Long-term sonographic evaluation of the peritoneum in peritoneal dialysis patients: A retrospective cohort study

Shinya Taguchi (✉ shinyataguchi27@gmail.com)

Shonan Kamakura General Hospital <https://orcid.org/0000-0002-4540-125X>

Takayasu Ohtake

Shonan Kamakura General Hospital

Yasuhiro Mochida

Shonan Kamakura General Hospital

Kunihiro Ishioka

Shonan Kamakura General Hospital

Hidekazu Moriya

Shonan Kamakura General Hospital

Sumi Hidaka

Shonan Kamakura General Hospital

Shuzo Kobayashi

Shonan Kamakura General Hospital

Research article

Keywords: Peritoneal dialysis, peritoneal membrane thickness, morphological change, peritoneum, transabdominal sonography, biocompatible dialysate, biopsy, permeability, PD duration

Posted Date: April 23rd, 2020

DOI: <https://doi.org/10.21203/rs.3.rs-22298/v1>

License: © ⓘ This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

Abstract

Background

Long-term peritoneal dialysis (PD) causes morphological changes to the peritoneum. However, the sequential morphological changes of the peritoneum remain unclear due to the invasiveness and ethical dilemmas surrounding peritoneal biopsies. We aimed to evaluate these long-term morphological peritoneal changes using sonography, which was recently reported to be useful for morphological peritoneal evaluation.

Methods

We retrospectively identified 115 PD patients who underwent sonographic peritoneal membrane thickness (PMT) measurement. Univariate and multivariate linear regression analyses identified factors related to PMT at baseline (bPMT), at last measurement (IPMT), and the PMT change rate. Of the 115 patients, 42 patients had at least two PMT measurements, including a bPMT measurement. We evaluated the PMT change between bPMT and IPMT. We also evaluated the annual PMT change for 3 years before PD withdrawal in patients who discontinued PD due to peritoneal dysfunction. Clinical characteristics and parameters were analyzed according to PMT change rates (≤ 0 [$n = 28$] or > 0 [$n = 20$]).

Results

The mean age at PD introduction and mean PD duration were 63.7 ± 12.7 years and 40.5 ± 30.1 months, respectively. There was a significant positive correlation between the dialysate to plasma ratio of creatinine (D/P Cr) and IPMT ($r = 0.386$, $p = 0.004$), but not bPMT ($r = -0.114$, $p = 0.326$). In the multivariate analyses, D/P Cr remained an independent predictor of IPMT ($r = 0.478$, $p = 0.001$) after adjusting for age, sex, body mass index, PD duration, diabetes, and peritonitis rate. The mean bPMT and IPMT were 0.67 ± 0.15 mm and 0.69 ± 0.10 mm, respectively, without statistical difference ($p = 0.49$). Annual PMTs for 3 years before PD withdrawal were 0.67 ± 0.13 mm, 0.66 ± 0.11 mm, and 0.67 ± 0.08 mm, respectively, with no significant differences among measurements ($p = 0.967$). There were no differences in PD duration, the use of a dialysate containing over 2.5% glucose or icodextrin, and the peritonitis rate between groups divided by the PMT change rate.

Conclusions

PMT, measured by sonography, was positively correlated with peritoneal permeability. Repeated evaluation of the peritoneum by sonography will enable the recognition of transition in peritoneal function in real time and allow for more appropriate PD management. Furthermore, the peritoneum was not necessarily thickened regardless of PD duration or cause of withdrawal.

Background

Peritoneal membrane dysfunction, including ultrafiltration and solute transport problems, is one of the major causes of withdrawal from peritoneal dialysis (PD) therapy [1, 2]. Moreover, ultrafiltration failure not only shortens PD duration but also worsens patient survival [3]. The peritoneum is thought to sustain injury with long-term PD therapy, uremia, long-term exposure to bio-incompatible dialysis solutions, and frequent episodes of peritonitis [4–6]. These factors cause structural and functional changes to the peritoneum, leading to peritoneal membrane dysfunction. Histological studies have shown mesothelial denudation, interstitial fibrosis, and vasculopathy in the peritoneum of patients on long-term PD [5, 7, 8]. However, since peritoneal biopsies are invasive and difficult to repeat due to ethical issues, the sequential morphological changes of the peritoneum associated with PD treatment remain unclear.

