# Original Article Study of right ventricular function with preserved left ejection fraction by three-dimensional speckle tracking in uremic patients undergoing peritoneal dialysis

Li Luo<sup>1\*</sup>, Jing Zhu<sup>1\*</sup>, Jianchang Chen<sup>1</sup>, Lan Gao<sup>1</sup>, Sheng Feng<sup>2</sup>

Departments of <sup>1</sup>Internal Medicine-Cardiovascular, <sup>2</sup>Nephrology, The Second Hospital Affiliated to Soochow University, Suzhou, Jiangsu, China. \*Equal contributors.

Received January 20, 2016; Accepted May 4, 2016; Epub June 15, 2016; Published June 30, 2016

**Abstract:** This study aimed to test the ability of real-time three-dimensional echocardiography (RT3DE) to characterize early abnormalities of right ventricular (RV) structure and function with preserved left ventricular (LV) ejection fraction (EF) in uremic patients undergoing peritoneal dialysis (PD). Sixty-six uremic patients with preserved left ventricular ejection fraction (> 50% LVEF) undergoing peritoneal dialysis and 20 healthy control participants underwent both standard and RT3DE assessment. The PD patients with right ventricular ejection fraction (RVEF) > 45% composed group A (45 patients), and all other patients were included in group B (21 patients). The RV volume and ejection fraction, global longitudinal strain (GLS), global circumferential strain (GCS), global area strain (GAS), and global radial strain (GRS) were calculated using RT3DE. GLS in Group A was significantly lower than the GLS in the control group. In patients with abnormal right ventricular function, GCS, GAS, GRS and GLS were lower in the group B than in healthy controls. Compared with the control subjects, GLS, GRS, and GAS were lower among PD patients, but the GCS was similar among the groups. The right ventricular GLS of patients undergoing peritoneal dialysis decreased prior to the decline in before the right ventricular ejection function became worse. GLS is a sensitive index marker for assessing right ventricular function in patients with peritoneal dialysis. In uremic patients undergoing peritoneal dialysis with obvious abnormal right ventricular systolic function, GLS, GRS, and GCS were all decreased.

**Keywords:** Peritoneal dialysis, real-time, three-dimensional echocardiography, speckle-tracking echocardiography, right ventricular function

#### Introduction

Traditionally, peritoneal dialysis (PD) without arteriovenous fistula, which can increase blood circulation pressure, has been recommended for uremic patients. Using this approach, the body volume changes occur slowly, and there is minimal risk of developing cardiovascular disease. PD patients do not require heparin treatment which can increase the bleeding risk and heart burden. Body circulation and metabolism remain stable. With residual renal function and controlled blood pressure, PD patients can experience improvement of anaemia and cardiac function [1, 2]. However, in clinical practice, even in patients in whom blood pressure is controlled, PD is not superior to haemodialysis (HD). With prolonged PD, increases in blood

pressure can lead to structural changes and ventricular dysfunction, especially if residual renal function decreases and peritoneal ultrafiltration capacity load increases. Although most available studies focused their attention on left ventricular (LV) dysfunction in end-stage renal disease (ESRD) patients, few studies have examined patients with right ventricular (RV) dysfunction. This type of dysfunction is important, as right ventricular dysfunction (RVD) has been associated with increased morbidity and mortality in many cardiovascular diseases [3, 4]. In a recent study, RV dysfunction was reported in two-thirds of patients on long-term dialysis [5]. Low RV ejection fraction was associated with increased mortality and hospitalization rates after adjustment for other prognostic variables. Thus, the assessment of RV function

rather than LV function is a necessary complement for determining the prognosis of patients with refractory heart failure. The impact of peritoneal dialysis treatments on the development of RVD has not been investigated. It is important to note that in patients with preserved left ventricular ejection fraction (EF), chronic volume overload may induce various adaptations of the right ventricle, thereby accelerating or delaying the progression toward right ventricular dysfunction [6]. However, accurate echocardiographic assessment of the right ventricle is difficult because of the ventricle's complex geometry, and the RV's retrosternal position limits echocardiographic imaging. More recently, three-dimensional (3D) speckle tracking echocardiography (3D-STE) has been introduced and demonstrated to be capable of accurately assessing myocardial deformation in all three spatial dimensions from 3D data sets [7-9]. 3D-STE has the potential to overcome the limitations of Doppler-based strain or 2D-based speckle-tracking strain [10]. 3D-STE measures myocardial deformation in the longitudinal, radial and circumferential directions by means of frame-by-frame tracking and may be used as a technique to assess RV volumes and function [11]. Other detection methods are limited in their ability to acquire a high-quality fullvolumetric 3D data set, whereas 3D-STE can assess the RV anterior wall and the RV apical lateral segments in patients with poor imaging windows and/or a dilated RV [12]. Data on the feasibility of 3D-STE in a routine clinical context are limited. The use of 3D-STE may be important in detecting the clinically asymptomatic RV dysfunction. This study aimed to identify early abnormalities of right ventricular structure and function in peritoneal dialysis patients using real-time three-dimensional echocardiography (RT3DE).

