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Original Article

ORIGINAL ARTICLE

Mesenteric elasticity assessed by shear wave elastography and its relationship with peritoneal function in peritoneal dialysis patients

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ABSTRACT

Background. We evaluated the mesenteric elasticity in patients undergoing continuous ambulatory peritoneal dialysis (CAPD) using shear wave elastography (SWE) and investigated its relationships with peritoneal function.
Methods. Patients were recruited in our peritoneal dialysis (PD) centre between 15 July 2019 and 31 December 2021 and followed up to 31 March 2022. Twelve chronic kidney disease (CKD) patients and nineteen healthy people were included as controls. Correlation, linear regression and Cox regression analyses were applied.
Results. Of the 218 PD patients, 104 (47.8%) were male. Their mean age was 48.0 ± 13.2 years and the median PD duration was 59.0 months [interquartile range (IQR) 17.0–105]. The median mesenteric SWE value was 8.15 kPa (IQR 5.20–16.1). The mesenteric SWE values of patients with a PD duration of <3 months [5.20 kPa (IQR 3.10–7.60)] were not significantly different from those of CKD patients [4.35 kPa (IQR 2.63–5.20), $P = .17$] and healthy controls [3.60 kPa (IQR 2.90–5.10), $P = .13$] but were lower than those of patients with a PD duration of 3 months–5 years [6.40 kPa (IQR 4.10–10.5), $P < .001$], 5–10 years [11.9 kPa (IQR 7.40–18.2), $P < .001$] and >10 years [19.3 kPa (IQR 11.7–27.3), $P < .001$]. Longer PD duration ($\beta = 0.58$, $P < .001$), high effluent interleukin-6 ($\beta = 0.61$, $P = .001$) and low effluent cancer antigen 125 ($\beta = -0.34$, $P = .03$) were independently associated with low mesenteric elasticity. The mesenteric SWE value was independently correlated with the dialysate:plasma creatinine ratio ($\beta = 0.39$, $P = .01$) and negatively correlated with the total daily fluid volume removed ($\beta = -0.17$, $P = .03$). High mesenteric SWE values were an independent risk factor for death-censored technique failure [adjusted hazard ratio 4.14 (95% confidence interval 1.25–13.7), $P = .02$).
Conclusions. SWE could be used to non-invasively characterize peritoneal textural changes, which were closely associated with changes in peritoneal function.

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LAY SUMMARY

Long-term peritoneal dialysis (PD) leads to structural and functional changes of the peritoneum. Accurate assessment of PD-related peritoneal damage can help predict PD technique failure and develop timely interventions. In this study we used shear wave elastography (SWE) to detect the morphology and texture changes of the peritoneum. A total of 218 patients were enrolled with a median follow-up of 16.1 months. We measured the stiffness of the mesentery by SWE, which was closely related to the small solute transport and fluid clearance functions of the membrane. High mesenteric SWE values, which indicate low peritoneal elasticity, may predict PD technique failure. This study provides a new and non-invasive method for assessing PD-related peritoneal changes.

Keywords: dialysate:plasma creatinine ratio, fluid removed, mesenteric elasticity, shear wave elastography, technique failure

INTRODUCTION

The thin, highly vascularized peritoneum that encloses the peritoneal cavity has been used as a dialysis membrane for peritoneal dialysis (PD) [1]. The morphological integrity and functional stability of the peritoneum are critical for efficient dialysis and the survival of patients undergoing maintenance PD [2]. Long-term PD can cause structural changes in the peritoneum, involving the gradual thickening and hardening of the peritoneum, which can result in reductions in solute and fluid removal or complications such as cardiovascular diseases [3]. Peritoneal fibrosis is the most common post-PD pathological change in the peritoneum [4]. A rigid peritoneum can surround the small intestine, ultimately resulting in encapsulating peritoneal sclerosis (EPS), which is a rare but life-threatening complication of PD [5]. Therefore the early identification of PD-related peritoneal damage and timely intervention may help prolong the utility of the technique and improve the prognosis of PD patients.

The assessment and monitoring of PD-related peritoneal damage in clinical practice is challenging [6–8]. Recent studies have shown that pathological changes such as inflammation, fibrosis or malignant lesions can cause changes in tissue elasticity [9]. Shear wave elastography (SWE) enables not only two-dimensional imaging of abdominal structures but also real-time quantitative measurement of absolute tissue stiffness [10]. SWE has been successfully used for the assessment of liver fibrosis and the differentiation of benign and malignant breast or thyroid nodules [11–13]. However, the use of SWE for the assessment of peritoneal changes has not been reported. Therefore, in the present study we used SWE to measure the stiffness of the mesentery and evaluated its relationships with peritoneal function.

MATERIALS AND METHODS

Study sample

We performed a single-centre study of patients undergoing continuous ambulatory peritoneal dialysis (CAPD) who were ≥18 years of age and underwent SWE examination at our PD centre between 15 July 2019 and 31 December 2021. Patients who were <18 years of age, those who had been switched to PD after acute kidney injury or long-term (>3 months) haemodialysis (HD) or following renal transplant failure or who had experienced peritonitis within the 4 weeks preceding the measurement were excluded. All the enrolled patients were followed up to 31 March 2022. In addition, 12 chronic kidney disease (CKD) patients and 19 healthy people were included for non-PD patient controls.