Faller et al. demonstrated the effectiveness of abdominal sonography in the morphological evaluation of the peritoneum. They measured the peritoneal membrane thickness (PMT) of 131 healthy children using transabdominal ultrasonography and showed that the variation coefficient for the measurement was only 5%; the PMT was significantly correlated with age, weight, and height; and peritoneal thickening was observed in PD patients who had a history of peritonitis [9]. Subsequently, several studies have reported that PMT, measured with sonography, correlates with peritoneal permeability [10–13], and sonography is expected to be an alternative method for peritoneal evaluation. However, although sonography is a simple and non-invasive method, evaluation of the peritoneum with sonography is limited to cross-sectional studies, and there have been no reports on the sequential evaluation of the peritoneum over time during PD treatment.

The aim of this study was to clarify the morphological changes that occur in the peritoneum during PD treatment and examine whether these changes were related to peritoneal function and PD prognosis by long-term observation of the peritoneum using sonography.

Methods

STUDY DESIGN AND POPULATION

We retrospectively reviewed the clinical records of patients at Shonan Kamakura General Hospital between January 2008 and February 2019 and identified 115 PD patients who had a recorded sonographic PMT measurement. Patients who had received a kidney transplantation, hemodialysis treatment for more than one month, or underwent any abdominal surgeries before the start of PD treatment were excluded. Written informed consent was waived due to the retrospective nature of the study and anonymity of the data. However, participants were able to opt-out of the study on the hospital's website. This study complied with the standards of the Declaration of Helsinki and was approved by the Ethics Committee for Human Research of Shonan Kamakura General Hospital (approval number: TGE01288-024).

CLINICAL DATA COLLECTION

Clinical and laboratory data were obtained by reviewing medical records. Patient characteristics included age, sex, height, weight, body mass index (BMI), PD duration, etiology of end-stage renal disease (ESRD), comorbidities, and cause of PD discontinuation. Biological data (serum albumin, creatinine [Cr], estimated glomerular filtration rate, C-reactive protein, calcium, phosphate, uric acid, β_2 -microglobulin, low-density lipoprotein-cholesterol, and urinary volume), concomitant medication, dialysis prescription, transport characteristics, and PMT were evaluated at the start of PD treatment and annually until PD discontinuation or the start of combination therapy with PD and hemodialysis. We evaluated the transport characteristics of the peritoneum using the standard peritoneal equilibration test, calculating the dialysate to plasma ratio of creatinine (D/P Cr) after a 4-h dwell.

PERITONEAL MEMBRANE THICKNESS MEASUREMENT

We examined the parietal peritoneum of PD patients using transabdominal ultrasonography. The peritoneal membrane was defined as the hyperechoic line surrounding the abdominal cavity (Fig. 1). We indwelled at least 1,000 mL of dialysate and measured the PMT on three different ventral windows with PD patients in the supine position, according to the study by Faller et al. [9]. Horizontal sections were made at the midclavicular line bilaterally in the upper and lower quadrants of the abdomen without the catheter port. We calculated the mean of the three measurements and used it in the analysis. All PMT measurements were taken with an 8.0 MHz linear probe (Canon Medical systems Corporation, Tokyo, Japan) and were performed at the start of the peritoneal equilibration test.

OUTCOMES AND STATISTICAL ANALYSIS

Data are shown as means $\pm$ standard deviations or medians (minimum–maximum) and percentages, as appropriate. To identify factors related to the PMT at baseline (measured within 4 weeks of the introduction of PD) (bPMT), at last measurement (IPMT), and the PMT change rate, univariate and multivariate linear regression analyses were performed. In the multivariate analysis, candidate variables, including age, sex, BMI, PD duration, having diabetes mellitus (DM), history of peritonitis, and D/P Cr, were selected by referencing previous studies [9–16]. Of the 115 patients, 42 patients had at least two PMT measurements, including a bPMT measurement. We evaluated the PMT change between bPMT and IPMT. We also evaluated the annual PMT change for 3 years before PD withdrawal in patients who discontinued PD due to peritoneal dysfunction. To compare the PMT at various points during PD treatment, the paired *t*-test and repeated-measures ANOVA were performed. The patients were divided into two groups according to the PMT change rate: PMT change rate ≤ 0 ($n = 22$) or > 0 ($n = 20$). We compared patients' characteristics and clinical parameters, including the PMTs of the two groups, using student's *t*-test (for normally distributed variables), the Mann-Whitney *U* test (for non-normally distributed variables), and Fisher's exact test (for categorical variables). A *p*-value < 0.05 was considered to be significant. Statistical analyses were performed using R software version 3.5.2 (R Foundation for Statistical Computing, Vienna, Austria).