# Methods

# Study population

The study population included sixty-six patients undergoing peritoneal dialysis in our hospital from 2012 June to 2014 June, including 36 males and 30 females. The patients' ages ranged from 27 to 80 years old, and the average age was  $51.50\pm14.71$  years. Patients were included if they had received peritoneal dialysis for 3 to 51 months. They did not show obvious symptoms of heart failure, such as shortness of

breath, chest tightness, leg edema, and so on. They were in a relatively stable state in peritoneal dialysis. Patients were excluded from the study if the clinical evaluation revealed that the patients exhibited any of the following: chronic obstructive pulmonary disease, interstitial lung disease, connective tissue disease, chronic thromboembolic disease, left-to-right shunt congenital heart disease, primary pulmonary hypertension, pulmonary artery stenosis, obstruction of the right ventricular outflow tract, right ventricular pacemaker placement, right ventricular myocardial infarction, tricuspid valve disorders or cardiomyopathy. The uremic patients were evaluated routinely by echocardiography, and patients with left ventricular ejection fraction (LVEF) > 50% were included in the study. According to the Recommendations for Cardiac Chamber Quantification by Echocardiography in Adults, 3DE-derived RVEF can be considered a method for quantifying RV systolic function. Generally, RVEF < 45% reflect abnormal RV systolic function [13]. The PD patients were divided into 2 groups according to whether the RVEF was greater or less than 45%. Group A included patients with RVEF > 45% (45 patients), and the remaining patients were included in group B (21 patients). Twenty healthy volunteers composed the normal control group (group N), with were age- and gendermatched to the patients. All patients and healthy volunteers underwent blood pressure measurement, ECG, echocardiography dynamic mapping and other examinations to exclude the influence of various diseases of cardiac function. All patients signed an informed consent form before entering the study. Our study was approved by ethics committee of The Second Hospital Affiliated with Soochow University.

# Procedures

Standard echo-Doppler examinations were performed using a M5S transducer with harmonic capability, and the RT3DE data sets of the right ventricle were obtained using a 3D volumetric transducer of a Vivid E9 ultrasound machine (GE Healthcare, Horten, Norway). Heart rate (HR) and blood pressure (BP) were recorded at the end of the echocardiographic examination.

Standard echo-Doppler examination

The 2D standards used in our laboratory have been previously described. The quantitative

Healthy		0	F		
Control (20)	PD (66)	Ρ	RV > 45% (45)	45% (45) RV < 45% (21)	
53.15±15.84	51.50±14.71	0.667	53.66±15.34	53.66±15.34	0.085
8/20	30/66	0.667	21/45	9/21	0.772
71.20±10.68	74.00±12.90	0.380	75.04±12.60	71.76±13.55	0.321
- -	36/66	-	26/45	10/21	0.440
123.35±7.49	142.27±17.78	0.000	144.33±19.24	137.85±13.52	0.127
81.60±4.41	84.60±10.33	0.211	84.26±11.26	85.33±8.22	0.668
145.20±9.43	98.39±20.09	0.000	99.44±20.89	96.14±18.54	0.497
5.21±1.11	19.81±7.38	0.000	19.56±7.89	20.34±6.33	0.654
246.45±88.56	443.46±112.54	0.000	449.11±119.97	431.38±96.32	0.536
76.85±8.44	866.87±321.63	0.000	845.51±317.14	912.66±334.22	0.372
0.73±0.10	5.90±1.32	0.000	5.87±1.39	5.96±1.19	0.764
	Healthy Control (20) 53.15±15.84 8/20 71.20±10.68 5 - 123.35±7.49 81.60±4.41 145.20±9.43 5.21±1.11 246.45±88.56 76.85±8.44 0.73±0.10	Healthy Control (20)         PD (66)           53.15±15.84         51.50±14.71           8/20         30/66           71.20±10.68         74.00±12.90           71.20±10.68         74.00±12.90           123.35±7.49         142.27±17.78           81.60±4.41         84.60±10.33           145.20±9.43         98.39±20.09           5.21±1.11         19.81±7.38           246.45±88.56         443.46±112.54           76.85±8.44         866.87±321.63           0.73±0.10         5.90±1.32	Healthy Control (20)         PD (66)         P           53.15±15.84         51.50±14.71         0.667           8/20         30/66         0.667           71.20±10.68         74.00±12.90         0.380           7         -         36/66         -           123.35±7.49         142.27±17.78         0.000           81.60±4.41         84.60±10.33         0.211           145.20±9.43         98.39±20.09         0.000           5.21±1.11         19.81±7.38         0.000           246.45±88.56         443.46±112.54         0.000           76.85±8.44         866.87±321.63         0.000           0.73±0.10         5.90±1.32         0.000	$\begin{array}{c} \mbox{Healthy}\\ \mbox{Control (20)} \end{array} & \mbox{PD (66)} & \mbox{P} & \frac{\mbox{F}}{\mbox{RV} > 45\% (45)} \\ \mbox{S1.5\pm15.84} & 51.50\pm14.71 & 0.667 & 53.66\pm15.34 \\ \mbox{S20} & 30/66 & 0.667 & 21/45 \\ \mbox{S20} & 30/66 & 0.667 & 21/45 \\ \mbox{S20} & 30/66 & - & 26/45 \\ \mbox{S20} & - & 36/66 & - & 26/45 \\ \mbox{S20} & - & 36/66 & - & 26/45 \\ \mbox{S20} & - & 36/66 & - & 26/45 \\ \mbox{S20} & 142.27\pm17.78 & 0.000 & 144.33\pm19.24 \\ \mbox{S1.60} & 443.60\pm10.33 & 0.211 & 84.26\pm11.26 \\ \mbox{S20} & 48.60\pm10.33 & 0.211 & 84.26\pm11.26 \\ \mbox{S20} & 145.20\pm9.43 & 98.39\pm20.09 & 0.000 & 99.44\pm20.89 \\ \mbox{S21} & 19.81\pm7.38 & 0.000 & 19.56\pm7.89 \\ \mbox{S246.45} & 88.56 & 443.46\pm112.54 & 0.000 & 449.11\pm119.97 \\ \mbox{76.85} & 8.44 & 866.87\pm321.63 & 0.000 & 5.87\pm317.14 \\ \mbox{O.73} & 0.73\pm0.10 & 5.90\pm1.32 & 0.000 & 5.87\pm1.39 \end{array}$	$\begin{array}{c c c c c c } & PD(66) & P & \hline PD(66) \\ \hline PD(66) & P & \hline RV > 45\%(45) & RV < 45\%(21) \\ \hline RV > 45\%(45) & 51.60 \pm 14.71 & 0.667 & 53.66 \pm 15.34 & 53.66 \pm 15.34 \\ \hline S3.15 \pm 15.84 & 51.50 \pm 14.71 & 0.667 & 21/45 & 9/21 \\ \hline S3.62 & 30/66 & 0.667 & 21/45 & 9/21 \\ \hline 71.20 \pm 10.68 & 74.00 \pm 12.90 & 0.380 & 75.04 \pm 12.60 & 71.76 \pm 13.55 \\ \hline 7. & 36/66 & - & 26/45 & 10/21 \\ \hline 123.35 \pm 7.49 & 142.27 \pm 17.78 & 0.000 & 144.33 \pm 19.24 & 137.85 \pm 13.52 \\ \hline 81.60 \pm 4.41 & 84.60 \pm 10.33 & 0.211 & 84.26 \pm 11.26 & 85.33 \pm 8.22 \\ \hline 145.20 \pm 9.43 & 98.39 \pm 20.09 & 0.000 & 99.44 \pm 20.89 & 96.14 \pm 18.54 \\ \hline 5.21 \pm 1.11 & 19.81 \pm 7.38 & 0.000 & 19.56 \pm 7.89 & 20.34 \pm 6.33 \\ \hline 246.45 \pm 88.56 & 443.46 \pm 112.54 & 0.000 & 449.11 \pm 19.97 & 431.38 \pm 96.32 \\ \hline 76.85 \pm 8.44 & 866.87 \pm 321.63 & 0.000 & 5.87 \pm 1.39 & 5.96 \pm 1.19 \\ \hline \end{array}$

