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ARTYKUŁ ORYGINALNY / *ORIGINAL ARTICLE*

Evaluation of left atrial function using two--dimensional speckle tracking echocardiography in end-stage renal disease patients with preserved left ventricular ejection fraction

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Abstract

Background: Left atrial (LA) deformation analysis by two-dimensional speckle tracking echocardiography (2D-STE) has recently been proposed as an alternative approach for estimating left ventricular (LV) filling pressure and dysfunction.

Aim: To assess the LA myocardial function using 2D-STE in end-stage renal disease (ESRD) patients with preserved LV ejection fraction (PLVEF) and to evaluate the relationship of the obtained results with echocardiographically estimated pulmonary capillary wedge pressure (ePCWP).

Methods: Eighty-five ESRD patients and 60 healthy individuals were enrolled in the study. Images of the LA were acquired from apical two- and four-chamber views. The LA volumes (LAV) were calculated using the biplane area-length method. The LA volume indices (LAVI) were calculated by dividing the LA volumes by the body surface area. The LA strain (%) (LA_S) parameters (systolic [$LA_{S\text{-}S}$], early diastolic [$LA_{S\text{-}E}$], late diastolic [$LA_{S\text{-}A}$] during atrial contraction) were assessed, and the ePCWP was calculated according to the following formula: ePCWP = 1.25(E/E') + 1.9. LA stiffness was calculated non-invasively and based on the ratio of E/E' to $LA_{S\text{-}S}$.

Results: In patients with ESRD, the $LA_{S\text{-}S}$ (32.22 ± 7.64% vs. 57.93 ± 8.71%; $p < 0.001$), $LA_{S\text{-}E}$ (–15.86 ± 5.7% vs. –33.37 ± 7.71%; $p < 0.001$), and the $LA_{S\text{-}A}$ (–15.41 ± 4.16% vs. –24.57 ± 4.68%; $p < 0.001$) values were observed to be lower than the healthy group; while the LA stiffness (0.4 ± 0.19 vs. 0.17 ± 0.05; $p < 0.001$) value was higher. When the patients with ESRD were divided into two groups as those with a maximum LAVI value over 31.34 mL/m^2 and those with a maximum LAVI below this value, the $LA_{S\text{-}S}$ (30.36 ± 8.32% vs. 34.11 ± 6.43%; $p = 0.023$) and the $LA_{S\text{-}E}$ (–14.97 ± 5.88% vs. –16.76 ± 5.42%; $p = 0.039$) values were lower in the group with a LAVI value over 31.34 mL/m^2; while the $LA_{S\text{-}A}$ (–16.06 ± 4.44% vs. –14.75 ± 3.8%; $p < 0.001$) and LA stiffness (0.4 ± 0.19 vs. 0.17 ± 0.05; $p < 0.001$) values were higher. An association was observed between the ePCWP and $LA_{S\text{-}S}$ ($p < 0.001$), $LA_{S\text{-}E}$ ($p = 0.01$), $LA_{S\text{-}A}$ ($p < 0.001$), and LA stiffness ($p < 0.001$) values.

Conclusions: The results of our study have demonstrated that LA myocardial function assessed using the 2D-STE method is associated with the ePCWP, which is an echocardiographically calculated marker of LV dysfunction. The LA deformation parameters may be used as echocardiographic findings to predict the LV dysfunction in ESRD patients with PLVEF. Further studies are needed to determine the independent prognostic power of the atrial strain measurement as a predictor of future cardiovascular events in ESRD patients.

Key words: end-stage renal disease, left atrial strain

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INTRODUCTION

Chronic renal failure leads to structural changes and functional abnormalities in the heart, which are known as uraemic cardiomyopathy. These changes may be progressive and relate directly to a grossly aggravated risk of cardiovascular (CV) events and reduced survival rates [1]. Previous studies have shown that increased left atrial volume (LAV) as measured by echocardiography is a common finding in end-stage renal disease (ESRD) patients. Therefore, it has emerged as a biomarker with a potential value for the risk stratification in ESRD patients. The LAV predicts mortality aside from left ventricular (LV) hypertrophy and LV dysfunction, or the other risk factors in ESRD patients. Monitoring the LAV provides prognostic information beyond the echocardiographic markers of high CV risk [2].

Because the LA is directly exposed to LV diastolic pressure through the mitral valve, the size of the LA reflects the duration and severity of increased LA pressure following increased LV diastolic pressure. Therefore, LAV is reported to be a sensitive marker of LV diastolic dysfunction. LA function plays a central role in maintaining optimal cardiac output despite impaired LV relaxation and reduced LV compliance [3]. Echocardiographic studies conducted on different patient groups have demonstrated that the phasic functions of LA diminish in parallel to the increase in the LAV. Especially in heart failure patients with preserved LV ejection fraction (PLVEF), the reduction in the LA function may lead to a decrease in the functional capacity and to CV complications [4].

Traditionally, the LA function was assessed by measuring the LA size or volume using two-dimensional (2D) echocardiography. Also, Doppler echocardiographic evaluations such as transmitral and pulmonary venous flow measurements can be used for this purpose. While these methods assess the myocardial functions of the LA indirectly, 2D speckle tracking echocardiography (2D-STE) can directly assess myocardial LA functions [5]. 2D-STE allows a direct and angle-independent analysis of the myocardial deformation, thus providing sensitive and reproducible indices of myocardial fibre dysfunction. This analysis may allow a more direct assessment of LA endocardial contractility and passive deformation. The 2D-STE strain (S%) has been validated against the sonomicrometry and tagged magnetic resonance imaging techniques. In several pathophysiological cardiac conditions, abnormalities in the LA strain (LA_S) have been revealed using 2D-STE [6, 7]. In recent years, LA_S parameters obtained by assessment of the LA through the 2D-STE method have been shown to be associated with LV filling pressure (LVEDP) — which is the haemodynamic marker of LV dysfunction — and pulmonary capillary wedge pressure (PCWP) [8].