Results

PATIENT CHARACTERISTICS

Patient characteristics are summarized in Table 1. The mean age at the start of PD and the mean PD duration were 63.7 ± 12.7 years and 40.5 ± 30.1 months, respectively. The most frequent cause of ESRD was diabetic nephropathy (29.6%), followed by primary glomerulonephritis (27.0%), unknown (18.3%), and hypertensive nephrosclerosis (12.2%). Among the 115 patients, 74.8% were taking angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers. Of the 115 patients, 87 patients had discontinued PD and 28 had continued PD at the end of the observation period. The causes of PD withdrawal were peritoneal dysfunction (29.9%), peritonitis (18.4%), death (17.2%), kidney transplantation (9.2%), other infections (6.9%), and others (18.4%).

Table 1
Patient characteristics

	All (N = 115)
Age at start PD, years	63.7 ± 12.7
Sex (Female), n (%)	38 (33.0)
Body height, cm	162.3 ± 7.9
Body weight, kg	61.2 ± 12.0
Body mass index, kg/m ²	23.1 ± 3.5
PD duration, months	40.5 ± 30.1
Etiology of ESRD, n (%)	
Diabetic nephropathy	34 (29.6)
Hypertensive nephrosclerosis	14 (12.2)
Primary glomerulonephritis	31 (27.0)
Polycystic kidney disease	5 (4.3)
Others	10 (8.7)
Unknown	21 (18.3)
Comorbidities, n (%)	
Hypertension	105 (91.3)
Diabetes	50 (43.5)
Cerebral infarction	16 (13.9)
Ischemic heart disease	24 (20.9)
Medication, n (%)	
ACE-I/ARB	86 (74.8)
Calcium-based phosphorus binders	32 (27.8)
Vitamin D receptor agonists	81 (70.4)
Cause of PD withdrawal, n (%)	
Peritoneal dysfunction	26 (29.9)
Peritonitis	16 (18.4)
Death	15 (17.2)

	All (N = 115)
Kidney transplantation	8 (9.2)
Other infections	6 (6.9)
Others	16 (18.4)
Variables are presented as means $\pm$ standard deviations.	
PD, peritoneal dialyses; ESRD, end-stage renal disease; ACE-I, angiotensin-converting enzyme inhibitors; ARB, angiotensin II receptor blocker	

FACTORS CORRELATED WITH PERITONEAL MEMBRANE THICKNESS

In the univariate linear analysis, there was a significant correlation between D/P Cr and IPMT ($r = 0.386$, $p = 0.004$), but not bPMT ($r = -0.114$, $p = 0.326$) (Fig. 2, Table 2). BMI was significantly correlated with bPMT ($r = 0.009$, $p = 0.047$). Having DM tended to correlate with the bPMT ($r = 0.057$, $p = 0.093$). The duration of PD, use of a dialysate containing icodextrin and high-concentration glucose, and the peritonitis rate were not significantly correlated with IPMT or the PMT change rate (Table 2). In the multivariate analysis, D/P Cr remained the only independent predictor of IPMT ($r = 0.478$, $p = 0.001$) after adjusting for age, sex, BMI, PD duration, DM, and peritonitis rate (Table 3).