Table 1. Clinical parameter in patients with PD patients and healthy subjects

SBP, systolic blood pressure; DBP, diastolic blood pressure; HGB, hemoglobin; CERA, creatinine; URCA, uric acid; CYC, Cystatin C.

analysis of the left ventricle was performed according to the recommended guidelines. Two-dimensional LVEF was derived from the LV end-diastolic and end-systolic volumes calculated according to the Simpson rule. Right atrial and ventricular lengths were measured in the apical four-chamber view. The LV study was used to measure the left ventricular internal diastolic diameter (LVIDd), left ventricular internal systolic diameter (LVIDs) and interventricular septal thickness at diastole (IVSd). In the presence of tricuspid valve regurgitation, systolic pulmonary artery pressure was calculated using the simplified Bernoulli equation: sPAP =  $4^{*}$ (tricuspid systolic jet)<sup>2</sup> + right atrial pressure. According to the echocardiographic criteria, pulmonary hypertension was defined as sPAP > 35 mmHg at rest [14].

# Real-time 3D echocardiography

Three-dimensional echocardiographic examination was performed from an apical position. RV measurements were performed by applying the LV model to fit the RV, with semiautomated border detection and manual editing of the borders to generate a 3D model from which volumes can be measured without geometric assumptions. To create a full-volume data set, 4 smaller real-time volumes acquired from 4 consecutive cardiac cycles were combined to form a larger pyramidal volume. Apical full-volume acquisition was obtained to visualize the entire RV in a volumetric image. While retaining the entire RV within the pyramidal volume, depth and sector width were decreased as much as possible to improve the temporal and spatial resolution of the image, resulting in a volume rate of > 25 volumes/sec. The full-volume mode was initiated after the acquisition of a satisfactory image of the apical four-chamber view, and the three-dimensional images of the right ventricle were obtained during a single breath-hold. Contour tracing was performed with semiautomatic border detection, after first identifying the apex and tricuspid annulus on each slice, the endocardial borders of each frame were fit to a preconfigured ellipse and adjusted. If the acquisition was considered suboptimal, the data set was re-acquired. Data sets were stored digitally in a raw data format and were exported to a separate workstation (Echopac, PC 110.1.1, GE Healthcare) equipped with commercially available software (4D Auto LVQ software, GE Healthcare) for off-line analysis of RV volumes, EF, RV mass, and 3DSTE deformation parameters. RV analysis was performed according to a previously described methodology [15]. The right ventricular wall was divided into 17 segments, and the strain curves and peak systolic strain values for each segment and overall right ventricular wall were obtained. Global longitudinal strain (GLS), global circumferential strain (GCS), global radial strain (GRS), and the global area strain (GAS) were generated, measured and statistically analysed. Contrary to directional strains, which are calculated from changes of distance in their respective directions, the area strain (AS) is a measure of the relative percentage change in the area of a given myocardial segment, thus representing the percentage change of the