Although the association between the increase in LAV and CV complications and prognosis of the disease in patients with ESRD has been investigated in a number of clinical and echocardiographic studies, no study has directly focused on the myocardial functions of the LA, and the relationship between these functions and LV dysfunction.

We here study the evaluation of the myocardial functions of the LA and their relationship with the echocardiographically estimated (ePCWP) in addition to the LAV and phasic functions observed using 2D echocardiography in ESRD patients with PLVEF.

METHODS

Study group

For the purposes of our study, 140 consecutive ESRD patients between the ages of 18–60, who were receiving haemodialysis treatment for at least three months at the Nephrology Department of the Akdeniz University School of Medicine between August 2010 and February 2011 and were referred to the Echocardiography Laboratory of the Akdeniz University School of Medicine for their routine echocardiographic evaluation, were enrolled. The control group consisted of 70 healthy individuals who had undergone an echocardiographic evaluation due to various reasons and were observed to have normal LV structure and function. The individuals in the control group did not carry the classic CV risk factors or any systemic diseases that may affect cardiac structure and function. 2D grey scale images of the participants, which were taken during the echocardiographic evaluation, were recorded for offline analysis. Informed consent forms were obtained from every individual enrolled and the study was approved by the local Ethics Committee of the Akdeniz University School of Medicine.

The exclusion criteria included suspected coronary artery disease (CAD) observed during the recruitment stage based on patient history, physical examination, electrocardiography, echocardiography, treadmill test or scintigraphy findings in patients who were deemed to need these tests, angiographically proven CAD, past coronary revascularisation, severe or moderate mitral/aortic regurgitation or stenosis, diabetes mellitus (fasting plasma glucose concentration > 126 mg/dL, glycosylated haemoglobin [HbA1c] > 6.5%, or use of hypoglycaemic medication), New York Heart Association class III–IV heart failure, pericarditis or massive pericardial effusion, cardiac rhythm anomalies, low ejection fraction (EF < 60%), suboptimal echocardiographic image, body mass index (BMI) > 35 kg/m^2, any metabolic or systemic diseases other than chronic kidney disease which may disrupt the cardiac structure or functions, smoking, and previous renal transplants that ended with rejection. Blood pressure, heart rate and anthropometric measurements of all the individuals were recorded before the echocardiography. Body surface area (BSA) and BMI were calculated from the anthropometric measurements.

Echocardiography

Echocardiography was performed in the left lateral decubitus position using the GE-Vingmed Vivid 7 system (GE-Vingmed Ultrasound AS, Horten, Norway) ultrasound device and a 3S-RS (3.5 Mhz) probe. Examinations were performed by

two experienced cardiologists who were blinded to the patient groups. Three cardiac cycles were stored in a cineloop format for offline analysis. Isochronous electrocardiographic recordings were obtained during the echocardiography procedures. In the ESRD group, echocardiograms were performed in the interdialytic day; midweek between 8am and 1pm as previously recommended [9].

Left ventricular assessment

Images were obtained from the parasternal and apical positions using the 2D, M-mode and Doppler echocardiographic techniques. The 2D, M-mode and Doppler echocardiographic examinations were performed according to the guidelines of the American Society of Echocardiography for the evaluation of LV structures, the systolic and diastolic functions, and calculation of the values dependent on these functions. The LV mass was calculated according to the anatomically validated Devereux formula and indexed by the BSA. The LVEF was measured using the biplane Simpson's method from apical four- and two-chamber views [10, 11].

Tissue Doppler images (TDI) were recorded from the apical four-chamber view using the pulsed-wave Doppler with a 3 mm sample volume placed on the septal and lateral mitral annulus. All the annular velocities and time intervals of tissue Doppler analyses were calculated as the average of the two annular sites. Pulsed wave TDI examinations were performed according to the guidelines of the American Society of Echocardiography [11]. The ratio of the mitral early diastolic flow velocity (E) and the mitral annular early diastolic myocardial velocity (E') were calculated [12]. The ePCWP was calculated according to the following formula: ePCWP = 1.25(E/E') + 1.9 [13].

Left atrial assessment

From the apical four- and two-chamber views, three separate LAV (maximum [max] – precontraction [preA] – minimum [min]) were calculated using the area-length method according to the guidelines of the American Society of Echocardiography. The LAV indices (LAVI) were calculated by dividing the LAV by the BSA. Following the calculation of the LAV, the phasic functions of the LA (total emptying fraction [TEF], passive emptying fraction [PEF], active emptying fraction [AEF] and expansion index [EI]) were calculated using similar methods to those used in previous studies [14].

For the LA 2D-STE analysis, images from the apical four- and two-chamber views were obtained using conventional, 2D grey scale echocardiography while holding the breath and simultaneously taking an electrocardiography reading. All images were obtained at a frame rate of 60–80 frames/s. Three consecutive heart cycles were recorded in digital format for offline analysis using EchoPAC software (version 8, GE, Healthcare). In order to calculate the LA_S, the atrial endocardium was first manually traced in end-systolic frame. The epicardial surface is calculated automatically, and after manually reducing the region of interest to the atrial thickness, the software automatically divides the atrial wall into six segments. Before acquiring the LA_S view from the apical four- and two-chambers, if speckle tracking is not adequate, the region of interest is manually adjusted to include only the atrial wall. Segments in which adequate tracking quality could not be obtained despite manual adjustments were excluded from the analysis. Patients in whom no adequate tracking quality was obtained in more than two segments were also excluded from the study. Finally, the software calculated the average LA_S for six segments for each apical view and the LA_S values for each view were calculated from the averages of the values obtained from the LA segments in each view. The final LA_S values were the averages of the values obtained for each apical view [7, 15].