The study was approved by the Clinical Research Ethics Committee of the First Affiliated Hospital of Sun Yat-sen University (ethical review [2019]388) and was performed in compliance with the Declaration of Helsinki. All the participants provided written informed consent.

Demographic, clinical and biochemical data

The participants were undergoing maintenance CAPD treatment using standard lactate–glucose dialysis solutions (1.5%, 2.5% or 4.25% dextrose; Baxter, Guangzhou, China). The following data were collected at the time of SWE: demographic data, including age, sex, body mass index (BMI), history of diabetes mellitus, comorbidities and the primary renal disease; PD-related information, including the duration of PD, the mean dialysate glucose concentration, weekly *Kt/V*, creatinine clearance (CCL), total volume of fluid removed daily, ultrafiltration (UF) volume, residual measured glomerular filtration rate (mGFR) and 4-hour dialysate:plasma creatinine concentration ratio (D:PCr) (the weekly *Kt/V* and CCL data were obtained using PD Adequest 2.0, Baxter, Deerfield, IL, USA); and biochemical data, including haemoglobin, high-sensitivity C-reactive protein, serum albumin, corrected calcium, phosphorus, urea nitrogen, creatinine and intact parathyroid hormone concentrations, and interleukin-6 (IL-6) and cancer antigen 125 (CA-125) concentrations in the dialysate. Daily UF within 1 week prior to the SWE examination were acquired from the patients' dialysis diary. That week's average daily UF was calculated as their UF data. The Charlson comorbidity index (CCI) was used to assess the participants' comorbidities [14]. Computed tomography (CT) images obtained within 6 months of the SWE examination were reviewed. The CT scores for EPS were calculated according to the literature [15]. PD death-censored technique failure was defined as transfer to HD for at least 3 months [16].

Mesenteric SWE examinations

Real-time SWE examinations were performed by a sonologist (Y.C.) with >10 years of experience in abdominal and bowel ultrasonography and who has completed several high-quality clinical studies on SWE [13, 17–18]. Examinations were performed using an Aixplorer ultrasound system (SuperSonic Imagine, Aix-en-Provence, France) and an SL10-2 probe (2–10 MHz) for elasticity measurements. The sonologist was blinded to the clinical, laboratory and radiological findings of each participant. Prior to the examination, ∼500 ml of dialysate was retained in the abdomen of the participant, who had fasted for >6 hours. During the examination, the participant adopted a supine position.

We first examined the whole abdomen to evaluate the abnormal morphology of the peritoneum and bowels, including calcification, wall thickening and encapsulated effusions. The mesentery was selected to perform SWE measurements instead of the parietal peritoneum, as the thickness of the latter is usually inadequate for placement of the region of interest (ROI). The pre-experimental test (Supplementary Tables S1 and S2) and methods for bowel wall SWE examinations are provided in the Supplementary materials. Based on the pre-experimental results, we subsequently measured the mesenteric SWE value in the lower right quadrant for all enrolled patients. Each participant held his/her breath for ∼5 seconds. The large blood vessels, ascites and hollow organs were avoided. The rectangular ROI was set as 1.0 cm × 0.5 cm to 2.0 cm × 1.0 cm in size. After the image stabilized (elastic filling >2/3 uniformity), a quantification box (Q-box) was drawn 1–2 cm below the mesenteric surface, with a diameter of ∼0.5–2 cm. Three measurements were obtained in each participant and the mean SWE values were calculated. Measurements were classified as failed when no or weak signals were obtained for all acquisitions [13, 17–19].

Statistical analysis

Numerical data are expressed as mean ± standard deviation (SD) or median [interquartile range (IQR)]. Differences in numerical variables were compared by Kruskal–Wallis H test and rates were compared by chi-squared test. Relationships were assessed using Spearman's correlation. Linear regression analysis was used to identify factors influencing mesenteric SWE values and the relationships between ultrasonographic parameters and peritoneal function. Variables with *P*-values <.05 in univariate analysis were included using the enter method and the results are expressed as β values and 95% confidence intervals (CIs). Receiver operating characteristics (ROC) analysis was used to identify the optimal cut-off mesenteric SWE value for the prediction of technique failure. Univariate and multivariate Cox regression models were used to explore the influence of mesenteric SWE values on technique failure. *P*-values <.05 were statistically significant. Statistical analyses were performed using SPSS version 20.0 (IBM, Armonk, NY, USA).

RESULTS

Clinical characteristics

A total of 222 eligible patients underwent SWE examinations during the study period. Examination failure occurred in four participants because of excessive thickening of the abdominal wall and therefore these individuals were excluded, such that data from a total of 218 participants were analysed. The mean age of the participants was 48.0 ± 13.2 years, 104 (47.8%) were male and 34 (15.6%) had concomitant diabetes mellitus (Table 1). Their mean BMI was 22.0 ± 2.93 kg/m^2 and the median duration of PD was 59.0 months (IQR 17.0–105). The prevalence of chronic glomerulonephritis, diabetic nephropathy and hypertensive nephropathy was 65.6%, 11.0% and 6.88%, respectively. The mean ages of the healthy control group and the CKD group were 47.8 ± 18.7 years and 46.0 ± 14.6 years, respectively, and the male ratios were 52.6% and 41.7%, respectively.