Verieble	Healthy		0	P	— P	
Variable	Control (20)	PD (66)	Р	RV > 45% (45) RV < 45% (		
LVEF (%)	62.27±4.35	60.83±6.48	0.355	61.59±6.79	59.54±5.62	0.135
LVFS (%)	35.00±3.82	32.55±5.36	0.061	32.84±5.96	31.92±3.84	0.498
LVIDd(mm)	45.44±2.66	51.55±6.21	0.000	51.18±6.60	52.34±5.33	0.438
LVIDs (mm)	28.23±4.85	34.65±5.92	0.000	34.37±6.52	35.62±4.43	0.558
IVSd (mm)	8.63±0.99	10.73±1.85	0.000	10.81±2.00	10.57±1.50	0.609
RV basal (mm)	33.40±3.73	32.83±6.19	0.699	32.77±6.30	32.95±6.08	0.909
RA long axis (mm)	38.05±3.11	44.72±7.12	0.000	44.51±7.05	45.19±7.42	0.692
RA minor axis (mm)	31.10±4.42	33.43±6.15	0.118	33.88±5.82	32.47±6.86	0.361
PA systolic pressure (mmHg)	22.91±4.45	27.50±8.01	0.017	26.82±7.10	28.96±9.73	0.275

 Table 2. 2D echocardiographic parameters

LVEF, left ventriculer ejection fraction; LVFS, left ventricular fractional shortening; LVIDd, left ventricular internal diastolic diameter; LVIDs, left ventricular internal systolic diameter; IVSI, interventricular septal thickness at diastole; RA, right atrium; RV, right ventriculer; PA: pulmonary artery.

myocardial surface from its original dimensions. Using this approach, RV end-diastolic (EDV, mL) and RV end-systolic volume (ESV, mL) were calculated, and the stroke volume (SV, mL EDV-ESV), cardiac output (CO, L/m SV × HR), and RVEF [(EDV-ESV)/EDV × 100%] were derived. RV mass [(RV, g epicardial volume-RV endocardial volume) × 1.05] was estimated at end-diastole using automated border detection with optional manual adjustment.

### Statistical analysis

Statistical analysis was performed using SPSS software version 17.0. Continuous variables are expressed as mean  $\pm$  SD, and nominal variables are expressed as percentages. Categorical variables were compared between groups using the ANOVA, which were adjusted for age and gender. The *p* values after adjustment are presented. The null hypothesis was rejected at  $P \le 0.05$ . Two-tailed values of  $P \le 0.05$  were considered statistically significant. Reproducibility analyses (intra- and interobserver variability) were performed by calculating intraclass correlation coefficients (rho). Bland-Altman plots for interobserver differences and average values were generated for GAS, GLS, GRS, and GCS.

### Results

### Clinical features (Table 1)

Age, gender, and heart rate were similar in the peritoneal dialysis group and in the control subjects. Compared with the control group, the PD group exhibited a significantly higher systolic blood pressure  $(142.27\pm17.78 \text{ mmHg})$  and urea  $(19.81\pm7.38 \text{ mmol/L})$ , creatinine  $(866.87\pm$ 321.63 umol/L) and cystatin  $(5.90\pm1.32 \text{ mg/L})$ levels but lower HGB  $(98.39\pm20.09 \text{ g/L})$ . These indexes did not significantly differ between in group A and group B.

### 2D echocardiographic parameters (Table 2)

The LV ejection fraction and left ventricular fractional shortening (LVFS) were similar in all groups, although the PD group exhibited a higher left ventricular LVIDd and LVIDs than did the control subjects. The interventricular septum in the PD group exhibited greater thickening than the control subjects (10.73±1.85 mm vs. 8.63±0.99 mm), indicating that the left ventricular function was normal but was accompanied by structural changes in the left ventricle. The pulmonary arterial pressure was significantly increased in the PD group compared with the normal control group (27.50±8.01 mmHg vs. 22.91±4.45 mmHg). There were significant differences (P < 0.0001) in the RA long axis diameter, whereas there were no differences (P=0.699) in the RV size. There were no significant differences in any 2D echocardiographic parameters between the subgroups of patients with RVEF < 45% or  $\geq 45\%$ .

### 3D echocardiographic parameters (Table 3)

RVEDV and RVESV were similar between the peritoneal dialysis group and the control subjects. The right ventricular diastolic volume did not significantly change in any of the three groups. RV mass was higher in the PD group.

				l la altibu	PD			PD	_
Variable	Control (20)	PD (66)	Р	Control (20)	RV > 45%	Р	Control (20)	RV < 45%	P
				. ,	(45)		. ,	(21)	
RVEDV, ml	47.35±11.28	50.09±17.36	0.509	47.35±11.28	50.04±17.64	0.540	47.35±11.28	50.19±17.17	0.578
RVESV, ml	18.95±7.27	22.57±9.13	0.108	18.95±7.27	20.20±8.10	0.574	18.95±7.27	27.66±9.31	0.001
GLS, %	-27.63±4.12	-23.40±5.18	0.001	-27.63±4.12	-24.09±5.00	0.009	-27.63±4.12	-21.92±5.37	0.000
GRS, %	74.16±21.52	62.56±19.09	0.023	74.16±21.52	66.42±19.82	0.136	74.16±21.52	54.27±14.66	0.001
GAS, %	-40.20±10.67	-32.90±10.97	0.010	-40.20±10.67	-35.35±6.50	0.089	-40.20±10.67	-27.65±15.98	0.000
GCS, %	-16.82±5.11	-15.94±3.79	0.406	-16.82±5.11	-16.75±3.93	0.945	-16.82±5.11	-14.21±2.83	0.041
CO, L/m	2.11±0.54	2.02±0.83	0.642	2.11±0.54	2.21±0.82	0.614	2.11±0.54	1.60±0.69	0.031
SV, mL	28.55±6.66	27.54±10.82	0.696	28.55±6.66	29.86±11.09	0.612	28.55±6.66	22.57±8.48	0.050
SPI	0.39±0.15	0.38±0.11	0.752	0.39±0.15	0.39±0.11	0.942	0.39±0.15	0.37±0.10	0.500
RVEF, %	61.25±7.97	54.07±9.90	0.004	61.25±7.97	59.64±6.44	0.338	61.25±7.97	42.14±2.81	0.000
RVmass, g	81.30±10.63	89.74±15.90	0.029	81.30±10.63	87.13±15.16	0.140	81.30±10.63	95.33±16.38	0.003