The LA_S during systole ($LA_{S\text{-}S}$) was obtained at the time of the aortic valve closure, and the strain during late diastole ($LA_{S\text{-}A}$) was obtained at the onset of the P wave on electrocardiography. The LA_S during early diastole ($LA_{S\text{-}E}$) was defined as $LA_{S\text{-}S} - LA_{S\text{-}A}$. The $LA_{S\text{-}S}$ left atrial reservoir, $LA_{S\text{-}E}$ left atrial conduit, and $LA_{S\text{-}A}$ values are related to the pump functions of the LA [15]. LA stiffness was calculated based on the ratio of the PCWP estimated from E/E' to the $LA_{S\text{-}S}$ [16]. The assessment of the LA myocardial functions using 2D-STE is presented in Figure 1.

Statistical analyses

The SPSS 18.0 statistical package was used for the statistical analyses. The parameters evaluated in our study are presented as frequency, percentage, mean ± standard deviation and median (minimum – maximum) values. Depending on the results of the normality test, either the Mann-Whitney U-test, or Student's t-test was used for the analysis of the differences between the independent measurements of both groups. For the inter-measurement relationships, Spearman's or Pearson's correlation tests were applied after the normality of the distribution of the data was verified. The independent variables which were found to be significant according to the result of the correlation test were selected and a linear regression model was formed with the specified dependent variable.

Inter and intra-observer variability

After the first measurement by an observer in randomly selected patients with ESRD and the control group, the intra-observer variability was determined by repeating the measurement of the LA global longitudinal strain by a different observer two weeks later. Inter-observer variability was determined through the measurement of the same variables in the same database by another observer. Bland-Altman analysis was used to assess the differences between the measurements.

RESULTS

During analysis of the data for the purposes of our study, 20 patients in the ESRD group were excluded from the evaluation

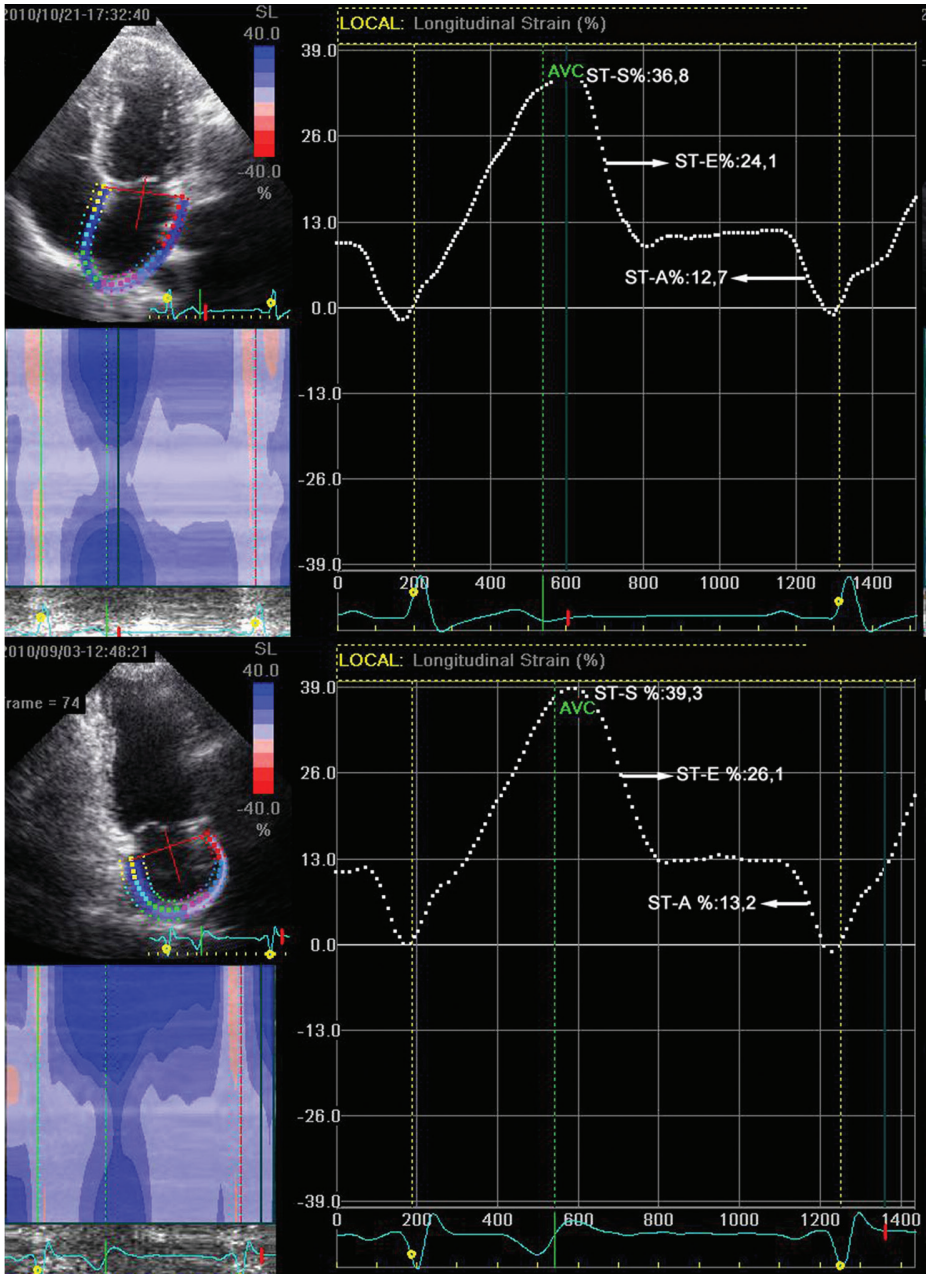

Figure 1. Assessment of the left atrial myocardial functions using the two-dimensional speckle tracking echocardiography method. The atrial endocardial border is traced manually. After automatic creation of a region of interest divided into six subregions, segmental tracking quality is analysed, after approval by the user, global longitudinal strain and strain rate curves. The systolic strain (ST-S), early diastolic strain (ST-E) and late diastolic strain (ST-A) values are determined from these curves. The averages of strain values determined from apical two- and four-chamber views were calculated