Abdominal ultrasonographic parameters, SWE values and their relationships

The median mesentery and bowel wall SWE values for the participants were 8.15 kPa (IQR 5.20–16.1) and 8.75 kPa (IQR 6.33–12.8), respectively. Fifty (22.9%) of the participants had bowel wall thickening, 40 (18.3%) had mesenteric or bowel wall calcification and 4 had encapsulated effusions (Figure 1). The SWE value of the mesentery was positively associated with bowel wall thickening, mesenteric/bowel wall calcification and the SWE value of the bowel wall ($P < .01$; Supplementary Table S3).

Table 1: Basic characteristics of subjects at the time of SWE measurement.

Variable	*n*	Values
Demographics		
Male, *n* (%)	218	104 (47.8)
Age (years), mean ± SD	218	48.0 ± 13.2
BMI (kg/m^2), mean ± SD	218	22.0 ± 2.93
Primary kidney disease, *n* (%)	218	
Chronic glomerulonephritis		143 (65.6)
Diabetic nephropathy		24 (11.0)
Hypertensive nephropathy		15 (6.88)
Other		36 (16.5)
Diabetes	218	34 (15.6)
CCI score, median (IQR)	218	3.00 (2.00–4.00)
Vintage (months), median (IQR)	208	59.0 (17.0–105)
PD-related parameters		
Solution glucose concentration (%), median (IQR)	218	1.70 (1.50–2.00)
Daily exchange volume (L), median (IQR)	218	8.00 (8.00–10.0)
D:PCr, mean ± SD	99	0.67 ± 0.11
UF from standard PET (ml/4 hours)	99	225 (170–320)
Weekly *Kt/V*, median (IQR)	204	2.10 (1.87–2.37)
CCL (l/week/1.73 m^2), median (IQR)	204	59.0 (52.2–72.5)
UF (ml/24 hours), median (IQR)	207	550 (250–750)
Residual mGFR (ml/min × 1.73 m^2), median (IQR)	213	0.22 (0.00–2.62)
Biochemical data at the time of SWE measurement		
Haemoglobin (g/dl), median (IQR)	218	11.5 (9.98–12.6)
hs-CRP (mg/l), median (IQR)	214	2.21 (0.75–7.81)
Urea nitrogen (mg/dl), median (IQR)	218	47.3 (40.4–57.3)
Creatinine (μmol/L), mean ± SD	218	959 ± 262
Albumin (g/l), median (IQR)	218	35.8 (33.1–38.3)
Corrected calcium (mg/dl), mean ± SD	218	9.58 ± 0.70
Phosphate (mmol/l), mean ± SD	218	1.55 ± 0.40
iPTH (pg/ml), median (IQR)	218	375 (204–703)
Effluent IL-6 (pg/ml), median (IQR)	176	30.7 (18.8–70.8)
Effluent CA-125 (U/ml), median (IQR)	176	12.3 (7.93–18.1)
Renin–angiotensin inhibitor use, *n* (%)	213	157 (73.7)

hsCRP: high-sensitivity C-reactive protein; iPTH: intact parathyroid hormone.

Comparison of abdominal ultrasonographic parameters and SWE values with CT

Twenty-six PD participants underwent abdominal CT within 6 months of their SWE examination. Compared with CT, SWE could not only measure the peritoneal morphological changes, but was also able to evaluate the elasticity of the mesentery (Supplementary Table S4). These patients' mesenteric SWE values were significantly positively correlated with their CT scores for EPS [15] ($r = 0.76$, $P < .001$).

