FLUID OVERLOAD IMPACT ON BOTH ARTERIAL STIFFNESS AND DIASTOLIC HEART FAILURE IN PERITONEAL DIALYSIS PATIENTS

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ABSTRACT

***Introduction**: Chronic subclinical volume overload, frequently observed in peritoneal dialysis (PD) patients, is associated with increased arterial stiffness (AS), diastolic heart failure (HF), and higher mortality and morbidity. Diastolic HF is also known as HF with preserved left ventricular (LV) ejection fraction (LVEF). We here in evaluated the effect of volume status on development of arterial stiffness and diastolic HF in patients with normal or near-normal LV systolic function.*

***Materials and methods**: A total of 75 chronic patients with PD and 52 age- and gender-matched control subjects were included in this study. Fluid overload (FO) was determined using multifrequency bioelectrical impedance analysis (mBIA). LVEF, peak velocity of atrial filling (E/A ratio), left atrium diameter (LAD), LV end-diastolic diameter (LVEDD), and LV end-systolic diameter (LVESD) were obtained using echocardiography (ECHO). Brachial-ankle artery pulse wave velocity (baPWV) and augmentation index (AIx) were measured to determine AS.*

***Results**: Of a total 75 patients, 56 (59.6%) were undergoing continuous ambulatory PD (CAPD). The mean values for systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial blood pressure (MAP), and pulse pressure (PP) were 130 ± 24, 80 ± 17, 103 ± 19, and 50 ± 16 mmHg, respectively. The mean SBP, LAD, and LV mass index (LVMI) (all $p < 0.005$) were higher and the E/A ratio ($p = 0,000$) was lower in patients with PD than in healthy controls. Comparison of hypervolemic and normovolemic patients showed that the mean SBP, LAD, LVEDD, LVESD, and LVMI (all $p < 0.005$) were significantly higher and the mean LVEF ($p = 0.003$) was significantly lower in the hypervolemic group, whereas the mean DBP, MAP, baPWV, PP, and AIx were not significantly different between the two groups (all $p > 0.005$). Multivariate regression analysis adjusted for ECHO parameters revealed that age ($\beta = 0.733$, $p = 0.001$), diabetes status ($\beta = 0.184$, $p = 0.027$), and SBP ($\beta = 0.519$, $p = 0.001$) were independently associated with increased baPWV.*

***Conclusions**: Overhydration (OH) was higher in patients with PD than in healthy controls and was associated with development of diastolic HF in patients with PD. Additionally, age, SBP, and diabetes status and not FO were independent predictors of baPWV in patients with PD.*

***Key words**: bioimpedance analysis, brachial-ankle artery pulse wave velocity, diastolic heart failure, peritoneal dialysis.*

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Introduction

Fluid overload (FO), commonly observed in patients undergoing peritoneal dialysis (PD), has a negative effect on cardiac structures[1]. PD treatment provides tight fluid and blood pressure (BP) control during the first year; however, hypervolemia may occur after several years of PD[2]. Multifrequency bioelectrical impedance analysis (mBIA) has been proposed as a method for objective assessment and monitoring of hydration status in dialysis patients[3]. Chronic subclinical FO leads to an increase in left ventricular (LV) end-diastolic diameter (LVEDD) that results in an enlarged LV and left atrium diameter (LAD) in patients with PD. Diastolic heart failure (HF) is also known as HF with preserved LV ejection fraction (LVEF)[4]. FO, arterial stiffness (AS), and LV hypertrophy (LVH) can all contribute

to diastolic HF in patients with PD. LVH is a predictor of cardiovascular (CV) events[5] that are the main cause of morbidity and mortality in patients on PD. Enia et al. and Cader et al. reported that FO was strongly associated with LVH[6-7]. Additionally, Wang et al. demonstrated the importance of HF with preserved ejection fraction (EF) in patients with PD[8].

