)	*p* value
Age (year)	0.997427 (0.969902–1.025913)	0.856	1.036209 (0.993983–1.08614)	0.0957
Planned induction	0.6491229 (0.1417638–2.1771561)	0.507		
DM	1.7142855 (0.6390125–5.1477196)	0.2919		
Duration (months)	1.020419 (1.005713–1.036291)	0.0065	1.044343 (1.0175–1.075341)	0.0009
Alb (g/dL)	1.30442 (0.621999–2.893441)	0.4885		
TC (mg/dL)	0.996178 (0.983332–1.008124)	0.5382		
LDL-C (mg/dL)	0.981459 (0.957613–1.002111)	0.081	0.965523 (0.93469–0.990848)	0.0054
TG (mg/dL)	0.998921 (0.992217–1.003703)	0.6912		
eGFR (mL/min/m^2)	0.92649 (0.785128–1.065996)	0.304		
Ca (mg/dL)	1.028434 (0.581224–1.884277)	0.9247		
P (mg/dL)	1.136351 (0.801089–1.579718)	0.457	1.658951 (0.968327–2.933482)	0.0650
iPTH (pg/mL)	0.99808 (0.9948–1.000679)	0.1596		
Hb (g/dL)	0.971873 (0.702058–1.347163)	0.8626		
CRP (mg/dL)	0.93241 (0.59953–1.237147)	0.6675		

DM, diabetes mellitus; Alb, albumin; TC, total cholesterol; LDL-C, low-density lipoprotein cholesterol; TG, triglyceride; eGFR, estimated glomerular filtration rate; iPTH, intact parathyroid hormone; Hb, hemoglobin; CRP, C-reactive protein; CI, confidence interval

creatinine levels at PD initiation were lower in the latter group, but no significant difference in eGFR was found between the two groups. This finding does not contradict our finding of an increase in the number of elderly patients newly undergoing PD. In addition, the continuance and survival rates were significantly different among patients aged ≤65 years. However, many patients over the age of 65 years completed "last PD", as evidenced by the lack of a significant difference between the continuance and survival rates in this group[6]. There is a tendency for

PD induction rate to decrease among elderly patients with the increasing number of elderly CRF patients and PD patients worldwide[7–9]. Compared with HD, PD has a minimal effect on hemodynamics and is more likely to facilitate home-based medical care in elderly CRF patients, which can lead to a desired reduction in the number of hospital visits[10]. However, mastering the procedure is difficult, and family support and at-home medical staff are often necessary[11]. Overall mortality is not significantly different between PD and HD, and the dialysis method is not identified as an independent factor that influences survival rate[12]. Furthermore, studies indicated no differences between the continuance rate and peritonitis incidence between elderly and young patients[13].

Changes in RRF were not sustained in elderly patients compared with those in young patients. Reports indicated that urine volume, which decreased below the ultrafiltration volume two years after PD initiation in patients younger than 70 years but not in patients aged >70 years, exceeded the ultrafiltration volume until five years after PD initiation[14]. Our results differ from those reported previously, probably due to the smaller number of cases. In addition, there are several factors that can affect RRF including eGFR at induction, use of diuretics, and proteinuria[15]. Due to the small sample size of the current study, further investigation with a larger patient cohort at this hospital is necessary to validate the current results.

Using the Cox proportional hazards model, we identified age and T-Cho level as independent risk factors for PD withdrawal, which imply that elderly patients and those with decreased T-Cho levels were more likely to withdraw from PD; this trend observed among patients with low T-Cho levels remained significant, independent of age. Decrease in cognitive function due to aging and deterioration of the nutritional status of the patient are suggested to lead to a reduction in the ability to perform the tasks needed for PD[16].

LDL-C levels and peritonitis were significant factors that were associated with PD duration. One study showed that patients treated with PD exhibited significantly higher serum T-Cho levels than patients treated with HD[17]. Patients undergoing PD have an energy burden as glucose is included in the dialysate, which is compounded with the leakage of Alb and high-density lipoprotein cholesterol into the dialysate. Hypoproteinemia due to Alb leakage accelerates lipoprotein synthesis, possibly precipitating hyperlipidemia. Serum LDL-C and T-Cho levels, together with serum Alb levels, are indicators of nutritional status[18], and malnutrition correlates with poor viability in all patients with renal failure, including those undergoing PD. However, the correlation of malnutrition with PD duration requires further investigation.

The incidence of peritonitis at our hospital was significantly lower (0.077 times per patient per year) than that reported by the National JSDT Survey (0.24 times per patient per year)[2]. Further, EPS was encountered in only one patient (0.87%), which reflects the staff's commitment to patient education. The Brazilian Peritoneal Dialysis Multicenter Study, a cohort study, showed that peritonitis incidence significantly decreased with at least 15 h of catheter operation training[19]. Furthermore, infection prevention is aided by the daily application of gentamicin cream when redness is found in the catheter exit region. According to a double-blind study by Bernardini *et al.* (2005), daily application of gentamicin reduced *Pseudomonas aeruginosa* infection rate and peritonitis onset by 35%[20]; another report suggested that peritonitis incidence should be decreased to prevent early PD withdrawal in patients[21].

We also identified PD duration and LDL-C levels as independent risk factors for peritonitis onset. As reported by the JSDT, as patients grow older, the incidence of peritonitis tends to increase, albeit with a lack of a correlation with PD duration[1,2]. Another study by Nisina *et al.* (2014) identified age, presence of DM, and use of a sterile tubing welder device as significant risk factors for peritonitis[22]. Therefore, sterile tubing welder devices are not used at our hospital. A potential reason for PD duration as a risk factor for peritonitis despite the low number of peritonitis cases is that patients receiving PD long-term might develop peritonitis multiple times. The mechanism underlying the relationship between LDL-C levels and peritonitis is currently unknown and requires further investigation for clarification.

For an aging society, nephrologists, nurses, and care managers should cooperate to provide appropriate renal failure care, including home medical care, for patients[5]. In Japan, where home HD is not common, PD therapy performed with cooperation from family or by home medical care are recognized as assisted PD, which might become an important medical option in an aging society in the future.

Limitations

This study has several limitations. First, this was a retrospective study conducted at a single center; therefore, the number of patients was too small to allow for robust sta-

tistical analyses. Second, data collection methods varied over the course of this long-term study encompassing 18 years. Finally, as certain doctors administered treatment, a medical bias cannot be ruled out.

Conclusion

This retrospective study of the long-term prognosis of 114 PD patients at the Nippon Medical School Musashi Kosugi Hospital revealed that, in conjunction with efforts to prevent peritonitis and EPS, long-term PD treatment was safe and conferred a high QOL. In addition, evaluation of the nutritional status of patients and a clear understanding of the aseptic techniques required for administering PD were important. Furthermore, in a rapidly aging society, with the inevitable increase in the proportion of patients requiring home medical care, the need for PD medical care is expected to increase. Thus, providing appropriate medical care, particularly in elderly patients desiring last PD, will become of paramount importance to meet the needs of patients, their families, and caregivers.

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

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(Received, September 25, 2017)
(Accepted, January 15, 2018)