Table 2
Univariate linear regression analyses of factors correlated with peritoneal thickness

	bPMT ^a		IPMT ^b		PMT change rate ^b	
	Regression coefficient (95% CI)	<i>p</i> value	Regression coefficient (95% CI)	<i>p</i> value	Regression coefficient (95% CI)	<i>p</i> value
Age at start PD	-0.002 (-0.004–0.001)	0.122	0.002 (0–0.004)	0.131	0.001 (0–0.003)	0.266
Female	0.022 (-0.047–0.092)	0.523	-0.010 (-0.073–0.054)	0.767	0.015 (-0.027–0.058)	0.464
Body mass index	0.009 (0.000–0.012)	0.047	0.005 (-0.004–0.014)	0.260	-0.002 (-0.010–0.004)	0.513
PD duration	-	-	-0.001 (-0.014–0.013)	0.924	0.001 (-0.011–0.014)	0.813
Diabetes	0.057 (-0.010–0.123)	0.093	0.022 (-0.039–0.084)	0.475	-0.033 (-0.076–0.009)	0.123
Taking ACE-I/ARB	-0.039 (-0.118–0.040)	0.329	0.021 (-0.047–0.089)	0.544	0.030 (-0.023–0.083)	0.255
Use of dialysate containing over 2.5% glucose	-	-	0.030 (-0.035–0.095)	0.356	-0.027 (-0.073–0.019)	0.237
Use of dialysate containing icodextrin	-	-	0.008 (-0.053–0.070)	0.786	-0.002 (-0.046–0.042)	0.922
Peritonitis rate	-	-	-0.003 (-0.042–0.036)	0.876	0.008 (-0.016–0.031)	0.509
Serum albumin	0.003 (-0.052–0.058)	0.919	0.010 (-0.050–0.070)	0.736	0.013 (-0.024–0.051)	0.473
C-reactive protein	-0.007 (-0.039–0.025)	0.654	0.013 (-0.016–0.041)	0.376	0 (-0.020–0.021)	0.952
eGFR	-0.014 (-0.034–0.007)	0.189	-	-	-	-

Serum calcium	0.006 (-0.026– 0.037)	0.717	0.029 (-0.013– 0.070)	0.174	0.010 (-0.016– 0.037)	0.417
Serum phosphate	-0.003 (-0.024– 0.017)	0.746	-0.002 (-0.023– 0.019)	0.859	-0.012 (-0.028– 0.036)	0.126
Serum uric acid	-0.003 (-0.020– 0.015)	0.769	0.002 (-0.019– 0.023)	0.823	-0.005 (-0.022– 0.011)	0.509
Serum β_2 -microglobulin	-0.003 (-0.012– 0.007)	0.596	-0.001 (-0.004– 0.002)	0.364	-0.001 (-0.003– 0.002)	0.433
LDL-Cholesterol	0 (-0.002–0)	0.177	0 (-0.002– 0)	0.226	0.001 (0– 0.002)	0.022
Urinary volume	-0.015 (-0.086– 0.054)	0.661	-0.001 (-0.06– 0.073)	0.966	0.046 (0– 0.093)	0.051
D/P Cr	-0.114 (-0.345– 0.116)	0.326	0.386 (0.129– 0.642)	0.004	-0.102(-0.330– 0.127)	0.373

Responsible variables are ^a at baseline, ^b at last measurement of PMT

PD, peritoneal dialyses; ACE-I, angiotensin-converting enzyme inhibitors; ARB, angiotensin II receptor blocker; eGFR, estimated glomerular filtration rate; LDL low-density lipoprotein; D/P Cr, dialysate to plasma ratio of creatinine; bPMT, peritoneal membrane thickness at baseline; IPMT; peritoneal membrane thickness at last measurement; CI, confidence interval

Table 3

Multivariate linear regression analyses of factors correlated with peritoneal membrane thickness at last measurement

	Regression coefficient (95% CI)	<i>p</i> value
Age at start PD	0.002 (-0.001–0.004)	0.142
Female	0.005 (-0.058–0.068)	0.883
Body mass index	0.085 (-0.257–0.428)	0.379
PD duration	0.011 (-0.004–0.027)	0.131
Diabetes	0.026 (-0.035–0.086)	0.404
History of peritonitis	-0.023 (-0.062–0.017)	0.261
D/P Cr	0.478 (0.195–0.762)	0.001
Adjusted R-squared: 0.0942, <i>p</i> = 0.047		
PD, peritoneal dialyses; D/P Cr, dialysate to plasma ratio of creatinine; IPMT peritoneum membrane thickness at last measurement; CI, confidence interval		