Table 3. 3D echocardiographic parameters of right ventriculer in with PD patients and healthy subjects

RVEDV, right ventricular end-diastolic volume; RVESV, right ventricular end-systolic volume; GLS, global longitudinal strain; GCS, global circumferential strain; GRS, global radial strain; GAS, global area strain; CO, cardiac output; SV, stroke volume; SPI, Spherical index; RVEF, right ventricular ejection fraction.



Figure 1. GLS: PD Group A VS. healthy subjects (the left one is the GLS of PD Group A and the right one is the GLS of the healthy subjects).

Compared with the control subjects, the right ventricle GLS (-23.40 $\pm$ 5.18%), GRS (62.56 $\pm$ 19.09%), and GAS (-32.90 $\pm$ 10.97%) were decreased in the PD group, although the GCS (-15.94 $\pm$ 3.79%) remained at a normal level. The GLS (-24.09 $\pm$ 5.00%) of Group A was significantly lower than the GLS (-27.63 $\pm$ 4.12%) of the control group (**Figure 1**). Among peritoneal dialysis patients with normal right ventricular EF, 3D speckle tracking technology revealed decreased GLS. Among the patients with abnormal right ventricular ejection function, the

GCS, GAS, GRS and GLS were all reduced in Group B relative to healthy controls ( $-14.21\pm$ 2.83% vs.  $-16.82\pm5.11\%$ ,  $-27.65\pm15.98\%$  vs.  $-40.20\pm10.67\%$ ,  $54.27\pm14.66\%$  vs.  $74.16\pm$ 21.52%, and  $-21.92\pm5.37\%$  vs.  $-27.63\pm4.12\%$ , respectively) (Figure 2).

### Reproducibility of 3D-STE measurements

A Bland-Altman plot of the GLS, GCS, GRS, and GAS interobserver differences were depicted in **Figure 3**; the extent of agreement between the two observers was adequate (**Figure 3**).

# Right ventricular function assessed by three-dimensional speckle tracking





Figure 2. PD group B VS. healthy subjects (the left were GLS, GCS, GAS and GRS of the PD Group B and the right were GLS, GCS, GAS and GRS of healthy subjects).

### Discussion

### The PD group vs. the control group

Due to the superior ability of peritoneal dialysis to preserve residual renal function compared with haemodialysis, mortality rates associated with dialysis have decreased during the first few years [16, 17]. A study reported that the mortality of patients on peritoneal dialysis was significantly associated with hypertension, decreased sodium removal, and low total fluid removal [18]. Peritoneal membranes remove mid-sized molecules and protein-bound molecules more efficiently but have fewer pores of greater diameter [16]. The retention of uremic toxins in the blood of PD patients can significantly inhibit the energy metabolism of myocardial cells. Peritoneal dialysis is unable to effectively clear all uremic toxins, resulting in sustained damage to the myocardium in PD patients. According to the results of this present study, we can infer that toxins can easily damage the myocardium, as evidenced by changes in the GAS, GRS, and GLS, although GCS damage was not obvious. The right ventricles are composed multiple layers, as described by Ho and Nihoyannopoulos, and the superficial and deep muscle layers mainly comprise the RV wall. The superficial layer fibres are arrayed circumferentially in a direction that is parallel to

the atrioventricular (AV) groove [19, 20]. The GCS is representative of the superficial myocardium strain rate, and the lack of change in this parameter suggests that the effects of toxins on the superficial layer in uraemia patients are less serious than effects on the inner layer. Compared with the control group, the pulmonary artery pressure of patients in the peritoneal dialysis group was increased. To adapt to the high pressure of pulmonary circulation, the end systolic pressure of the right ventricle increases. This study demonstrated that sPAP and RV mass increased in the peritoneal dialysis group. Long-term right ventricular pressure overload leads to functional tricuspid valve insufficiency, initiating pathological RV remodelling and resulting in decreased wall stress, which ultimately induces right heart failure. Our study also revealed that the LV volume increased and that the LV wall thickened, suggesting the development of LV hypertrophy in the PD group. A long-term increase in peripheral resistance can result in cardiac muscle thickening and interstitial fibrous proliferation, eventually leading to ventricular wall hypertrophy. Additionally, the quality of the right ventricle increased before any obvious changes in right ventricular morphology were observed. A previous study confirmed that LV hypertrophy was more severe in patients on long-term continuous peritoneal dialysis than in patients on hae-



Figure 3. Bland-Altman plot of inter-observer difference of the GLS, GCS, CRS, GAS. Continuous lines are 95% confidence intervals of between-measure differences.

modialysis [21]. These results suggest that the toxins induced both LV hypertrophy and RV hypertrophy and that these changes may therefore represent pathological adaptations.