since they were on peritoneal dialysis, 25 patients were excluded because they failed to meet the study criteria, and ten patients were excluded due to inferior quality of the echocardiographic images. In the healthy control group, two patients were excluded since they did not meet the study criteria, and eight were excluded due to inadequate echocardiographic image quality. Thus, a total of 145 patients were evaluated in our study, of whom 85 were ESRD patients and 60 were healthy individuals. The mean duration of haemodialysis in ESRD patients was found to be 57.72 ± 44.9 months. When the demographic and clinical data of the groups was evaluated, the mean age of the healthy group was found to be higher than the ESRD group (39.17 ± 10.08 vs. 33.79 ± 9.08; $p = 0.002$), while no difference was observed between the groups in terms of BMI (26.02 ± 4.07 vs. 22.26 ± 3.33; $p > 0.05$) or sex (males 51.7 [n = 31] vs. 54.1% [n = 46],

Table 1. Conventional and tissue Doppler echocardiographic variables of healthy individuals and patients with end-stage renal disease (ESRD)

	ESRD	Healthy	P
Bp-EF [%]	64.85 ± 5.33	65.73 ± 3.62	0.061
IVSDt [cm]	1.12 ± 0.21	0.86 ± 0.08	< 0.001
PWDt [cm]	1.13 ± 0.04	0.87 ± 0.08	< 0.001
LVMI [g/m^2]	186.37 ± 58.51	132.52 ± 24.31	< 0.001
E [m/s]	0.86 ± 0.24	0.82 ± 0.16	0.697
A [m/s]	0.8 ± 0.19	0.66 ± 0.15	< 0.001
E/A	1.12 ± 0.33	1.29 ± 0.35	0.002
E-DecT [s]	234.4 ± 47.03	161.45 ± 29.38	< 0.001
IVRT [s]	85.21 ± 16.79	68.17 ± 10.57	< 0.001
Tissue Doppler imaging parameters:			
S [m/s]	0.09 ± 0.02	0.11 ± 0.02	< 0.001
E' [m/s]	0.11 ± 0.03	0.14 ± 0.06	< 0.001
A' [m/s]	0.1 ± 0.02	0.11 ± 0.02	0.015
E/E'	12.43 ± 2.86	7.28 ± 1.67	< 0.001
ePCWP	13.52 ± 3.61	9.64 ± 2.11	< 0.001

Data is presented as mean ± standard deviation; A — mitral valve late diastolic velocity; A' — mitral annulus late diastolic velocity; Bp-EF — biplane Simpson ejection fraction; E — mitral valve early diastolic velocity; E' — mitral annulus early diastolic velocity; E-DecT — E wave deceleration time; ePCWP — estimated pulmonary capillary wedge pressure; IVSDt — interventricular septum diastolic thickness; IVRT — isovolumic relaxation time; LVMI — left ventricular mass index; PWDt — posterior wall diastolic thickness; S — mitral annulus systolic velocity

females 48.3% [n = 29] vs. 45.9% [n = 39]; p > 0.05). The systolic (119.42 ± 10.97 vs. 132.57 ± 19.93; p < 0.001) and diastolic (72.96 ± 8.21 vs. 83.47 ± 11.23; p < 0.001) blood pressures were found to be higher in the ESRD group. No difference was observed between the groups in terms of heart rates (75.13 ± 10.38 vs. 74.75 ± 10.4; p > 0.05).

When the 2D and TDI LV echocardiographic data of the groups was compared, the LV wall thickness, LV mass index (LVMI), mitral late diastolic flow velocity (Mit A), E-wave deceleration time (E-DT), E/E' ratio, isovolumic relaxation time (IVRT) and the ePCWP values were observed to be higher in the ESRD group. On the other hand, the Mit E/A; mitral annulus systolic, early diastolic and late diastolic velocities were found to be lower in the ESRD group. No difference was observed between the groups in terms of the LVEF and the Mit E values. The results of the echocardiographic evaluation of the LV in both groups are presented in Table 1.

When the atrial parameters of the groups were assessed, the anteroposterior diameter (LAD) and the volumes of the LA were found to be higher in the ESRD group. The LATEF, LAPEF, LAAEF and LAEI values indicating the phasic functions of the LA; and the LA_{S-S}, LA_{S-E} and LA_{S-A} values of the LA assessed through the 2D-STE were observed to be lower in the ESRD group. On the other hand, the LA stiffness was found to be higher. An assessment of the LA structure and function in the groups is presented in Table 2.

When the ESRD group was divided into two groups to include those with a median LAVImax value higher than 31.34 mL/m^2 and those with lower values, the LVMI, E/E', and ePCWP values were observed to be higher in the group with LAVI > 31.34 mL/m^2. When the LA parameters were assessed, the LAD, LAVI, LA_{S-A}, and LA stiffness values were found to be higher in the group with LAVI > 31.34 mL/m^2; while the LA_{S-S}, and LA_{S-E} values were lower. No difference was observed between the LA phasic functions of the groups. The LV echocardiographic data of the groups according to the LAVImax values are presented in Table 3, and the results related to the LA structure and functions are shown in Table 4.