Compared with atheromatous changes, sclerotic changes in the arterial wall, which can be determined by brachial-ankle artery pulse wave velocity (baPWV), has only recently been studied in patients with PD, and the results are contradictory and sometimes inconsistent. The baPWV measurement was developed due to its noninvasive and simple utiltiy[9]. PWV promotes cardiac hypertrophy by increasing the impact of arterial wave reflection in the central arteries[10]. Increased AS detected by PWV was shown as an independent risk predictor of all-cause and CV mortality in patients with PD[11], with significant increases in PWV observed over time[12]. Previous studies demonstrated that AS was increased in patients with PD with FO[13,14] and that strict FO control might allow for regression of AS[15].

FO and AS have been considered as risk factors of mortality in patients with PD; however, the relationship between these parameters remains controversial. The aim of the present study was to evaluate the effect of volume status on development of AS and diastolic HF in patients with normal or near-normal LV systolic function.

Material and methods

Study population

In this study, we evaluated a total of 75 adult patients (44 males and 31 females) with a mean age of 53.7 ± 13.3 years (range, 22-79) who were treated for more than three months with PD as renal replacement therapy in the outpatient clinic of Antalya Training and Research Hospital, Turkey. Of these, 56 (59,6%) patients were treated by continuous ambulatory PD (CAPD), whereas the remaining patients (n = 19, 20.2%) were treated by automated PD (APD). Patients were compared with age- and gender-matched 52 healthy control subjects. Data on demographic characteristics, body mass index (BMI), end stage renal disease etiology, PD treatment duration, cardiac functions, and baPWV measurement were collected from all subjects. Patients with significant valvular heart disease, any prior coronary intervention, non-sinus rhythm, LV global or regional systolic dysfunction (EF < 50%), previous myocardial infarction, uncontrolled hypertension, active infectious or inflammatory disease, malignancy, and history of peritonitis within the last three months before the study were excluded. For ethical reasons, subjects on antihypertensive medications were studied without washing out antihypertensive medications. The ethics committee of Antalya Training and Research Hospital approved this study. The purpose of this study was fully explained and informed consent was obtained from all subjects. All procedures were conducted in accordance with the Helsinki Declaration of 1975, as revised in 2000.

Multifrequency bioelectrical impedance analysis

A body composition monitor (BCM; Fresenius Medical Care, Bad Homburg, Germany) was used to determine extracellular water (ECW), intracellular water (ICW), total body water (TBW), lean tissue index (LTI), fat tissue index (FTI), dry lean mass (DLM), and adipose tissue mass (ATM). [Remark 2] Briefly, after the patient was in a recumbent position for at least 15 minutes with an empty stomach, [Remark 3] electrodes were attached to one hand and one foot on the ipsilateral side (16), measurements were recorded using multifrequency bioelectrical impedance analysis (mBIA). For excess fluid measured by mBIA, the value obtained from the receiver operating characteristic (ROC) curve was used as an FO indicator.

Biochemical analysis

Two milliliters of fasting blood samples were collected from patients with PD and healthy control subjects. Serum was separated after 30 minutes and was stored at -80 °C. [Remark 4]

Echocardiography

Echocardiography (ECHO) measurements were performed at the cardiology department of our hospital by the same cardiologist. The LV systolic and diastolic volumes and EF were derived from M-mode images according to standard criteria[17]. The LV mass was calculated by Devereux's method[18]. The LV mass index (LVMI) was calculated as LV mass divided by body surface area. LVH was accepted as LVMI ≥ 134 g/m2 in males and ≥ 110 g/m2 in females. The peak velocity of early rapid filling (E velocity) and peak velocity of atrial filling (A velocity) were recorded to obtain

the E/A ratio. Relative wall thickness at diastole (RWTd) [Remark 5] was calculated by the following formula: RWTd = 2 × thickness of LV posterior wall/LV diameter at diastole.

Brachial-ankle artery pulse wave velocity

The baPWV was performed in PD patients with empty abdomen after drainage of dialysate and at least 15 minutes of supine rest. Two measurements were performed in each arm, and the average value was recorded. [Remark 6] The baPWV was assessed using VP-1000 vascular profiler that allowed on-line pulse wave recording and automatic calculation of pulse wave velocity (PWV).