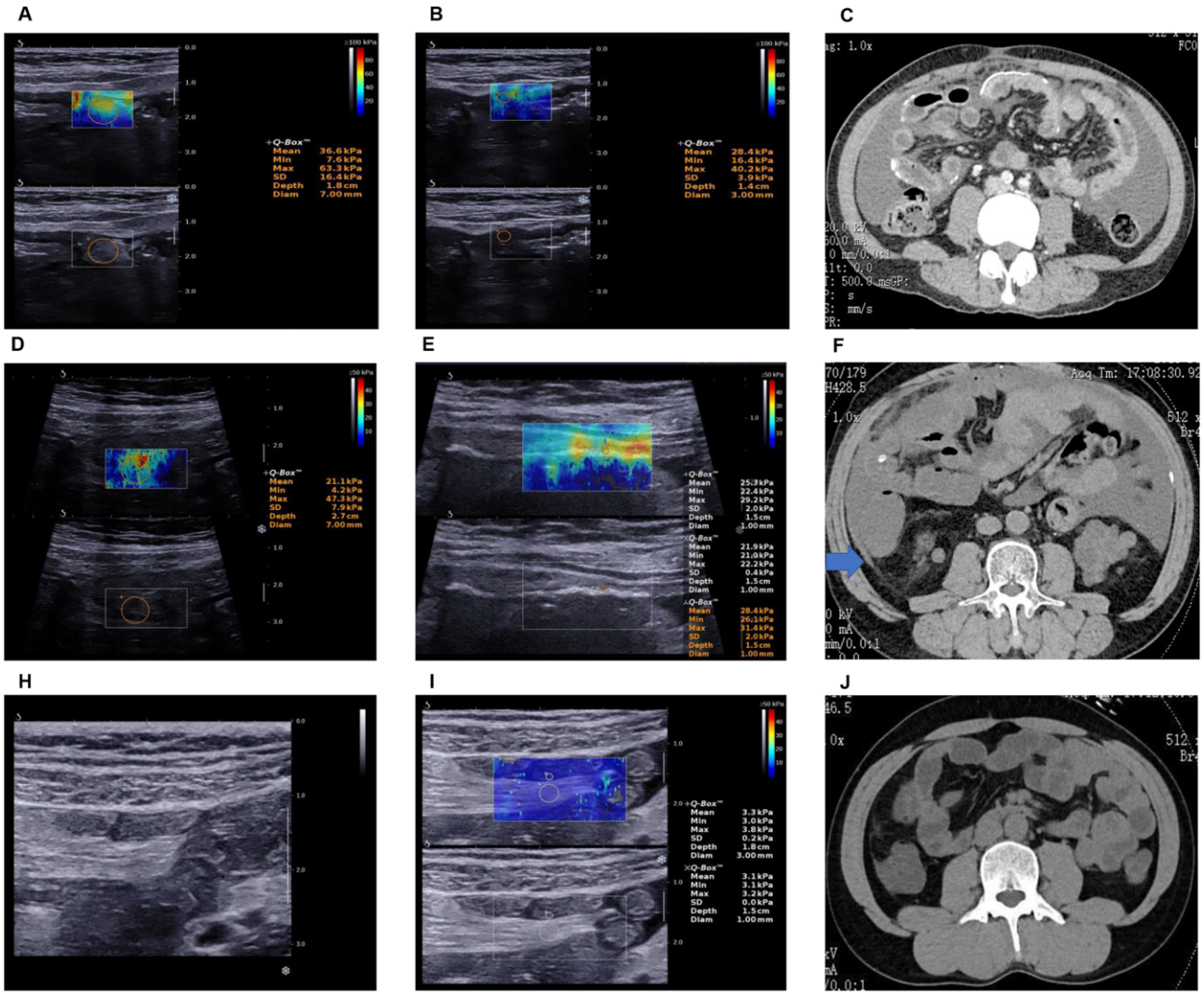

Figure 1: SWE images and CT manifestations of three participants undergoing CAPD. **(A–C)** Images of a 38-year-old male patient with a duration of PD of 115 months and no history of peritonitis. (A) His mean mesentery SWE value was 27.1 kPa, (B) part of the small intestinal wall (<25%) was thickened by 0.57 cm and the mean SWE value of the intestinal wall was 28.4 kPa and (C) abdominal CT during the same period showed intestinal wall thickening and calcification and mesenteric hyperplasia. **(D–F)** Images of a 44-year-old female participant with a duration of PD of 138 months and a history of one episode of peritonitis. (D) Her mean mesenteric SWE value was 21.1 kPa; (E) the parietal peritoneum of the right lower abdominal wall was thickened and hardened, with calcification; and (F) CT also showed peritoneal thickening. **(H–J)** Images of a 57-year-old male participant with a duration of PD of 23 months and no history of peritonitis. (H, J) No mesenteric hyperplasia or thickening of the intestinal wall was present and (I) the mean SWE values of the mesentery and intestinal wall were 3.3 kPa and 3.1 kPa, respectively.

Factors associated with peritoneal changes assessed using SWE

The SWE values of the mesentery and bowel wall positively correlated with the duration of PD ($r = 0.61$, $P < .001$). Differences between the PD vintage <3 months group [5.20 kPa (IQR 3.10–7.60)] and the healthy control group [3.60 kPa (IQR 2.90–5.10), $P = .13$] as well as the CKD group [4.35 kPa (IQR 2.63–5.20), $P = .17$] were not statistically significant, but were lower than those of patients with a PD duration of 3 months–5 years [6.40 kPa (IQR 4.10–10.5), $P < .001$; see Figure 2A and Table 2], 5–10 years [11.9 kPa (IQR 7.40–18.2), $P < .001$] and >10 years [19.3 kPa (IQR 11.7–27.3), $P < .001$]. In addition, the prevalence of bowel wall thickening and mesenteric/bowel wall calcification increased with the duration of PD (Table 2).

The prevalence of bowel wall thickening and mesenteric/bowel wall calcification in patients with anuria was significantly higher than in those with urine output (37.4% versus 9.17%, $P < .001$ and 32.7% versus 4.59%, $P < .001$; respectively). The SWE values of the mesentery were significantly higher in anuric patients [6.95 kPa (IQR 4.30–10.1) versus 11.8 kPa (IQR 6.28–20.2), $P < .01$].

Participants with bowel wall thickening and calcification had higher effluent concentrations of IL-6 than participants without these changes ($P < .01$; Figure 2B). The SWE values of the mesentery ($r = 0.44$, $P < .001$) and bowel wall ($r = 0.38$, $P < .001$) positively correlated with the effluent concentration of IL-6.