PMT CHANGE RATE

Figure 3a shows the change in the PMT from baseline to the last measurement in all patients who had at least two PMT measurements, including a bPMT measurement (*n* = 42). The mean bPMT and IPMT measurements were 0.67 ± 0.15 mm and 0.69 ± 0.10 mm, respectively, with no statistical difference between these measurements (*p* = 0.49) (Fig. 3b). The mean D/P Cr at baseline and at last measurement were 0.72 ± 0.15 and 0.77 ± 0.09 , respectively, with no statistical difference between these values (*p* = 0.11) (data not shown). Of the 42 patients, seven patients had discontinued PD due to peritoneal dysfunction. The mean bPMT and IPMT in these patients were 0.69 ± 0.10 mm and 0.67 ± 0.06 mm, respectively, with no significant difference between measurements (*p* = 0.68) (Fig. 3c). In patients who discontinued PD due to peritoneal dysfunction, the mean PMTs at 3, 2, and 1 year before PD withdrawal were 0.67 ± 0.13 mm, 0.66 ± 0.11 mm, and 0.67 ± 0.08 mm, respectively, with no significant differences between these measurements (*p* = 0.967) (Fig. 3d).

COMPARISON BETWEEN TWO GROUPS DIVIDED BY PMT CHANGE RATE

There were no significant differences in PD duration, the use of a dialysate containing more than 2.5% glucose or icodextrin, and the peritonitis rate between the groups divided by the PMT change rate (Additional File 1). The bPMT was higher in the group with a decreased PMT over time than in the group with an increased PMT over time (0.76 ± 0.14 mm versus 0.57 ± 0.09 mm, *p* < 0.001); however, there was no difference in the IPMT between the groups (0.67 ± 0.12 mm versus 0.70 ± 0.07 mm, *p* = 0.184).

Discussion

In this study, we showed that the PMT and peritoneal permeability, represented by D/P Cr, were significantly correlated, and PMT was not necessarily increased with an increase in PD duration. To our knowledge, this study is the largest study evaluating the peritoneum by sonography and is the first study in which the PMT was repeatedly measured over time during PD treatment.

Duman et al. measured the PMT of 42 PD patients who had undergone PD for > 12 months using sonography and showed, for the first time, that the PMT was positively correlated with D/P Cr [10]. Subsequently, the correlation between PMT and peritoneal permeability has been reported in several studies using sonography [11–13]. Honda et al. showed in their study, which evaluated peritoneal specimens of 253 patients before and during PD treatment, that the PMT increased and the lumen/vessel diameter ratio, which was reported as an indicator of vasculopathy in their study, decreased with an increase in PD duration [8]. They also showed that the PMT was significantly higher in patients with ultrafiltration failure than in patients with a preserved ultrafiltration capacity. Plum et al. showed that patients characterized as being high transporters, according to the peritoneal equilibration test, had an increased submesothelial fibrous layer thickness [17]. Based on these pathological studies, PMT may reflect vasculopathy or fibrosis of the peritoneum.

Conversely, bPMT tended to correlate with BMI and the presence of DM, but not with D/P Cr in this study. A previous morphological study evaluating the peritoneum of PD patients with or without DM at the start of PD showed that the submesothelial connective tissue thickness and the number of capillaries were significantly greater in the DM group than in the non-DM group [16]. However, to date, there have been no studies evaluating the correlation between PMT and peritoneal permeability at the start of PD using either peritoneal specimens or sonography.

There were no significant differences between bPMT and IPMT in all patients. These measures were not significantly different even among patients who discontinued PD due to peritoneal dysfunction. Moreover, the annual PMT, measured for 3 years prior to PD withdrawal, was preserved, contrary to our hypothesis that the PMT would be higher in patients who had discontinued PD due to peritoneal dysfunction. Inconsistent with the findings of our study, several previous studies have shown that PMT increased with a longer PD duration [8, 10, 12–14]; however, these studies had cross-sectional study designs. Williams et al. evaluated the peritoneal biopsy specimens of 130 PD patients and showed that the thickness of the submesothelial compact zone increased significantly with an increase in PD duration [5]. However, these findings were not observed in patients without PD-related problems or membrane failure. Similarly, Lee et al. showed, based on sonographic examination, that the PMT was not associated with PD duration [11].