Statistical analysis

Statistical analysis was performed using SPSS® statistical package (version 21; Chicago, IL, USA), and p values of 0.05 were considered statistically significant. Quantitative variables were described using means and standard deviation, and qualitative variables were described using frequencies and percentages. The independent sample t test and Mann-Whitney U test were used to analyze quantitative variables. The ROC curve was used to analyze patients with FO. Multiple linear regression analysis was used to assess independent determinants of increased baPWV.

Results

A total of 75 patients (31 females and 44 males) were included in the study. The mean time of PD duration was 41.5 ± 31.9 (range, 3-132) months. Causes of renal failure were diabetic nephropathy, hypertensive nephrosclerosis, glomerulonephritis, polycystic renal disease, nephrolithiasis, and other etiologies in 22 (29.3%), 57 (76.0%), 6 (8.0%), 3 (4.0%), 1 (1.3%), and 7 (9.3%) patients, respectively. Medications for hypertension included angiotensin-converting enzyme inhibitors or angiotensin-II receptor blockers (29.3%), calcium channel blockers (37.3%), beta receptor blockers (38.7%), alpha receptor blockers (14.7%), sympatholytic agents (6.7%), and diuretics (38.7%) (Table 1).

The mean systolic BP (SBP), diastolic BP (DBP), mean arterial pressure (MAP), and pulse pressure (PP) were 130 ± 24, 80 ± 17, 103 ± 19, and 50 ± 16 mmHg, respectively. The mean baPWV was 8.1 ± 1.8 m/s (range, 4.9-13.4), and the mean AIx was 22 ± 13 m/s (range, 1-58). The mean

Variable	Mean ± S.D./n-%	Med (Min–Max)
Age (years)	53.7 ± 13.3	56 (22–79)
Male	44 58.7%	
Female	31 41.3%	
BMI (kg/m2)	27.8 ± 5.2	28.1 (17.8–39.3)
PD duration (months)	41.5 ± 31.9	35 (3–132)
Etiology of ESRD		
Diabetic nephropathy	22 29.3%	
Hypertensive nephrosclerosis	57 76.0%	
Glomerulonephritis	6 8.0%	
Polycystic kidney disease	3 4.0%	
Nephrolithiasis	1 1.3%	
Others	7 9.3%	
Use of antihypertensive drugs		
ACEi/ARB	22 29.3%	
Calcium channel blockers	28 37.3%	
Alpha receptor blockers	11 14.7%	
Beta receptor blockers	29 38.7%	
Sympatholytic agents	5 6.7%	
Diuretics	29 38.7%	

Table 1: Demographic and Clinical Characteristics of Patients included in this study.
BMI: body mass index; ESRD: end-stage renal disease; ACEi/ARB: angiotensin-converting enzyme inhibitors /angiotensin-II receptor blockers; PD: peritoneal dialysis

LAD was 38.3 ± 8.3 mm, which was more than 40 mm in 29 (38.7%) patients. The mean LVEDD was 46.7 ± 6.1 mm, which was more than 55 mm in 10 (13.3%) patients. The mean LVESD was 30 ± 6, which was more than 35 mm in 9 (12,.0%) patients. The E/A ratio was ≤ 0.75 in 33 (44.0%) patients; 12 (16%) male and 22 (29.3) female patients had LVH based on ECHO evaluation, with a mean LVMI of 125.2 ± 39.5 g/m2. Eccentric and concentric hypertrophy were found in 5 (6.7%) and 43 (57.3%) patients, respectively (Table 2).

Comparison of patients with age- and gender-matched 52 healthy controls revealed that overhydration (OH) as well as the mean SBP, LAD, and LVMI (all $p < 0.005$) were significantly higher and

the E/A ratio was significantly lower in patients with PD than in healthy controls (Table 3).