In our study, the relationship between age, BMI, echocardiographic parameters related to the LV, dimensions of the LA, phasic functions of the LA, the 2D-STE parameters, and the ePCWP were evaluated through the correlation analysis. The LVMI, S', IVRT, LAVImax, LA stiffness, LA_{S-S}, LA_{S-E}, and the LA_{S-A} parameters were found to be associated with the ePCWP. In the regression analysis carried out after the formation of the model using the related parameters, the relationship between the ePCWP and LA stiffness, LA_{S-S}, LA_{S-E} and LA_{S-A} was observed to prevail. The related analysis results are presented in Table 5.

Intra- and inter-observer variability

Twenty patients were randomly selected for the assessment of intra- and inter-observer variability in the measurements of the LA_{S-S}, LA_{S-E}, and LA_{S-A} parameters. Confidence intervals and mean differences for inter-observer and intra-observer variability for the S values are shown in Table 6.

Table 2. Left atrium functional and structural parameters of healthy individuals and patients with end-stage renal disease (ESRD)

Left atrium parameters	ESRD	Healthy	P
LAD [cm]	35.25 ± 4.79	31.53 ± 3.69	< 0.001
LAVImax [mL/m^2]	34.25 ± 13.91	23.6 ± 5.76	< 0.001
LAVIPreP [mL/m^2]	21.84 ± 9.05	14.12 ± 4.38	< 0.001
LAVImin [mL/m^2]	13.35 ± 6.91	7.84 ± 3.13	< 0.001
TEF [%]	61.38 ± 10.16	67.09 ± 8.33	< 0.001
PEF [%]	35.67 ± 10.82	44.42 ± 12.2	0.008
AEF [%]	39.85 ± 13.16	44.42 ± 12.2	0.036
EI [%]	187.79 ± 133.24	214.7 ± 75.51	< 0.001
LA_{S-S} [%]	32.22 ± 7.64	57.93 ± 8.71	< 0.001
LA_{S-E} [%]	15.86 ± 5.7	33.37 ± 7.71	< 0.001
LA_{S-A} [%]	15.41 ± 4.16	24.57 ± 4.68	< 0.001
Stiffness	0.4 ± 0.19	0.17 ± 0.05	< 0.001

Data is presented as mean ± standard deviation; AEF — active empyting fraction; EI — expansion index; LA_{S-S} — left atrium systolic strain; LA_{S-E} — left atrium eraly diastolic strain; LA_{S-A} — left atrium late diastolic strain; LAD — left atrium diameter; LAVImax-PreP-min — left atrium volume index maximum-precontraction-minimum; PEF — passive empyting fraction; TEF — total empyting fraction

Table 3. Comparison of left ventricular parameters in end-stage renal disease patients according to median left atrium volume indices (LAVI) max values

Left ventricular parameters	LAVImax > 31.34 mL/m^2	LAVImax < 31.34 mL/m^2	P
Bp-EF [%]	64.3 ± 5.33	65.4 ± 5.34	0.264
IVSDt [cm]	1.17 ± 0.24	1.07 ± 0.16	0.05
PWDt [cm]	1.18 ± 0.23	1.08 ± 0.16	0.42
LVMI [g/m^2]	218.1 ± 59.07	153.9 ± 36.13	< 0.001
E [m/s]	0.9 ± 0.25	0.81 ± 0.23	0.063
A [m/s]	0.81 ± 0.22	0.78 ± 0.17	0.563
E/A	1.16 ± 0.31	1.08 ± 0.36	0.154
E-DecT [s]	236.05 ± 50.59	232.71 ± 43.65	0.746
IVRT [s]	89.56 ± 17.18	80.75 ± 15.33	0.022
Tissue Doppler imaging parameters:			
S [m/s]	0.09 ± 0.02	0.09 ± 0.02	0.362
E' [m/s]	0.1 ± 0.02	0.11 ± 0.03	0.273
A' [m/s]	0.1 ± 0.02	0.1 ± 0.02	0.695
E/E'	11.27 ± 3.35	9.7 ± 2.07	0.05
ePCWP	13.49 ± 4.18	11.53 ± 2.6	0.05

Datais presented as mean ± standard deviation; A — mitral valve late diastolic velocity; A' — mitral annulus late diastolic velocity; Bp-EF — biplane Simpson ejection fraction; E — mitral valve early diastolic velocity; E' — mitral annulus early diastolic velocity; E-DecT — E wave deceleration time; ePCWP — estimated pulmonary capillary wedge pressure; IVSDt — interventricular septum diastolic thickness; IVRT — isovolumic relaxation time; LVMI — left ventricular mass index; PWDt — posterior wall diastolic thickness; S — mitral annulus systolic velocity

DISCUSSION

In the present study, the comparison between ESRD patients and the healthy individuals revealed that as the LAV increased, the phasic functions and deformation parameters decreased in patients with ESRD. The changes in the LA structure and functions were accompanied by an increase in ePCWP, which is an echocardiographically calculated haemodynamic marker of LV dysfunction. When the ESRD patients were divided into two groups according to the median LAVImax value of 31.34 mL/m^2, no difference was observed between the groups in terms of the diastolic function parameters and the phasic functions of the LA. In the group with higher LAVI values, the LA_{S-S}, LA_{S-E} values were lower; while the LAV, LA stiffness and LA_{S-A} values were higher. Although a relationship