In Japan, since around 2005, most PD patients have used a pH-neutral, low-glucose degradation product (GDP) dialysate, which is more biocompatible than conventional dialysates. Since then, several studies have shown that a pH-neutral low-GDP dialysate might prevent morphological and functional changes in the peritoneum [15, 18–20]. Tawada et al. compared the peritoneal biopsy samples of 54 PD patients treated with a conventional acidic dialysate to those of 73 PD patients treated with a pH-neutral low-GDP

dialysate [15]. They showed that the PMT was higher and the lumen/vessel diameter ratio was smaller in the conventional dialysate group than in the pH-neutral dialysate group and that the lumen/vessel diameter ratio negatively correlated with PD duration and D/P Cr in the conventional dialysate group but not in the pH-neutral dialysate group. From these findings, they suggested that a pH-neutral low-GDP dialysate might prevent morphological and functional changes in the peritoneum. Among the 115 patients in this study, only seven patients started PD therapy before 2005, and most patients were treated with a pH-neutral dialysate from the onset of treatment. Based on these facts, one of the reasons as to why the PMT was not correlated with PD duration in this study might possibly be explained by the use of a biocompatible dialysate.

Several studies showed that inhibition of the renin-angiotensin-aldosterone system (RAAS) prevented the morphological deterioration of the peritoneum in animal models [21, 22]; although, the effectiveness of RAAS inhibitors in protecting the peritoneal membrane function of PD patients has remained unclear [23]. In this study, a greater percentage of patients were taking RAAS inhibitors than that reported in a previous study [14], and this may have contributed to the preservation of the peritoneal membrane.

In this study, we were unable to identify factors related to the PMT change rate. The bPMT was higher in the group with a decreased PMT over time than in the group with an increased PMT over time. This might be partly explained by the percentage of patients with DM in both groups. We found that the complications of DM tended to correlate with the bPMT. Of those with a decreased PMT over time, 45.5% had DM, whereas 25.0% of patients in the group with an increased PMT over time had DM. However, this difference was not significantly different.

There were some limitations to this study. First, this study was a retrospective single-center study. Therefore, selection bias could not be completely eliminated. Second, the timing of the IPMT during PD treatment varied depending on the patients, because sonographic examinations were not necessarily conducted every year. However, we evaluated the annual change in PMT for 3 years before PD withdrawal and found that the PMT was preserved over time. Third, the concentration of glucose in the dialysate was not adjusted for statistically, because detailed PD prescription data were not compiled in this study. However, the use of a dialysate containing more than 2.5% glucose was not correlated with IPMT or the PMT change rate in the univariate analysis.

Conclusions

Herein, we have demonstrated that the peritoneal thickness, measured by sonography, was positively correlated with peritoneal permeability. Repeated evaluation of the peritoneum using sonography may enable the recognition of the transition in peritoneal function in real time and allow for the more appropriate management of PD.

Furthermore, the peritoneum was not necessarily thickened regardless of the PD duration or cause of PD withdrawal, and this may be partly explained by the widespread use of a biocompatible dialysate.

Abbreviations

PD, peritoneal dialysis

PMT, peritoneal membrane thickness

BMI, body mass index

ESRD, end-stage renal disease

Cr, creatinine

D/P Cr, dialysate to plasma ratio of creatinine

bPMT, peritoneal membrane thickness at baseline

IPMT, peritoneal membrane thickness last measurement

GDP, low-glucose degradation product

RAAS, renin-angiotensin-aldosterone system

DM, diabetes mellitus

Declarations

Ethics approval and consent to participate:

This study complied with the standards of the Declaration of Helsinki and was approved by the Ethics Committee for Human Research of Shonan Kamakura General Hospital (approval number: TGE01288-024). Written informed consent was waived due to the retrospective nature of the study and anonymity of the data. However, participants were able to opt-out of the study on the hospital's website.