The prevalence of bowel wall thickening and calcification was higher in participants with a history of peritonitis than in those with no such history (36.1% versus 17.8%, $P = .004$ and 37.7% versus 10.8%, $P < .001$; respectively; Figure 2C). The SWE values of the mesentery and bowel wall were also higher in participants with a history of peritonitis ($P < .05$; Figure 2D).

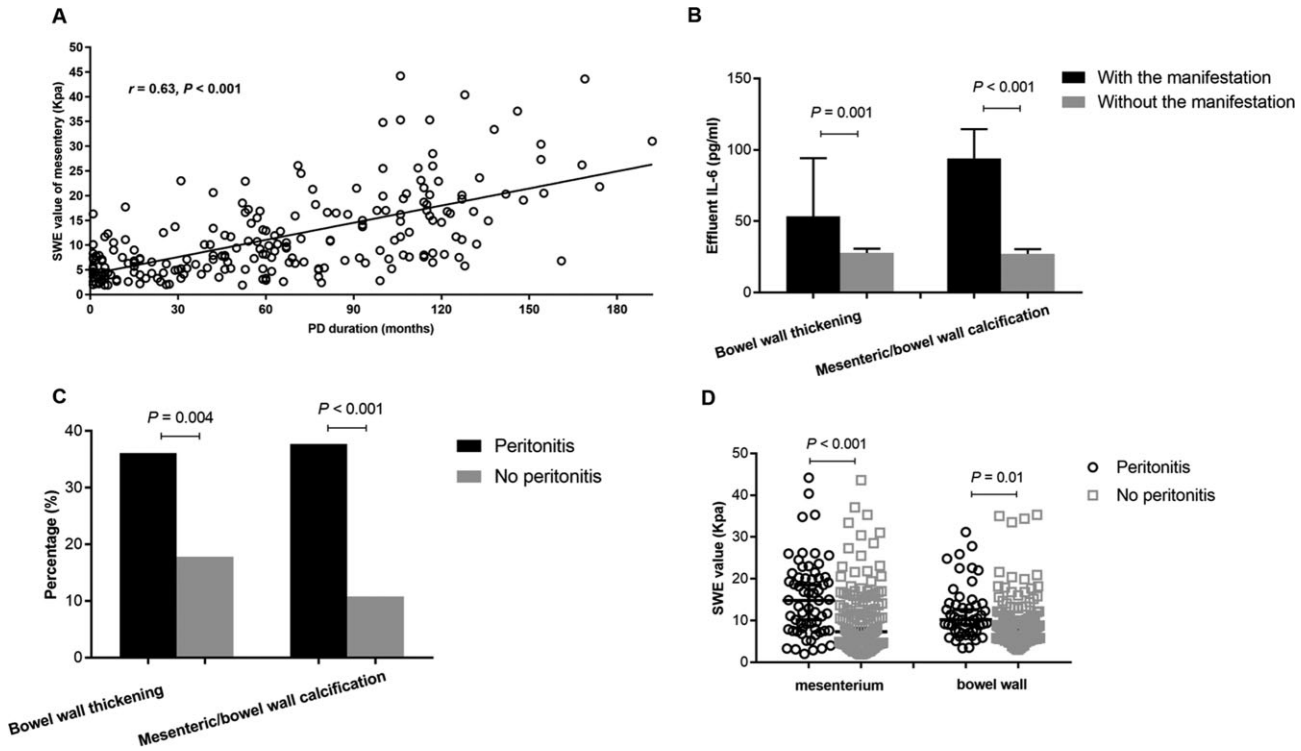

Figure 2: Relationship between ultrasonographic parameters and indicators of peritoneal injury. **(A)** Comparison of mesenteric SWE values in the healthy control group, CKD group and patients with different PD vintages. **(B)** Patients with bowel wall thickening [52.9 pg/ml (IQR 30.3–129) versus 28.6 (18.6–54.6), P = .001] and calcification [94.7 pg/ml (IQR 48.2–235) versus 28.1 (18.6–44.5), P < .001] had higher effluent IL-6 concentrations than those without these changes. **(C)** The prevalence of bowel thickening and calcification was higher in participants with a history of peritonitis than in those without (36.1% versus 17.8%, P = .004; 37.7% versus 10.8%, P < .001, respectively). **(D)** The mesenteric [14.9 kPa (IQR 7.83–20.6) versus 7.10 (4.50–11.8), P < .001] and bowel wall [10.2 kPa (IQR 7.40–14.2) versus 7.80 (6.00–11.2), P = .01] SWE values were also higher in participants with a history of peritonitis.

Table 2: The abdominal SWE manifestations of the study population and different PD vintage groups.