# The group A vs. the control group

This comparison demonstrated early right ventricular dysfunction in peritoneal dialysis patients with preserved left ventricular ejection fraction. Global longitudinal strain (GLS) was assessed by the software as the average strain of all segments in the 17-LV-segment model and was calculated by averaging values observed in all RV segments [22]. The deep muscle fibres of the RV are longitudinally ordered from base to apex. The GLS is representative of the superficial myocardium strain rate. The creatinine and urea in the uremic patients undergoing peritoneal dialysis were relatively unchanged. Changes in the levels of creatinine, urea and other toxins may firstly affect the sub-

endocardial layer, which suggests that the deep muscle fibres in the uremic patients undergoing peritoneal dialysis were impaired in the early stage of right ventricular dysfunction. Furthermore, the subendocardial layer is vulnerable to the effect of pressure and ischemia, which are more commonly associated in elderly or hypertensive patients [23]. Other studies have reported that the changes in the serum levels of tissue inhibitor of matrix metalloproteinase indicate that a change in collagen turnover and the myocardial fibrotic process may be associated with impaired longitudinal strain generated in this early LV dysfunction [24], and this association may extend to the right ventricle. A previous study reported that the rate of decline in residual renal function has more influence than the baseline residual renal function in pretesting all-cause mortality and technique failure in patients on long-term peritoneal dialysis. Differences in loading conditions, compliance with a lower after load in the RV, and

the predominance of longitudinal and oblique myocardial fibres in the RV may also influence mortality [25]. Longitudinal strain was reduced when the EF and both radial and circumferential strain remained normal [26]. The GLS was precociously reduced, although the area and radial and circumferential strain were preserved, suggesting normal RV systolic function. The longitudinal strain was lower in patients undergoing peritoneal dialysis with right ventricular EF > 45% compared with the control subjects. Therefore, we can conclude that the longitudinal stain has the high sensitivity in the assessment of right ventricular function. When right ventricular function is normal in PD patients, three-dimensional speckle tracking can detect dysfunction using the global longitudinal strain.

# Group B vs. the control group

PD patient exhibit a reduced ability to remove water to reduce volume load and decrease blood pressure. The development of overhydration may be exacerbated by the limited capacity for sodium removal during peritoneal dialysis. An EF < 45% in uremic PD patients is suggestive of abnormal right ventricular function. Overhydration promotes the development of left ventricular hypertrophy (LVH) and elevated serum concentrations of natriuretic peptides due to increased production by the myocardium, particularly the right ventricle. Threedimensional speckle tracking revealed that GLS, GRS, GAS, and GCS were decreased in Group B patients. These results indicated that if the right ventricular EF is < 45%, the longitudinal, radial, circumferential and area strain were impaired. Additionally, these abnormalities involving the GLS, GRS, GCS and GAS were evident in uremic patients and resulted in only minor changes of the RV geometry and abnormal EF. In a recent study, Cho et al explained that more advanced myocardial involvement is associated with a decrease in and that circumferential strain is more closely associated with prognosis than longitudinal strain in ischemic HF. Longitudinal contraction, circumferential shortening, and radial thickening are all involved in RV systolic function; circumferential strain is triggered by muscle fibres in the midwall [27] and may better reflect intrinsic contractility than the contraction of fibres in the endocardium [24]. RT3DE-derived STE can track the motion of the speckles irrespective of their direction because the speckles remain within the selected scan volume, an aspect that might be particularly relevant in the quantification of radial strain. GRS is less robust and less reproducible than GLS or GCS due to the need to evaluate variable levels of heartbeat function and the different effect of the undetectable third displacement vector. Because area strain is a parameter integrating longitudinal and circumferential deformation, a more global and comprehensive evaluation of right ventricular systolic function should be provided. Thus, unlike radial, circumferential, or longitudinal strain, area strain represents the percentage change in the endocardial surface area from its original dimension, whereas direction strain reflects changes in distance in the respective directions. In the comparison of RV dysfunction and control subjects. GAS was significantly lower in patients with RV dysfunction. Similarly, Yu et al reported that RV GAS was impaired in association with RV dyssynchrony, volume overload and reduced EF in adults after tetralogy of Fallot repair [28]. Associations between peritoneal ultrafiltration and mortality have been conformed in anuric patients. When fluid intake is not adapted to peritoneal ultrafiltration, patients will develop overhydration, and the risk of cardiovascular events will increase. The effect of the RV on the pumping action of the heart tends to be influenced by capacity, volume load and pressure load. Thus, the systolic function of the RV is almost exclusively dependent on the afterload that the cardiac chamber must confront [29]. Indeed, in patients with advanced HF, independent of LV function, impairment of RV systolic function is consistently associated with worse outcomes [30]. In the largest study to date evaluating the impact of RV function on outcomes in patients with advanced systolic HF, chronic volume overload was demonstrated to affect right ventricular function independent of post-load conditions. In chronic volume overload, an increase in body water amplifies the effects of the predisposing factors, leading right ventricular dysfunction, demonstrating a correlation between hydration status and pulmonary pressure [31]. We believe that overhydration may be the most important of the cardiovascular risk factors specific to peritoneal dialysis. The risk of overhydration increases with deteriorating residual renal function and is obviously highest in anuric

patients. All of the above factors lead to decreased GLS, GRS, GAS, and GCS in uremic patients undergoing peritoneal dialysis and are indexes of RV function reflect intrinsic myocardial function.