Consent for Publication:

Written informed consent was waived due to the retrospective nature of the study and anonymity of the data. However, participants were able to opt-out of the study on the hospital's website.

Availability of Data and Materials

All data generated or analyzed during this study are included in this published article [and its supplementary information files].

Competing Interests

The authors declare that they have no conflict of interest.

Funding

None.

Authors' Contributions

ST and TO conceived the research question and study design. ST, TO, KI, YM, HM, and SH acquired the data. ST and TO performed the data analysis and interpretation. ST wrote the first draft of the manuscript. ST, TO, SH, and SK reviewed and edited the manuscript. All authors have approved the submitted version of the manuscript and agreed to be accountable for the author's own contributions.

Acknowledgments

Not applicable.

References

1. Davies SJ, Phillips L, Griffiths AM, Russell LH, Naish PF, Russell GI. What really happens to people on long-term peritoneal dialysis? *Kidney Int.* 1998;54:2207–17.
2. Davies SJ, Bryan J, Phillips L, Russell GI. Longitudinal changes in peritoneal kinetics: the effects of peritoneal dialysis and peritonitis. *Nephrol Dial Transplant.* 1996;11:498–506.
3. Brown EA, Davies SJ, Rutherford P, Meeus F, Borrás M, Riegel W, et al. Survival of functionally anuric patients on automated peritoneal dialysis: the European APD Outcome Study. *J Am Soc Nephrol.* 2003;14:2948–57.
4. Jörres A, Bender TO, Finn A, Witowski J, Fröhlich S, Gahl GM, et al. Biocompatibility and buffers: Effect of bicarbonate-buffered peritoneal dialysis fluids on peritoneal cell function. *Kidney Int.* 1998;54:2184–93.
5. Williams JD, Craig KJ, Topley N, Ruhland C, Von, Fallon M, Newman GR, et al. Morphologic changes in the peritoneal membrane of patients with renal disease. *J Am Soc Nephrol.* 2002;11:717–28.
6. Lai KN, Tang SCW, Leung JCK. Mediators of inflammation and fibrosis. *Perit Dial Int.* 2007;27(Suppl 2 Supplement 2):65–71.
7. Honda K, Nitta K, Horita S, Yumura W, Nihei H. Morphological Changes in the Peritoneal Vasculature of Patients on CAPD with Ultrafiltration Failure. *Nephron.* 1996;72:171–6.