Doppler indexes	All ($N = 218$)	<3 months ($n = 21$)	≥3 months–<5 years ($n = 91$)	≥5–< 10 years ($n = 79$)	≥10 years ($n = 27$)	P-value
SWE value of mesentery, median (IQR)	8.15 (5.20–16.1)	5.20 (3.10–7.60)	6.40 (4.10–10.5)	11.9 (7.40–18.2)	19.3 (11.7–27.3)	**<.001**
Mesenteric/bowel wall calcification, *n* (%)	40 (18.3)	0 (0)	3 (3.16)	21 (26.6)	16 (59.3)	**<.001**
Bowel wall thickening, *n* (%)	50 (22.9)	2 (9.52)	8 (8.79)	28 (35.4)	12 (44.4)	**<.001**
SWE value of bowel wall, median (IQR)	8.75 (6.33–12.8)	6.10 (5.50–8.20)	7.55 (6.00–10.1)	10.4 (7.33–15.2)	11.4 (9.25–21.3)	**<.001**
Encapsulated fluid, *n* (%)	4 (1.83)	0 (0)	2 (1.54)	2 (2.53)	0 (0)	0.76

Differences between numerical variables were compared by Kruskal–Wallis H test and rates were compared by chi-squared test.
Significant values in bold.

Table 3 shows the results of the univariate and multivariate regression analyses of the factors associated with the SWE value for the mesentery. A long duration of PD ($\beta = 0.58$, $P < .001$), high effluent IL-6 concentration ($\beta = 0.61$, $P = .001$) and low effluent CA-125 concentration ($\beta = -0.34$, $P = .03$) were independently associated with a high mesenteric SWE value.

Relationships between peritoneal changes assessed using SWE and peritoneal function

The mesenteric SWE value positively correlated with D:PCr ($r = 0.32$, $P = .001$; Supplementary Figure S1). After adjustment for age, sex and effluent IL-6 and CA-125 concentrations, we found that the mesenteric SWE value was independently associated with D:PCr ($\beta = 0.39$, $P = .01$; Table 4). After adjustment for age, sex, residual mGFR, solution glucose concentration, daily exchange volume and the effluent IL-6 and CA-125 concentrations, the mesenteric SWE value was also independently correlated with peritoneal *Kt/V* ($\beta = 0.24$, $P = .01$; Supplementary Table S5).

No catheter-related UF dysfunction or dialysate leakage occurred in the participants. Univariate analysis showed that the mesenteric SWE value was negatively associated with UF from standard positron emission tomography [$\beta = -0.24$ (95% CI −0.43

Table 3: Univariable and multivariate analysis of predictive clinical variables for SWE value of the mesentery.

	Univariate model		Multivariate model 1		Multivariate model 2	
Variables	β (95% CI)	*P*-value	β (95% CI)	*P*-value	β (95% CI)	*P*-value
Demographic and PD profile						
Maler	−0.28 (−0.55 to −0.02)	**.04**	−0.05 (−0.26–0.16)	.65	−0.16 (−0.38–0.06)	.16
Age	0.13 (−0.004–0.26)	.06	0.02 (−0.09–0.13)	.71	−0.03 (−0.14–0.10)	.53
Diabetes	0.04 (−0.33–0.41)	83	–	–	–	–
PD duration	0.64 (0.53–0.74)	**<.001**	0.57 (0.45–0.70)	**<.001**	0.58 (0.45–0.71)	**<.001**
Residual renal function						
Residual mGFR	−0.37 (−0.49 to −0.24)	**<.001**	−0.01 (−0.13–0.11)	.87	−0.002 (−0.14–0.13)	.98
Inflammation and dialysate biomarkers						
Number of peritonitis episodes	0.33 (0.22–0.43)	**<.001**	0.18 (0.08–0.28)	**<.001**	–	–
Effluent IL-6	0.37 (0.23–0.50)	**<.001**	–	–	0.61 (0.31–0.90)	**<.001**
Effluent CA-125	0.27 (0.13–0.42)	**<.001**	–	–	−0.34 (−0.63 to −0.05)	**.03**

Univariable and multivariable linear regression analyses were used.
Significant values in bold.

Table 4: Association between SWE value of the mesentery and D:PCr.

	Univariate model		Multivariate model	
Variables	β (95% CI)	*P*-value	β (95% CI)	*P*-value
Male	0.56 (0.18–0.95)	**.005**	0.70 (0.29–1.12)	**.001**
Age	0.15 (−0.05–0.36)	.14	0.09 (−0.12–0.31)	.38
Effluent IL-6	18.0 (3.97–32.0)	**.01**	12.1 (−3.06–27.2)	.12
Effluent CA-125	0.55 (−0.60–1.70)	.34	0.19 (−0.92–1.30)	.73
SWE value of the mesentery	0.38 (0.18–0.58)	**.001**	0.39 (0.11–0.68)	**.01**

Univariable and multivariable linear regression analyses were used.
Significant values in bold.

to −0.04), $P = .02$]. After adjustment for age, sex, residual urine volume status and effluent IL-6 concentration, the mesenteric SWE value independently negatively correlated with the total volume of fluid removed daily across all the participants ($\beta = -0.17$, $P = .03$; Table 5) and the UF volume in those with anuria ($\beta = -0.28$, $P = .02$).

During a median follow-up period of 16.1 months (IQR 12–28.3), 23 patients were transferred to HD. The reasons are shown in Supplementary Table S6. ROC analysis generated an optimum cut-off mesenteric SWE value of 9.30 kPa for the prediction of death-censored technique failure (sensitivity 82.6%, specificity 57.9%, area under the ROC curve 0.75, $P < .001$). Univariate [hazard ratio 4.74 (95% CI 1.61–14.0), $P < .01$] and multivariate [adjusted hazard ratio 4.14 (95% CI 1.25–13.7), $P = .02$; Table 6] Cox regression revealed that mesenteric SWE values >9.30 kPa were a risk factor for death-censored technique failure.