Variable	Mean ± S.D./n-%	Med	(Min-Max)
SBP (mmHg)	130 ± 24	130	(80-177)
DBP (mmHg)	80 ± 17	82	(41-119)
MAP (mmHg)	103 ± 19	101	(61-146)
PP (mmHg)	50 ± 16	48	(17-94)
AIx (%)	22 ± 13	20	(1-58)
baPWV (m/sec)	8.1 ± 1.8	8.0	(4.9-13.4)
RWT			
≥ 0.42	14 18.7%		
< 0.42	61 81.3%		
LVEF (%)	62 ± 4	65	(45–66)
LAD (mm)	38.3 ± 8.3	38,0	(8.0–74.0)
40≤	46 61.3%		
40>	29 38.7%		
LVESD (mm)	30 ± 6	29	(20–61)
≥ 35	66 88,0%		
< 35	9 12,0%		
LVMI (g/m2)	125.2 ± 39.5	123	(46–236)
Male ≥ 134 g/m2	12 16%		
Female ≥ 110 g/m2	22 29.3%		
LVH			
Eccentric hypertrophy	5 6.7%		
Concentric hypertrophy	43 57.3%		
Concentric remodeling	23 30.7%		
Normal	4 5.3%		
E/A ratio	0.9 ± 0.4	0.8	(0.4–2.2)
≤ 0.75	33 44.0%		
> 0,75	42 56.0%		

Table 2: Brachial-Ankle Artery Pulse Wave Velocity and Echocardiography values of subjects in this study.
SBP: systolic blood pressure; DBP: diastolic blood pressure; MAP: mean arterial pressure; AIx: augmentation index; baPWV: brachial-ankle pulse wave velocity; RWT: relative wall thickness; LAD: left atrium diameter; LVEDD: left ventricular end-diastolic diameter; LVESD: left ventricular end-systolic diameter; E/A ratio: ratio of early transmitral peak velocity to late transmitral peak velocity; LVEF: left ventricular ejection fraction; LVMI: left ventricular mass index; LVH: left ventricular hypertrophy

	Male PD Mean ± S.D	Male Healthy Mean ± S.D.	*p*	Female PD Mean ± S.D.	Female Healthy Mean ±S.D.	*p*
OH (L)	1.57 ± 1.86	0.06 ± 1.15	***0.006***	0.73 ± 1.35	−0.13 ± 0.80	***0.002***
SBP (mmHg)	125.22 ± 21.51	114.28 ± 9.37	***0.015***	121.61 ± 20.50	109.74 ± 12.66	***0.002***
DBP (mmHg)	82.18 ± 14.19	76.43 ± 6.33	***0.02***	77.52 ± 20.19	72.63 ± 10.57	0.22
LAD (mm)	39.34 ± 9.03	34.64 ± 4.13	***0.004***	36.74 ± 6.87	32.63 ± 3.58	***0.001***
LVEDD(mm)	47.57 ± 6.19	46.07 ± 3.85	0.433	45.35 ± 5.92	43.11 ± 4.17	0.058
LVESD (mm)	30.10 ± 7.39	28.86 ± 3.35	0.964	28.94 ± 4.90	27.13 ± 3.53	0.114
LVEF (%)	61.50 ± 4.67	64.29 ± 1.82	***0.025***	63.55 ± 3.21	64.21 ± 1.85	0.445
LVMI (g/m2)	122.24 ± 35.89	86.35 ± 18.02	***0.001***	129.79 ± 44.32	79.6 ± 16.76	***0***
E/A ratio	0.9 ± 0.4	1.17 ± 0.4	***0.012***	0.9 ± 0.3	1.2 ± 0.3	***0***

Table 3: Comparison of Peritoneal Dialysis Patients with Healthy Control Subjects.
Independent sample t test/Mann-Whitney U test
OH: overhydration; SBP: systolic blood pressure; DBP: diastolic blood pressure; LAD: left atrium diameter; LVEDD: left ventricular end-diastolic diameter; LVESD: left ventricular end-systolic diameter; LVEF: left ventricular ejection fraction; LVMI: left ventricular mass index; E/A ratio: ratio of early transmitral peak velocity to late transmitral peak velocity

To assess OH, excess fluid volume was determined from available parameters obtained by mBIA. The LVEDD values of > 55 mm obtained by ECHO were used to generate the ROC curve. The resulting threshold values for females and males were +1.75 L/m (sensitivity = 0.67, specificity = 0.75) and for men was + +2.25 L/m (sensitivity = 0.80, specificity = 0.66), respectively. The optimal threshold value for OH was determined to be +1.75 L/m (sensitivity = 0.73, specificity = 0.68), and patients were divided into normovolemic and hypervolemic groups based on this value (Figure 1).