8. Honda K, Hamada C, Nakayama M, Miyazaki M, Sherif AM, Harada T, et al. Impact of uremia, diabetes, and peritoneal dialysis itself on the pathogenesis of peritoneal sclerosis: a quantitative study of peritoneal membrane morphology. *Clin J Am Soc Nephrol*. 2008;3:720–8.
9. Faller U, Stegen P, Klaus G, Mehls O, Troger J. Sonographic determination of the thickness of the peritoneum in healthy children and paediatric patients on CAPD. *Nephrol Dial Transplant*. 1998;13:3172–7.
10. Duman S, Ozbek SS, Gunay ES, Bozkurt D, Asci G, Sipahi S, et al. What does peritoneal thickness in peritoneal dialysis patients tell us? *Adv Perit Dial*. 2007;23:28–33.
11. Lee T-C, Yang J-Y, Wang H-P, Tsai T-J, Yang Y. Peritoneal thickening is not inevitable in long-term peritoneal dialysis and is associated with peritoneal transport characteristics: a two-centre sonographic study. *Nephrol Dial Transplant*. 2007;23:1005–10.
12. Caltik A, Akyüz SG, Bülbül M, Çınar G, Erdogan Ö, Demircin G. Can sonographic peritoneal thickness be used to follow pediatric patients on peritoneal dialysis? *Pediatr Nephrol*. 2013;28:811–7.
13. Yavaşcan Ö, Aksu N, Alparslan C, Sarıtaş S, Elmas CH, Eraslan AN, et al. The importance of ultrasonographic measurement of peritoneal wall thickness in pediatric chronic peritoneal dialysis patients. *Ren Fail*. 2015;37:381–6.
14. Temiz G, Sahin G, Mukerrem G, Ozkurt S, Degirmenci NA, Yalcin AU. Ultrasonographic evaluation of peritoneal membrane thickness and comparison with the effectiveness and duration of CAPD. *Int Urol Nephrol*. 2013;45:1761–6.
15. Tawada M, Hamada C, Suzuki Y, Sakata F, Sun T, Kinashi H, et al. Effects of long-term treatment with low-GDP, pH-neutral solutions on peritoneal membranes in peritoneal dialysis patients. *Clin Exp Nephrol*. 2019;23:689–99.
16. Mizumasa T, Hirakata H, Kuroki Y, Katafuchi R, Yotsueda H, Mitsuiki K, et al. Diabetes influences peritoneal morphology in uremic patients at the initiation of peritoneal dialysis. *Perit Dial Int*. 2013;33:175–81.
17. Plum J, Hermann S, Fussoller A, Schoenicke G, Donner A, Röhrborn A, et al. Peritoneal sclerosis in peritoneal dialysis patients related to dialysis settings and peritoneal transport properties. *Kidney Int*. 2001;59:42–7.
18. Kawanishi K, Honda K, Tsukada M, Oda H, Nitta K. Neutral solution low in glucose degradation products is associated with less peritoneal fibrosis and vascular sclerosis in patients receiving peritoneal dialysis. *Perit Dial Int*. 2013;33:242–51.
19. Hamada C, Honda K, Kawanishi K, Nakamoto H, Ito Y, Sakurada T, et al. Morphological characteristics in peritoneum in patients with neutral peritoneal dialysis solution. *J Artif Organs*. 2015;18:243–50.
20. Peso G, Jiménez-Heffernan JA, Selgas R, Remón C, Ossorio M, Fernández-Perpén A, et al. Biocompatible Dialysis Solutions Preserve Peritoneal Mesothelial Cell and Vessel Wall Integrity. A Case-Control Study on Human Biopsies. *Perit Dial Int*. 2016;36:129.

21. Nishimura H, Ito Y, Mizuno M, Tanaka A, Morita Y, Maruyama S, et al. Mineralocorticoid receptor blockade ameliorates peritoneal fibrosis in new rat peritonitis model. *Am J Physiol - Ren Physiol.* 2008;294.
22. Nakamoto H, Imai H, Fukushima R, Ishida Y, Yamanouchi Y, Suzuki H. Role of the renin-angiotensin system in the pathogenesis of peritoneal fibrosis. *Perit Dial Int.* 2008;28(Suppl 3):83-7.
23. Phatthanasobhon S, Nochaiwong S, Thavorn K, Noppakun K, Panyathong S, Suteeka Y, et al. Effectiveness of Renin-Angiotensin-Aldosterone System Blockade on Residual Kidney Function and Peritoneal Membrane Function in Peritoneal Dialysis Patients: A Network Meta-Analysis. *Sci Rep.* 2019;9:1–13.

Figures

Figure 1

Transabdominal ultrasonography image The peritoneal membrane is represented by a hyperechoic line surrounding the abdominal cavity.

Figure 2

Relationship between D/P Cr and (a) bPMT and (b) IPMT (a) D/P Cr and bPMT show no significant correlation. (b) D/P Cr and IPMT show a positive correlation. D/P Cr, dialysate to plasma ratio of creatinine; bPMT, baseline peritoneal membrane thickness; IPMT, last measurement peritoneal membrane thickness

Figure 3

The change in peritoneal membrane thickness (a) Change in PMT between bPMT and IPMT measurements in all patients who had at least two PMT measurements, including a bPMT measurement (n=42). (b) Change in PMT among all patients (n=42). There is no significant difference (p=0.49). (c) Change in PMT in patients who discontinued PD due to peritoneal dysfunction. There is no significant difference (p=0.68). (d) Annual change in PMT 3 years before PD withdrawal in patients who discontinued PD due to peritoneal dysfunction. There are no significant differences between measurements (p=0.967). PMT, peritoneal membrane thickness; PD, peritoneal dialysis; bPMT, baseline peritoneal membrane thickness; IPMT, last measurement peritoneal membrane thickness

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [SupplementalTable1.docx](#)