DISCUSSION

In the present study we have pioneered the use of SWE for the assessment of mesenteric textural changes. A long duration of PD, high effluent IL-6 concentration and low effluent CA-125 were found to be independently associated with low mesenteric elasticity. In addition, the SWE value of the mesentery was independently correlated with D:PCr and peritoneal Kt/V and negatively correlated with the total volume of fluid removed daily across all the participants. Finally, low mesenteric elasticity was found to be a risk factor for technique failure.

Biopsy is the gold standard method of assessing peritoneal pathological changes. However, it is unsuitable for longitudinal monitoring or routine follow-up purposes. CT is regarded as a reliable alternative method for the assessment of peritoneal changes and is especially useful for the diagnosis of EPS [15, 20]. Ultrasonography, a non-invasive and radiation-free method, has also been widely used in patients undergoing PD. In 1998, Faller *et al.* [21] characterized the abdominal ultrasonographic features of 131 healthy children, 8 paediatric patients who were undergoing HD and 18 paediatric patients who were undergoing CAPD and found those undergoing CAPD had a significantly thicker peritoneum and showed less peritoneal movement than either of the other two groups. Caltik *et al.* [22] asserted that the ultrasonographic measurement of peritoneal thickness is useful for the assessment of structural and functional changes in the peritoneum of patients undergoing PD. Temiz *et al.* [23] found that the lower quadrant of the parietal peritoneum was thicker than that of the upper quadrant in PD patients by abdominal ultrasonography. They speculated that it was due to more exposure of the lower quadrant to the dialysis solution caused by the postural state of patients and the effect of gravity. In this study we observed that the mesenteric stiffness of the lower quadrant was higher than the upper quadrant by SWE examinations, confirming that the peritoneal changes in PD patients did not occur synchronously. Areas of the peritoneum with more exposure to peritoneal fluid may develop earlier or more severe peritoneal changes than areas with less exposure.

Fibrosis is one of the most important factors that leads to a decrease in tissue elasticity [9]. Long-term exposure to acidic dialysate, advanced glycation end-products and uraemic toxins leads to interstitial fibroblast activation, collagen fibre secretion and interstitial fibrosis [4]. It has been reported that during the first 2 years, structural changes in the peritoneum were

Table 5: Association between SWE value of the mesentery and daily fluid removal.

	Total volume in all patients				Ultrafiltration in anuric patients			
	Unadjusted		Adjusted		Unadjusted		Adjusted	
Variables	β value (95% CI)	P-value	β value (95% CI)	P-value	β value (95% CI)	P-value	β value (95% CI)	P-value
Age	−0.01 (−0.15–0.13)	.88	0.02 (−0.11–0.14)	.79	0.07 (−0.13–0.26)	.49	0.11 (−0.12–0.33)	.35
Male	0.13 (−0.14–0.40)	.35	−0.17 (−0.44–0.10)	.22	−0.01 (−0.40–0.37)	.95	−0.17 (−0.66–0.31)	.48
Residual mGFR	0.52 (0.40–0.64)	**<.001**	0.50 (0.32–0.68)	**<.001**	–	–	–	–
Solution glucose concentration	−0.26 (−0.39 to −0.13)	**<.001**	0.02 (−0.14–0.19)	.78	0.05 (−0.14–0.24)	.61	0.21 (−0.06–0.47)	.12
Daily exchange volume	−0.27 (−0.40 to −0.14)	**<.001**	0.03 (−0.14–0.20)	.72	0.01 (−0.19–0.20)	.96	0.03 (−0.21–0.26)	.83
Effluent IL-6	−0.08 (−0.23–0.07)	.27	−0.22 (−0.57–0.14)	.23	−0.08 (−0.31–0.15)	.49	−0.63 (−1.32–0.07)	.08
Effluent CA-125	0.01 (−0.14–0.15)	.92	0.23 (−0.11–0.57)	.18	0.01 (−0.22–0.24)	.92	0.58 (−0.08–1.25)	.08
SWE value of mesentery	−0.35 (−0.47 to −0.22)	**<.001**	−0.17 (−0.31 to −0.02)	**.03**	−0.29 (−0.47 to −0.10)	**.003**	−0.28 (−0.52 to −0.04)	**.02**

Univariable and multivariable linear regression analysis were used.
Significant values in bold.

uncommon except for the occurrence of mesothelial–mesenchymal transition (MMT); if PD treatment is administered for >2 years, an increase in fibrotic tissue can be found in the peritoneum [24]. Williams *et al.* [25] performed a comprehensive comparison of the peritoneal biopsies of patients undergoing long-term PD, uraemic patients and healthy individuals and confirmed that submesothelial thickening and fibrosis were directly related to the duration of PD therapy. The present results indicate that the elasticity of the mesentery and bowel wall decrease as the PD vintage increases; the mesenteric SWE values of CKD patients and healthy controls were not significantly different from those with a PD vintage of <3 months and were significantly lower than other patients with longer PD vintages. Therefore, we think that the progression of peritoneal fibrosis after PD is one of the important reasons attributed to the positive relationship between mesenteric SWE values and PD vintage.