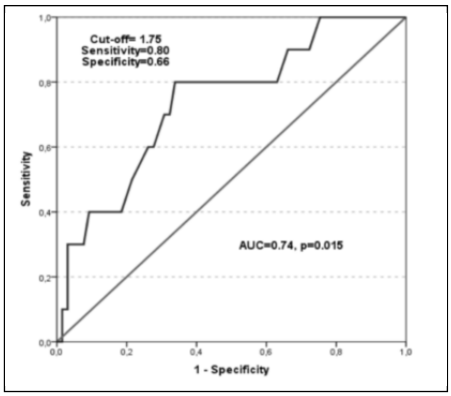

Figure 1:The Receiver Operating Characteristic Curve for Determining Patients with Fluid Overload.

FO was detected in 37.4% (n = 28) of the patients. Comparison of hypervolemic patients with those who were normovolemic revealed that the mean SBP, LAD, LVEDD, LVESD, and LVMI (all

p < 0.005) were significantly higher and the mean LVEF (p = 0003) was significantly lower in hypervolemic patients, whereas the mean DBP, MAP, baPWV, PP, and AIx were not different between the two groups (all p > 0.005; Table 4).

In multivariate regression analysis, baPWV was found to be an independent contributor to age (β coefficient = 0.733, p = 0.001), diabetes status (β coefficient = 0.184, p = 0.027), and SBP (β coefficient = 0.519, p = 0.001) (Table 6).

	Patients with FO (n = 28) Mean ± S.D/n-% Med(Min-Max)	Patients without FO (n = 47) Mean ± S.D/n-% Med(Min-Max)	p
Age (years)	52.31 ± 15.50 57 (22–77)	50.16 ± 10.62 49 (26-79)	0.234
Male	17 60.7%	27 57.4%	0.266
Female	11 39.3%	20 42.6%	
DM	10 35.7%	12 25.5%	0.349
PD duration (months)	40.47 ± 33.24 29 (3-132)	42.97 ± 33.56 36 (5-120)	0.617
SBP (mmHg)	131.32 ± 23.15 137.00 (80.00-177.00)	128.82 ± 24.44 128.50 (80.00-160.00)	***0.001***
DBP (mmHg)	80.11 ± 17.43 82.00 (41.00-119.00)	80.50 ± 16.47 82.00 (41.00-105.00)	0.602
MAP (mmHg)	103.55 ± 18.64 102.00 (61.00–146.00)	102.57 ± 18.67 101.00 (61.00-129.00)	0.943
PP(mmHg)	51.32 ± 16.21 50.00(17.00-94.00)	48.32 ± 16.60 46.50 (17.00-94.00)	0.547
AIx (%)	22.32 ± 13.99 20.00 (1.00-58.00)	21.64 ± 10.02 17.5 (9.00-42.00)	0.987
baPWV (m/sec)	8.10 ± 1.74 8.10 (4.90-13.40)	7.99 ± 2.01 7.95 (5.10-12.50)	0.634
LAD (mm)	39.59 ± 6.69 39 (25 ± 57)	34.45 ± 6.69 35 (8 ± 51)	***0.001***
LVEDD (mm)	49.47 ± 6.36 49 (38 ± 61)	44.58 ± 4.70 44 (32 ± 56)	***0.001***
LVESD (mm)	31.25 ± 7.99 30.00 (20.00-61.00)	28.57 ± 5.20 29.00 (20.00-44.00)	***0.001***
LVEF (%)	61.28 ± 4.61 60 (50-66)	63.49 ± 3.48 65 (45-65)	***0.003***
LVMI (g/m2)	141.25 ± 38.68 136.5 (63-233)	98.83 ± 34.90 88 (49-236)	***0.001***
E/A ratio	0.9 ± 0.4 0.8 (0.4-2.2)	0.9 ± 0.4 0.8 (0.6-1.8)	0.999

Table 4: Comparison of hypervolemic patients with normovolemic patients according to the multifrequency bioelectrical impedance analysis.