Table 4. Comparison of left atrial functional and structural parameters in end-stage renal disease patients according to median left atrium volume indices (LAVI) max values

Left atrium parameters	LAVImax > 31.34 mL/m²	LAVImax < 31.34 mL/m²	P
LAD [cm]	37.14 ± 3.84	33.31 ± 4.92	< 0.001
LAVImax [mL/m²]	44.38 ± 11.85	23.88 ± 5.94	< 0.001
LAVIPreP [mL/m²]	27.53 ± 8.51	16.03 ± 5.01	< 0.001
LAVImin [mL/m²]	17.38 ± 6.98	9.23 ± 3.67	< 0.001
TEF [%]	60.97 ± 9.67	61.79 ± 10.73	0.709
PEF [%]	37.88 ± 19.06	33.41 ± 1.22	0.057
AEF [%]	37.33 ± 11.98	42.45 ± 13.94	0.083
EI [%]	179.08 ± 113.43	196.7 ± 151.77	0.847
LA_{S-S} [%]	30.36 ± 8.32	34.11 ± 6.43	0.023
LA_{S-E} [%]	14.97 ± 5.88	16.76 ± 5.42	0.045
LA_{S-A} [%]	16.06 ± 4.44	14.75 ± 3.8	0.039
Stiffness	0.45 ± 0.24	0.36 ± 0.13	0.04

Data is presented as mean ± standard deviation; AEF — active empyting fraction; EI — expansion index; LA_{S-S} — left atrium systolic strain; LA_{S-E} — left atrium eraly diastolic strain; LA_{S-A} — left atrium late diastolic strain; LAD — left atrium diameter; LAVImax-PreP-min — left atrium volume index maximum-precontraction-minimum; PEF — passive empyting fraction, TEF — total empyting fraction

was observed between the ePCWP and the LA deformation parameters, no such association was found between the LAV, phasic functions and ePCWP.

LA functions play a central role in maintaining the optimal cardiac output despite impaired LV relaxation and reduced LV compliance in ESRD patients with PLVEF. LV diastolic dysfunction, LV hypertrophy, and volume overload may lead to elevated LV filling pressure and LA afterload in patients with ESRD [17]. Consequently, these alterations produce a compensatory mechanism in the LA characterised by LA dilatation and the stretching of the atrial myocardium. This contributes to an enhanced LA emptying volume activation of the Frank-Starling mechanism, which is partially responsible for the maintenance of the stroke volume in ESRD patients. However, late stage chronic increases in the LA afterload in addition to LA remodelling may produce an alteration in the compliance, reservoir function, and pump performance of the LA [9, 18]. The LA remodelling process has been shown to increase the LA wall thickness and focal collagen, contributing to fibrosis in the atrial myocardium. In addition, the impaired calcium uptake in the cardiomyocytes in LA remodelling leads to a slow and incomplete relaxation. LA remodelling is also associated with atrial interstitial fibrosis and cell hypertrophy, which may contribute to the LA systolic and diastolic dysfunction [19, 20].

Myocardial functions of the LA can be evaluated through the regional active and passive deformation parameters of the LA measured using the 2D-STE method. The myoarchitecture of the LA is complex, and the fibres are predominantly arranged in two layers: the subendocardial layer (responsible for the longitudinal functions of the LA) and the subepicardial layer (responsible for the radial functions of the LA) [21]. Although the longitudinal functions of the LA can be evaluated with the 2D-STE method, radial functions cannot be evaluated with the same method. The radial strain of the atria cannot be obtained from the parasternal views because the atrial wall is thinner than the LV wall and does not allow speckle tracking analysis [22].

The LA reservoir function is assessed in two consecutive phases as early and late function. While the early reservoir function depends on LA relaxation (or LA stiffness), the late reservoir function depends on the descent of the base during the systole [23]. We demonstrated a reduction in LA expansion index, LA total emptying fraction, and LA_{S-S} in parallel with increased LA stiffness index, which reflects a reduced atrial reservoir function in ESRD patients. In our study, although there was no difference between the LVEF measurements of the control and ESRD groups, the fact that the mitral annular systolic velocities were lower in ESRD patients suggests that, in addition to atrial myopathy, subclinical LV systolic dysfunction may also contribute to reduced LA reservoir function [24].

During early LV diastole, a portion of the external energy stored in the LA during LV systole is transferred back to the LV, and some of the remainder is coupled with the blood flow from the pulmonary veins [25]. The LA conduit function can be assessed by the LA_{S-E} and passive emptying fraction; and a reduction was observed in patients with ESRD. In relation to the changes in the LV structure and functions that occur in ESRD patients, due to the disturbances in LV relaxation and passive filling in early diastole, the conduit function of LA is reduced [26].

In this study, the LA_{S-A} and LA active emptying fractions were observed to be reduced in ESRD patients, suggesting a de-

Table 5. Correlation of estimated pulmonary capillary wedge pressure with clinical and echocardiographic parameters

Correlation analysis	R	P
Age	0.146	0.184
Body mass index	0.03	0.788
LVMI	0.291	0.006
Biplane Simpson ejection fraction	–0.133	0.226
Mitral valve late/early diastolic velocity	0.012	0.913
E wave deceleration time	–0.172	0.115
S	–0.304	0.005
IVRT	0.291	0.007
LAVImax	0.359	0.001
Total empyting fraction	–0.170	0.12
Passive empyting fraction	–0.118	0.282
Active empyting fraction	–0.08	0.465
Expansion index	–0.70	0.12
Stiffness	0.794	< 0.001
LA_{S-S}	–0.286	0.008
LA_{S-E}	–0.650	< 0.001
LA_{S-A}	0.960	< 0.001
Regression analysis	**β**	**Lower/upper limit 95% confidence interval**	**P**
LVMI	–0.003	–0.006/0.005	0.949
S	0.011	–12.832/17.790	0.748
IVRT	–0.012	–0.018/0.013	0.729
LAVImax	0.034	–0.017/0.034	0.495
Stiffness	0.689	9.784/15.225	< 0.001
LA_{S-S}	0.409	0.140/0.246	< 0.001
LA_{S-E}	–0.125	–0.139/–0.019	0.01
LA_{S-A}	0.461	0.3/0.498	< 0.001