Local inflammation is an important component of the mechanism of PD-associated peritoneal damage [26]. The present results indicate that the effluent IL-6 concentration and peritonitis are closely associated with mesenteric stiffness. The reasons for this may be that inflammation in the peritoneum can result in hypervascularization of the peritoneal membrane, which may increase local vascular density and results in elevated tissue SWE values [27–29]. In addition, inflammation also promotes peritoneal fibrosis by mechanisms such as MMT [4]. We also found that the effluent CA-125 concentration negatively correlated with the mesenteric SWE value. Dialysate CA-125 concentration is a marker of mesothelial cell mass, and its decline represents the integrity of the peritoneum being destroyed [30]. The loss of peritoneal mesothelial cells, together with the accumulation of matrix collagen fibres, and vascular disease are typical pathological findings in the peritoneum after the long-term use of a bio-incompatible dialysate. These findings imply that abdominal SWE values reflect the changes in the peritoneum during PD.

We further analysed the relationship between mesenteric SWE values and peritoneal function and found that mesenteric SWE values were positively correlated with D:PCr. In the clinical setting, the solute D:PCr concentration ratio was used to estimate the mass transfer area coefficient, reflecting the transport capacity of the peritoneal membrane. Changes in the D:P ratio of a low molecular-weight solute such as creatinine can be considered to represent changes in the vascular peritoneal surface area [31]. Studies showed that the more abundant the neovascularization, the less elasticity [32]. It may partially explain the positive relationship between mesenteric SWE values and D:PCr. We also found that mesenteric SWE values were negatively correlated with fluid clearance. The latest guidelines suggest that UF insufficiency is principally caused by two mechanisms: a high peritoneal solute transfer rate and a decrease in the peritoneal osmotic conductance of glucose [33]. The former is mainly determined by local peritoneal inflammation, associated with increased vascular peritoneal surface area, whereas the latter is mainly caused by changes in the properties of the peritoneum that relate to progressive fibrosis [33]. As discussed earlier, pathological changes like neovascularization and fibrosis decrease the elasticity of the mesentery, which may account for the negative correlation between the mesenteric SWE values and fluid clearance.

Owing to the relatively few outcome events that occurred during the short study period, we only adjusted age, sex, PD vintage and UF in the analysis of potential factors influencing the incidence of technique failure. We found that low mesenteric

Table 6: Univariate and multivariate Cox regression analysis of mesentery SWE values and technique failure.

	Univariate model		Multivariate model	
Variables	Unadjusted HR (95% CI)	*P*-value	Adjusted HR (95% CI)	*P*-value
Age	1.23 (0.81–1.87)	.33	1.08 (0.69–1.70)	.74
Male	1.39 (0.61–3.16)	.43	1.77 (0.76–4.11)	.19
PD vintage	1.56 (1.06–2.29)	**.02**	1.23 (0.80–1.91)	.35
Ultrafiltration	0.99 (0.65–1.54)	.99	–	–
SWE value of mesentery	4.74 (1.61–14.0)	**.005**	4.14 (1.25–13.7)	**.02**

Significant values in bold.

elasticity is an independent risk factor for technique failure, which was consistent with the previously published finding that changes in the peritoneum affect prognosis [34, 35].

The present study had some limitations. First, sufficient peritoneal samples were not obtained for further analysis of the pathological changes in PD patients. Second, although our preliminary test confirmed that the mesenteric SWE value of the right lower quadrant was significantly correlated with the average mesenteric SWE value of the four quadrants, we only measured local mesenteric stiffness, which may not be representative of overall peritoneal stiffness. Third, because of the experimental design, we were able to identify relationships among various factors, but causality could not be inferred. Fourth, since no patient in this study used icodextrin or other biocompatible dialysis fluids, the generalizability of the results of this study to the population using these dialysis fluids is limited. Also, this is a single-centre study and the results need multicentre validation. Future research efforts should also include the measurement of peritoneal elasticity in multiple quadrants to compare the clinical significance of local peritoneal stiffness and the overall changes in the peritoneum.

CONCLUSION

In conclusion, we have pioneered the use of SWE for the assessment of mesenteric textural changes in the present study. We demonstrated that the peritoneal elasticity of patients with PD was closely related to their peritoneal function. In the future, SWE may help us to determine peritoneal damage after PD and may even have a predictive role in prognosis.

SUPPLEMENTARY DATA

Supplementary data are available at *ckj* online.

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AUTHORS' CONTRIBUTIONS

X.D. and X.Y. were responsible for the research idea and study design. Y.C., J.L., M.X. and Y.P. were responsible for data acquisition. X.D., H.W. and Y.C. were responsible for data analysis/interpretation and statistical analysis. X.Y., X.X., X.Y., H.M. and F.H. were responsible for supervision or mentorship.

DATA AVAILABILITY STATEMENT

The datasets generated during and/or analysed during the current study are available from the corresponding author upon reasonable request.

CONFLICT OF INTEREST STATEMENT

None declared.

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