Independent sample t test /Mann-Whitney U test/Pearson chi square test/Fisher's exact test

FO: fluid overload; DM: diabetes mellitus; PD: peritoneal dialysis; SBP: systolic blood pressure; DBP: diastolic blood pressure; MAP: mean arterial pressure; PP: pulse pressure; AIx: augmentation index; baPWV: brachial-ankle pulse wave velocity; LAD: left atrium diameter; LVEDD: left ventricular end-diastolic diameter; LVESD: left ventricular end-systolic diameter; LVEF: left ventricular ejection fraction; LVMI: left ventricular mass index; E/A ratio: ratio of early transmitral peak velocity to late transmitral peak

When patients were divided into the high and low baPWV groups according to mean baPWV values, compared with those in the low baPWV group, patients in the high baPWV group were significant older (p = 0.000) and their mean SBP (p = 0.000), PP (p = 0.001), and AIx (p = 0.001) were significantly higher. There were no significant differences in BMI, gender, diabetes status, LAD, LVEDD, LVESD, or LVMI between the two subgroups (all p > 0.05) (Table 5).

Discussion

Increased AS detected by PWV was shown as an independent risk predictor of all-cause and CV mortality in patients with PD, and significant increases in PWV over time were observed in patients with PDPD patients[11,12]. Kwan et al. demonstrated that the OH value was ≥ +1 L/m in 72.1% of patients with PD and that 20.5% of those had an OH value ≥ +5 L/m[12].

	baPWV ≤ 8. 1(n = 38) Mean ± S.D/n-%	baPWV > 8. 1(n = 37) Mean ± S.D/n-%	p
Age (years)	48. 24 12. 84	59. 27 11. 53	***0. 000***
BMI (kg/m²)	27. 76 ± 5. 11	27. 94 ± 5. 27	0. 695
Male	20 52.6%	24 64.9%	0. 282
Female	18 47.4%	13 35.1%	
DM	9 23.7%	13 35.1%	0. 278
PD duration (months)	40 ± 33	43 ± 31	0. 442
LAD (mm)	37. 61 ± 6. 61	38. 95 ± 9. 72	0. 307
LVEDD (mm)	47. 08 ± 6. 79	46. 22 ± 5. 37	0. 315
LVESD (mm)	29. 35 ± 4. 81	29. 79 ± 7. 81	0. 793
LVEF (%)	61. 89 ± 4. 77	62. 79 ± 3. 64	0. 373
LVMI (g/m²)	122. 47 ± 36. 91	128. 03 ± 42. 24	0. 828
E/A	0. 96 ± 0. 40	0. 85 ± 0. 30	0. 218
SBP (mmHg)	121. 53 ± 20. 51	139. 49 ± 23. 14	***0. 000***
DBP (mmHg)	77. 42 ± 17. 17	83. 16 ± 16. 48	0. 171
MAP (mmHg)	97. 66 ± 18. 03	108. 86 ± 17. 50	0. 013
PP (mmHg)	44. 16 ± 10. 42	56. 41 ± 18. 89	***0. 001***
AIx (%)	17. 61 ± 10. 31	26. 65 ± 13. 18	***0. 001***

Table 5: Comparison of patients according to the mean brachial-ankle pulse wave velocity.

Mann-Whitney U test/Pearson chi square/Fisher's exact test
BMI: body mass index; DM: diabetes mellitus; PD: peritoneal dialysis; LAD: left atrium diameter; LVEDD: left ventricular end-diastolic diameter; LVESD: left ventricular end-systolic diameter; LVEF: left ventricular ejection fraction; LVMI: left ventricular mass index; E/A ratio: ratio of early transmitral peak velocity to late transmitral peak velocity; SBP: systolic blood pressure; DBP: diastolic blood pressure; MAP: mean arterial pressure; PP: pulse pressure; AIx: augmentation index

Cader et al. reported that over 50% of patients were considered to be overhydrated with an OH threshold value of + 2 L/m; in the same study, the average OH value was ± 2.4 L/m[19].