IVRT — isovolumic relaxation time; LA_{S-S} — left atrium systolic strain; LA_{S-E} — left atrium early diastolic strain; LA_{S-A} — left atrium late diastolic strain; LAVImax — left atrium volume index maximum; LVMI — left ventricular mass index; S — mitral annulus systolic velocity

Table 6. Bland-Altman analysis for interobserver and intraobserver variability

	Interobserver		Intraobserver	
	Change in mean difference	95% confidence interval	Change in mean difference	95% confidence interval
Systolic strain	–0.1	–0.58 to 0.38	0.28	–0.15 to 0.7
Early diastolic strain	0.22	–0.36 to 0.8	–0.66	–1.26 to –0.07
Late diastolic strain	–0.26	–0.81 to 0.28	–0.25	–0.75 to 0.25

crease in the LA myocardial pump function. This may be associated with two problems related to LA myocardial contractility: 1) The afterload, becoming a major determinant of LA ejection when the LA preload reaches its limit (afterload mismatch); 2) Atrial myopathy triggered by the structural changes that occur in the myocardium of the LA [27]. Several studies have suggested that elevated LV filling pressures may not fully explain LA failure and that LA myocardial fibrosis and myopathy may play a role in the systolic dysfunction of the LA. In pathologies that affect the LA structure and functions, the severity of the LA fibrosis evaluated with magnetic resonance imaging, as well as the correlation between the LA longitudinal strain values,

prove the relationship between the involved parameters and LA fibrosis [7]. Several experimental studies, however, have shown that fibrosis is a common finding in the hearts of patients and animals with chronic kidney disease [28, 29].

When the ESRD patients were divided into two groups as those with a LAVImax above the median value of 31.34 mL/m^2 and those with a value below this limit, the $LA_{S\text{-}S}$ and $LA_{S\text{-}E}$ diastolic strain values were found to be lower, while the $LA_{S\text{-}A}$ and LA stiffness values were higher, in the group with higher LAVI. Among the patients with a LAVI > 31.34 mL/m^2, the LA reservoir and conduit functions were reduced due to the increase in LVEDP accompanying the LV dysfunction, while the LA pump function could show a compensatory augmentation due to the increase in the LAV before the LA systole and the increased tension in LA myocardium [4, 16]. The increase in the LA pump function may enable adequate LV filling.

In our study, when the ESRD patients were divided into two groups based on their LAVImax values, although no difference was observed in terms of their LA phasic functions and Doppler diastolic function parameters, their LA strain values were observed to be different. The exclusion of the ESRD patients with CAD, diabetes mellitus and low EF from the study; and the study population consisting of low-risk patients in terms of the impact on the LV structure and functions due to the low mean age may explain why no difference was observed between the groups in terms of LV diastolic function parameters or LA phasic functions. In addition to these clinical features of the patients, the sensitivity of the Doppler method and the volumetric analysis of LA to the volume load, as well as the technical limitations of the methods, may have contributed to these results. Recent work has shown that the Doppler indices of diastolic filling are very load-dependent, fluctuating widely with changes in the intravascular status during dialysis [30]. LA size, which has previously been shown to correlate with LV dysfunction, may be a more stable measurement option that is preload independent. A recent study showed that fluctuations in the LAV are less pronounced than the changes in the intravascular status during dialysis. However, the evaluation of LAV by 2D echocardiography is limited by the use of geometric models that determine the volume of a nonsymmetric chamber, and by errors that occur due to foreshortening [31]. This finding may support previous evidence showing that a large proportion of the variability in the standard indices of LAV and function is likely to be explained by the changes in the LA size, whereas abnormalities in the LA strain are relatively independent from LA dilatation and volume overload [22, 32].

PCWP measurement, which is a surrogate marker of LV filling pressure, is directly associated with functional capacity and prognosis in patients with heart failure. In the studies conducted on various patient groups with cardiac failure, a relationship has been demonstrated, particularly between LA systolic and late diastolic strain values and LV filling pressures [10, 16]. Although there are studies showing that the E/E' values in ESRD patients can be used to estimate LV filling pressures, there are no studies focusing on the LA deformation parameters, LV dysfunction and filling pressures [33]. While a relationship between the ePCWP value calculated based on the echocardiographic E/E' value and the LA deformation parameters has been observed in our study, no such relationship was observed between the LAVI and other echocardiographic parameters.

Our findings imply that LA myocardial deformation may have the potential to predict LV filling pressures and LV diastolic dysfunction in ESRD patients.