## Conclusion

The right ventricular GLS of patients undergoing peritoneal dialysis decreased prior to decreases in right ventricular ejection function. Therefore, GLS is a sensitive index for assessing right ventricular function in patients undergoing peritoneal dialysis. GCS was the last mark to be affected by RV function. In uremic patients with abnormal right ventricular systolic function, GLS, GRS, GAS, and GCS all decreased upon peritoneal dialysis. These factors are indexes of RV function specifically reflect intrinsic myocardial function. Therefore, threedimensional (3D) speckle tracking echocardiography (3D-STE) is capable of accurately assessing myocardial deformation of the RV function, and subclinical intrinsic myocardial dysfunction may be detectable by 3D-STE. This new approach presents an additional, reliable detection method for early myocardial deformation by standard echocardiography abnormalities. All of the parameters obtained by RT3DE were sufficiently reliable.

# Limitations

One limitation of this study was the lack of randomization. Thus, a control group of patients undergoing HD or uremic patients not undergoing any dialysis were not included in the analysis. Another limitation was that the effect of abnormal RV was not specifically described as part of this study. Furthermore, the largest proportion of patients were enrolled from the Soochow site. Technical limitations of each speckle-tracking method include endocardial border tracing, where care must be taken to manually fine-tune the width or the region of interest for appropriate tracking. A relatively high degree of intraobserver variability of speckle tracking analysis was observed in this present study, even with an experienced core lab. Accordingly, speckle tracking, similar to tissue Doppler dyssynchrony analysis, requires training and experience to achieve reproducible results. Another limitation was that other measures of dyssynchrony, such as using tissue Doppler, were not compared in this same group

of patients. However, this multiple method comparison was beyond the scope of the present study, which focused on speckle-tracking echocardiography. Future larger studies would be useful to further elucidate the role of speckle-tracking echocardiography for the assessment of right ventricular function.

## Disclosure of conflict of interest

### None.

Address correspondence to: Dr. Jianchang Chen, Department of Internal Medicine-Cardiovascular, The Second Hospital Affiliated to Soochow University, Suzhou, Jiangsu, China. Tel: 86-512-67784077; Fax: 86-512-67783689; E-mail: chenjcsz@126.com

### References

- Fassett RG, Driver R, Healy H, Coombes JS. Cardiovascular disease in peritoneal dialysis patients. Panminerva Med 2009; 51: 151-61.
- [2] Krediet RT, Balafa O. Cardiovascular risk in the peritoneal dialysis patient. Nat Rev Nephrol 2010; 6: 451-60.
- [3] de Groote P, Millaire A, Foucher-Hossein C, Nugue O, Marchandise X, Ducloux G, Lablanche JM. Right ventricular ejection fraction is an independent predictor of survival in patients with moderate heart failure. J Am Coll Cardiol 1998; 32: 948-54.
- [4] Voelkel NF, Quaife RA, Leinwand LA, Barst RJ, McGoon MD, Meldrum DR, Dupuis J, Long CS, Rubin LJ, Smart FW, Suzuki YJ, Gladwin M, Denholm EM, Gail DB; National Heart, Lung, and Blood Institute Working Group on Cellular and Molecular Mechanisms of Right Heart Failure. Right ventricular function and failure: report of a National Heart, Lung, and Blood Institute working group on cellular and molecular mechanisms of right heart failure. Circulation 2006; 114: 1883-91.
- [5] Paneni F, Gregori M, Ciavarella GM, Sciarretta S, De Biase L, Marino L, Tocci G, Principe F, Domenici A, Luciani R, Punzo G, Menè P, Volpe M. Right ventricular dysfunction in patients with end-stage renal disease. Am J Nephrol 2010; 32: 432-8.
- [6] Piazza G, Goldhaber SZ. The acutely decompensated right ventricle: pathways for diagnosis and management. Chest 2005; 128: 1836-52.
- [7] Gayat E, Ahmad H, Weinert L, Lang RM, Mor-Avi V. Reproducibility and inter-vendor variability of left ventricular deformation measurements by three-dimensional speckle-tracking

echocardiography. J Am Soc Echocardiogr 2011; 24: 878-85.

- [8] de Isla L P, Balcones DV, Fernandez-Golfin C, Marcos-Alberca P, Almería C, Rodrigo JL, Macaya C, Zamorano J. Three-dimensionalwall motion tracking: a new and faster tool for myocardial strain assessment: comparison with two-dimensional-wall motion tracking. J Am Soc Echocardiogr 2009; 22: 325-30.
- [9] Cheung YF. The role of 3D wall motion tracking in heart failure. Nat Rev Cardiol 2012; 9: 644-57.
- [10] Luo XX, Fang F, Lee AP, Sun JP, Li S, Zhang ZH, Sanderson JE, Kwong JS, Zhang Q, Wang J, Yu CM. What can three-dimensional speckletracking echocardiography contribute to evaluate global left ventricular systolic performance in patients with heart failure. Int J Cardiol 2014; 172: 132-7.
- [11] Hammoudi N, Cohen A. Right ventricular systolic function assessment by echocardiography in routine clinical practice: simple and feasible. Arch Cardiovasc Dis 2014; 107: 505-7.
- [12] Lang RM, Badano LP, Tsang W, Adams DH, Agricola E, Buck T, Faletra FF, Franke A, Hung J, de Isla LP, Kamp O, Kasprzak JD, Lancellotti P, Marwick TH, McCulloch ML, Monaghan MJ, Nihoyannopoulos P, Pandian NG, Pellikka PA, Pepi M, Roberson DA, Shernan SK, Shirali GS, Sugeng L, Ten Cate FJ, Vannan MA, Zamorano JL, Zoghbi WA; American Society of Echocardiography; European Association of Echocardiography. EAE/ASE recommendations for image acquisition and display using three-dimensional echocardiography. Eur Heart J Cardiovasc Imaging 2012; 13: 1-46.
- [13] Lang RM, Badano LP, Mor-Avi V, Afilalo J, Armstrong A, Ernande L, Flachskampf FA, Foster E, Goldstein SA, Kuznetsova T, Lancellotti P, Muraru D, Picard MH, Rietzschel ER, Rudski L, Spencer KT, Tsang W, Voigt JU. Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. J Am Soc Echocardiogr 2015; 28: 1-39, e14.
- [14] Rosenkranz S. Pulmonary hypertension: current diagnosis and treatment. Clin Res Cardiol 2007; 96: 527-41.
- [15] Muraru D, Badano LP, Piccoli G, Gianfagna P, Del Mestre L, Ermacora D, Proclemer A. Validation of a novel automated border-detection algorithm for rapid and accurate quantitation of left ventricular volumes based on three-dimensional echocardiography. Eur J Echocardiogr 2010; 11: 359-68.
- [16] Dhondt A, Vanholder R, Van Biesen W, Lameire N. The removal of uremic toxins. Kidney Int Suppl 2000; 76: S47-59.