Similarly, Luo et al. found that the threshold value for OH was +2 L/m in hypervolemic patients with PD[20]. Conversely, Hur et al. and Lindley et al. reported average OH values of 1.3 ± -1.7 L/m[21], and +1.3 L/m in hypervolemic patients with PD[22]. One of the parameters used to evaluate LV diastolic function is LVEDD. Hypervolemia and subsequently increased SBP might lead to increased LV dimensions in patients with PD. In this study, we determined patients with FO by using LVEDD values above 55 mm, as measured by ECHO, and performed the ROC curve analysis. The optimal threshold OH value was +1.75 L/m (sensitivity = 0.73, specificity = 0.68). Further, our analysis revealed that the OH threshold values for males and females were +2.25 L/m (sensitivity = 0.80, specificity = 0.66) and +1.75 L/m (sensitivity = 0.67, specificity = 0.75), respectively. In this study, 37.4% of the patients had OH. According to the OH threshold value, patients were divided into two groups: the normovolemic group (n = 47) with an OH of less than +1.75 L/m and the hypervolemic group with an OH of more than +1.75 L/m (n = 28). Interestingly, while Jung et al. did not find a relationship between FO and BP[23], Kwan et al. reported significantly higher SBP levels in hypervolemic patients[12]. Wong et al. demonstrated that patients with PD with high BP were more hypervolemic[24]. Similar to a previous study[25], in our study, we found that hypervolemic patients had higher SBP than normovolemic patients.

Variables	*β*	t	*p*
Age (years)	0.733	9.101	***0.001***
Gender	-0.021	-0.275	0.785
DM	0.184	2.263	***0.027***
PD duration (months)	0.073	0.911	0.366
LAD (mm)	0.051	0.654	0.516
LVEDD (mm)	0.07	0.887	0.379
LVESD (mm)	0.007	0.092	0.927
LVEF (%)	-0.021	-0.272	0.786
LVMI (g/m²)	-0.006	-0.052	0.959
E/A ratio	0.095	1.171	0.247
SBP (mmHg)	0.519	6.597	***0.001***
DBP (mmHg)	0.007	0.067	0.947
MAP (mmHg)	0.019	0.085	0.933
PP (mmHg)	-0.006	-0.045	0.964
AIx (%)	-0.176	-1.488	0.141

Table 6: Multivariate linear regression analysis of factors associated with baPWV.

DM: diabetes mellitus; PD: peritoneal dialysis; LAD: left atrium diameter; LVEDD: left ventricular end-diastolic diameter; LVESD: left ventricular end-systolic diameter; LVEF: left ventricular ejection fraction; LVMI: left ventricular mass index; E/A ratio: ratio of early transmitral peak velocity to late transmitral peak velocity; SBP: systolic blood pressure; DBP: diastolic blood pressure; MAP: mean arterial pressure; PP: pulse pressure; AIx: augmentation index

In the current study, patients with FO had worse LVH and LV dilation, LAD, and higher E/A ratios than those without FO. Hypervolemia was previously demonstrated as an independent predictor of LVH in patients with PD[26]. LVH appeared to be associated with high CV morbidity and mortality rates in patients undergoing PD[27]. Konings et al. demonstrated an association between FO and LVH

in patients with PD[28]. Yet another study reported that hypervolemic patients with PD had elevated LAD, LVEDD, and LVMI[29]. Furthermore, Wang et al reported that increased LVMI was related to worse CV outcome[30], whereas Cader et al. reported that FO was strongly associated with LVH and that effective control of FO could reduce the development of LVH[7]. Similar to a study by Hassan and colleagues[31], our results herein indicated that patients with FO had significantly worse LVH than normovolemic subjects.

LVH leads to the development of diastolic dysfunction, and concentric hypertrophy is the most common cause of diastolic dysfunction in patients with PD. In the current study, we included patients who had an EF of > 50% with no history of cardiac disease prior to the study. In a previous study, LVH was detected in 57.9% of patients with PD[32]. Herein, we found that 34 (45.3%) of the patients had LVH; 5 (6.7%) of those had eccentric hypertrophy, whereas 43 (57.3%) had concentric hypertrophy. These results indicated that diastolic dysfunction preceded deterioration of systolic function in these patients with PD. An E/A ratio of ≤ 0.75 was considered to indicate cardiac diastolic dysfunction[33]. Consequently, 33 (44.0%) of our patients had an E/A ratio of ≤ 0.75. We also found that patients with PD had significantly lower E/A ratio than healthy group, suggesting that patients with PD had worse diastolic dysfunction than healthy subjects.