Limitations of the study

Our study had several limitations. Although the efficiency of the 2D-STE method was validated on our study population, the limited number of patients may present a limitation for the validation of the efficiency of the method. Since the number of patients investigated in our study was small, and the aim of the study was the evaluation of the relationship between ESRD and the LA deformation parameters, the influence of the metabolic and haemodynamic changes observed in patients with ESRD and those brought about by the administered medications have not been assessed. Also, since our study included ESRD patients undergoing haemodialysis, but excluded those on peritoneal dialysis and pre-emptive patients, our results do not comprise all chronic kidney disease patients. Volume status was not directly assessed in our patients, and the influence of volume changes on the study results was not evaluated. Another limitation of the study was the lack of invasive haemodynamic data. Cardiac catheterisation provides more accurate information about the LV filling pressures than echocardiographic measurements. Nonetheless, several studies have demonstrated the high sensitivity, specificity and accuracy of the mitral E/E' ratio in the assessment of LV filling pressures [34]. We have also used the ePCWP value calculated from the E/E' ratio in order to assess LV filling in our study. The evaluation of the LA through 2D-STE is more difficult and time-consuming than the assessment of the segmental LV function. However, because a dedicated software for LA strain analysis has not been released yet, we used the current software for the LV analysis to study the LA pattern strain. Since our study was an observational study and did not include the clinical follow-up of the patients, no evaluation has been made in terms of the relationship between the results and the CV prognosis of the patients.

CONCLUSIONS

The present study demonstrated that in ESRD patients with preserved systolic function who are undergoing haemodialysis, the LA myocardial function assessed through the 2D-STE method is an independent correlative of increased ePCWP, which is an echocardiographically calculated haemodynamic

marker of LV dysfunction. LA deformation parameters may be used as echocardiographic findings to predict LV dysfunction in ESRD patients with PLVEF. In addition to echocardiographic parameters like LVEF, LAV and LVMI, the assessment of LA myocardial function may provide further insights into the clinical prognosis and CV complications in ESRD. Further study is required to determine the independent prognostic power of the atrial strain measurement as a predictor of future CV events in ESRD patients.

Conflict of interest: *none declared*

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Ocena czynności lewego przedsionka metodą echokardiografii dwuwymiarowej z algorytmem śledzenia markerów akustycznych u osób w schyłkowym stadium choroby nerek z zachowaną frakcją wyrzutową lewej komory

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Streszczenie

Wstęp: Analiza deformacji lewego przedsionka (LA) metodą echokardiografii dwuwymiarowej z algorytmem śledzenia markerów akustycznych (2D-STE) może być alternatywną metodą oceny ciśnienia wypełniania lewej komory (LV) i jej dysfunkcji.

Cel: Badanie przeprowadzono w celu oceny czynności LA metodą 2D-STE u osób w schyłkowym stadium choroby nerek (ESRD) z zachowaną frakcją wyrzutową lewej komory (PLVEF) i określenia zależności między uzyskanymi wynikami a oszacowanym echokardiograficznie ciśnieniem zaklinowania w kapilarach płucnych (ePCWP).

Metody: Do badania włączono 85 chorych z ESRD i 60 osób zdrowych. Obrazy LA uzyskano w projekcjach koniuszkowych — 2- i 4-jamowej. Objętość LA (LAV) obliczano, posługując się dwupłaszczyznową metodą pole/wymiar podłużny. Wskaźnik objętości LA (LAVI) obliczano, dzieląc LAV przez powierzchnię ciała. Oceniono parametry odkształcenia LA (%) (LA_S) [skurczowe (LA_{S-S}), wczesnorozkurczowe (LA_{S-E}), późnorozkurczowe (LA_{S-A}), w czasie skurczu przedsionków] i obliczono ePCWP, stosując następujący wzór: ePCWP = 1,25 (E/E') + 1,9. Sztywność LA określono metodą nieinwazyjną na podstawie stosunku E/E' do LA_{S-S}.

Wyniki: U chorych z ESRD wartości LA_{S-S} (32,22 ± 7,64% *vs*. 57,93 ± 8,71%; p < 0,001), LA_{S-E} (–15,86 ± 5,7% *vs*. –33,37 ± 7,71%; p < 0,001) i LA_{S-A} (–15,41 ± 4,16% *vs*. –24,57 ± 4,68%; p < 0,001) były niższe, a wskaźniki sztywności LA (0,4 ± 0,19 *vs*. 0,17 ± 0,05; p < 0,001) — wyższe niż u osób zdrowych. Po podzieleniu chorych z ESRD na dwie grupy (osoby z maksymalnym LAVI > 31,34 ml/m^2 i osoby z maksymalnym LAVI < 31,34 ml/m^2) stwierdzono, że w grupie, w której LAVI wynosił ponad 31,34 ml/m^2 wartości LA_{S-S} (30,36 ± 8,32% *vs*. 34,11 ± 6,43%; p = 0,023) i LA_{S-E} (–14,97 ± 5,88% *vs*. –16,76 ± 5,42%; p = 0,039) były niższe; natomiast LA_{S-A} (–16,06 ± 4,44% *vs*. –14,75 ± 3,8%; p < 0,001) i wskaźnik sztywności LA (0,4 ± 0,19 *vs*. 0,17 ± 0,05; p < 0,001) były większe niż w drugiej grupie chorych z ESRD. Zaobserwowano zależności między ePCWP a wartościami LA_{S-S} (p < 0,001), LA_{S-E} (p = 0,01), LA_{S-A} (p < 0,001) i wskaźnika sztywności LA (p < 0,001).

Wnioski: W niniejszym badaniu wykazano, że wyniki oceny czynności LA miokardium z zastosowaniem metody 2D-STE wiążą się z wartościami ePCWP, które stanowi obliczany echokardiograficznie wskaźnik dysfunkcji LV. Parametry odkształcenia LA mogą być przydatne jako echokardiograficzne wskaźniki pozwalające prognozować dysfunkcję LV u chorych z ESRD i PLVEF. Należy przeprowadzić dalsze badania w celu określenia znaczenia pomiarów odkształcenia przedsionka jako niezależnych czynników prognostycznych przyszłych zdarzeń sercowo-naczyniowych u osób z ESRD.

Słowa kluczowe: schyłkowa choroba nerek, odkształcenie lewego przedsionka

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