- [17] Lameire N, Vanholder R, De Smet R. Uremic toxins and peritoneal dialysis. Kidney Int Suppl 2001; 78: S292-7.
- [18] Ates K, Nergizoglu G, Keven K, Sen A, Kutlay S, Ertürk S, Duman N, Karatan O, Ertuğ AE. Effect of fluid and sodium removal on mortality in peritoneal dialysis patients. Kidney Int 2001; 60: 767-76.
- [19] Dell'Italia ⊔. The right ventricle: anatomy, physiology, and clinical importance. Curr Probl Cardiol 1991; 16: 653-720.
- [20] Ho SY, Nihoyannopoulos P. Anatomy, echocardiography, and normal right ventricular dimensions. Heart 2006; 92 Suppl 1: i2-13.
- [21] Enia G, Mallamaci F, Benedetto FA, Panuccio V, Parlongo S, Cutrupi S, Giacone G, Cottini E, Tripepi G, Malatino LS, Zoccali C. Long-term CAPD patients are volume expanded and display more severe left ventricular hypertrophy than haemodialysis patients. Nephrol Dial Transplant 2001; 16: 1459-64.
- [22] Meris A, Faletra F, Conca C, Klersy C, Regoli F, Klimusina J, Penco M, Pasotti E, Pedrazzini GB, Moccetti T, Auricchio A. Timing and magnitude of regional right ventricular function: a speckle tracking-derived strain study of normal subjects and patients with right ventricular dysfunction. J Am Soc Echocardiogr 2010; 23: 823-31.
- [23] Sun AL, Wu YY, Hung MJ. Quantification of left ventricular regional myocardial function using two-dimensional speckle tracking echocardiography in healthy volunteers-a multi-center study. 2013.
- [24] Lang RM, Bierig M, Devereux RB, Flachskampf FA, Foster E, Pellikka PA, Picard MH, Roman MJ, Seward J, Shanewise JS, Solomon SD, Spencer KT, Sutton MS, Stewart WJ; Chamber Quantification Writing Group; American Society of Echocardiography's Guidelines and Standards Committee; European Associationof Echocardiography. Recommendations for chamber quantification: a report from the American Society of Echocardiography's Guidelines and Standards Committee and the Chamber Quantification Writing Group, developed in conjunction with the European Association of Echocardiography, a branch of the European Society of Cardiology. J Am Soc Echocardiogr 2005; 18: 1440-63.
- [25] Torrent-Guasp F, Ballester M, Buckberg GD, Carreras F, Flotats A, Carrió I, Ferreira A, Samuels LE, Narula J. Spatial orientation of the ventricular muscle band: physiologic contribution and surgical implications. J Thorac Cardiovasc Surg 2001; 122: 389-92.
- [26] Galderisi M, Lomoriello VS, Santoro A, Esposito R, Olibet M, Raia R, Di Minno MN, Guerra G, Mele D, Lombardi G. Differences of myocardial systolic deformation and correlates of diastolic

function in competitive rowers and young hypertensives: a speckle-tracking echocardiography study. J Am Soc Echocardiogr 2010; 23: 1190-8.

- [27] Hurlburt HM, Aurigemma GP, Hill JC, Narayanan A, Gaasch WH, Vinch CS, Meyer TE, Tighe DA. Direct ultrasound measurement of longitudinal, circumferential, and radial strain using 2-dimensional strain imaging in normal adults. Echocardiography 2007; 24: 723-31.
- [28] Kleijn SA, Aly MF, Terwee CB, van Rossum AC, Kamp O. Three-dimensional speckle tracking echocardiography for automatic assessment of global and regional left ventricular function based on area strain. J Am Soc Echocardiogr 2011; 24: 314-21.

- [29] Hunt SA. Pulmonary hypertension in severe congestive heart failure: how important is it. J Heart Lung Transplant 1997; 16: S13-5.
- [30] Kalogeropoulos AP, Vega JD, Smith AL, Georgiopoulou VV. Pulmonary hypertension and right ventricular function in advanced heart failure. Congest Heart Fail 2011; 17: 189-98.
- [31] Paneni F, Gregori M, Ciavarella GM, Sciarretta S, De Biase L, Marino L, Tocci G, Principe F, Domenici A, Luciani R, Punzo G, Menè P, Volpe M. Right ventricular dysfunction in patients with end-stage renal disease. Am J Nephrol 2010; 32: 432-8.