AS was shown as an independent risk predictor of mortality in patients with PD[9]. A new PWV measurement based on the analysis of brachial and ankle sites, baPWV, was developed to determine AS in patients with PD[10]. Using this approach, Mimura et al. showed that the duration of dialysis therapy was one of the factors affecting AS[34]. Similar to a report by Stróżecki et al., we found no correlation between the duration of dialysis therapy and PWV[35].

Diabetes contributes to development of AS in end-stage renal disease (ESRD) patients[36]. Huang et al. reported that age, diabetes status, and MAP were independently correlated with baPWV[37]. Another study determined that age and SBP were major determinants of PWV[38]. In addition, Zhe et al. reported that increased PWV in patients with PD was significantly associated with age[39], whereas Blacher et al. demonstrated that arterial PWV correlated with SBP in ESRD patients[40]. In the present study, multivariate regression analysis used to identify factors correlating with changes in baPWV, after adjusting for CV risk factors, showed that age, diabetes status, and SBP were independently correlated with increased baPWV.

AS determined by PWV was previously shown to be a predictor of CV mortality[41]. Increased AS, as assessed by baPWV, affects vascular as well as cardiac alterations through modulation of central arterial pressure. Sipahioglu et al. reported that AS was an independent risk predictor of adverse CV outcomes in patients with PD[9]. A study by Nitta et al. reported that baPWV was significantly and positively correlated with LVH in dialysis patients[42], whereas a separate study failed to show such a relationship between baPWV and LVH[43]. Covic et. reported that a PWV value of ≥ 8.3 m/sec was associated with significantly higher CV and overall mortality rates than a PWV value of < 8.3 m/sec[44]. In the present study, the mean baPWV value was 8.1 ± 1.8 m/sec, and the LVH and LVMI did not differ between the high and low baPWV groups. In contrast to several previous studies and similar to a report by Hur et al.[45], we observed a correlation between AS and LV diastolic dysfunction and/or LVH development. The reason for the discrepancy between our findings and previous studies was unclear; however, comorbidities, treatment duration, and type of antihypertensive medications and PD prescriptions might be partially responsible for this outcome.

A study reported that FO was an independent predictor of AS in patients with PD[13]. Chung et al. reported that increased AS was observed in patients with PD[46]. In addition, Hur et al. reported that treatment of FO in dialysis patients led to the regression of LVMI and improvement in AS[47]. Similar to a study by Gao and colleagues, we found no relationship between FO and baPWV[48]. Different diagnostic devices might have different sensitivities this might be associated with differences observed between the studies.

Limitations

Our study has several limitations. First, the study was performed in a single center and included a small number of patients. Furthermore, the percentage of patients with abnormal baPWV was small. Second, the measurements for mBIA and baPWV were performed only once; repeated measurements might be helpful to achieve more accurate results. Third, due to the technical limitations associated with baPWV evaluation, patients with

atrial fibrillation and those with amputated extremities were excluded from this study. Finally, the majority of patients included in this study were stable with no overt FO, which was achieved by tight salt and fluid restriction and use of antihypertensive agents. These measures might have had a negative impact on our findings. Consequently, future, longitudinal studies including larger patient cohorts with different dialysis modalities are needed to confirm and expand our findings.

Conclusions

The present study failed to show a relationship between AS and FO and further demonstrated that LV structure was not affected, as assessed by baPWV. The reason for the differences between our findings and earlier studies might be the variety in PD prescriptions. AS, which was assessed by baPWV, was independent correlated with age, SBP, and diabetes mellitus in patients with PD. Further, FO was associated with LVH and LVMI development in patients on PD. Prevention of FO, which is linked to development of HF with preserved LVEF, should be a major goal in treatment of patients with PD.

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