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The effect of hemodialysis on left ventricular global longitudinal strain in chronic hemodialysis patients with preserved left ventricular ejection fraction

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ABSTRACT

Objectives: In the present study, we aimed to evaluate the acute effects of hemodialysis (HD) on left ventricular functions with left ventricular (LV) global longitudinal strain (GLS).

Patients and methods: This prospective study included a total of 38 patients (24 males, 14 females; mean age: 60.8±13.8 years; range, 31 to 82 years) who were on chronic HD for at least six months and had a LV ejection fraction of ≥50% between December 2021 and January 2022. The clinical and echocardiographic features of the patients were recorded before and after HD. The GLS was calculated using two-dimensional speckle-tracking method.

Results: The mean dialysis time of the patients was 6.3±3.9 years. The left atrial volume index was significantly lower after HD than before (30.1±10.0 *vs.* 27.5±8.2 mL/m^2, p=0.005). Pulsed Doppler echocardiography showed significantly decreased E and A wave peak velocity after HD (99.3±38.2 *vs.* 80.4±27.8 cm/s, p=0.001 and 99.4±23.2 *vs.* 90.4±25.5 cm/s, p=0.022), but no significant change in the E/A ratio (1.1±0.5 *vs.* 1±0.6, p=0.660). There was no significant change on the LV GLS between before and after HD (-17.3±2.6 *vs.* -16.9±2.6%, p=0.088).

Conclusion: Hemodialysis has no significant effect on LV GLS in the acute phase in patients with end-stage chronic renal disease.

Keywords: End-stage renal disease, global longitudinal strain, hemodialysis, speckle-tracking echocardiography.

Cardiac morbidity and mortality are higher in patients with end-stage renal disease (ESRD) than in the normal population.[1] Structural and functional cardiac changes can be observed in ESRD patients undergoing hemodialysis (HD) due to causes such as chronic volume and pressure overload, anemia, uremia, high-flow arteriovenous shunts, abnormal calcium and phosphate metabolism, and hyperparathyroidism.[2,3] In addition, rapid blood volume and electrolyte changes during HD may cause acute deterioration in cardiac functions. Cardiac functions in HD patients have been extensively studied by conventional echocardiography; however, this method offers only a semiquantitative assessment and cannot detect subclinical cardiac dysfunctions.

Despite a high prevalence of cardiovascular insults and progressive symptoms of heart failure, left ventricular ejection fraction (LVEF) remains preserved in the majority of patients with chronic kidney disease (CKD).[4] Speckle-tracking echocardiography with myocardial deformation (two-dimensional [2D] strain) analysis is a quantitative method for the assessment of subtle left ventricular (LV) dysfunction, which cannot be evaluated by semiquantitative conventional echocardiography.[5] Left ventricular global longitudinal strain (GLS) has been proposed to be a new indicator of systolic function. However, using speckle-tracking echocardiography to assess acute effects of HD on cardiac function has resulted in contradictory results.[6] Although some studies have reported that HD improves cardiac functions in the acute period, others have shown that it affects them negatively.[7-10] In the current study, we aimed to investigate the acute effect of HD on LV GLS in chronic HD patients with preserved LVEF.

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PATIENTS AND METHODS

This single-center, prospective study was conducted at Izmir Bakırçay University, Department of Cardiology between December 2021 and January 2022. A total of 38 patients (24 males, 14 females; mean age: 60.8±13.8 years; range, 31 to 82 years) who were on chronic HD for at least six months and had an LVEF of ≥50% were included. Exclusion criteria were as follows: age <18 years, LVEF <50%, undergoing acute HD, presenting with the acute coronary syndrome and/or pulmonary edema within the last one month, presence of cardiac resynchronization therapy, and inadequate echocardiography imaging quality. A written informed consent was obtained from each patient. The study protocol was approved by the Bakırcay University Non-interventional Clinical Research Ethics Committee (Approval number: 2021/471). The study was conducted in accordance with the principles of the Declaration of Helsinki.

Echocardiography was performed immediately before and immediately after HD in all patients included in the study. Two-dimensional conventional and speckle-tracking echocardiography data of the patients were recorded. Clinical information on comorbidities, medical history, and current cardiovascular medication was obtained by careful review of each patient's medical record and a self-reported questionnaire. All patients were assured to receive adequate clearance by dialysis. The blood pressure and pulse rate values of the patients were recorded before and after HD. The patients were weighed before and after HD and their body weights were recorded. Hemodialysis times, ultrafiltration volumes, and rates of all patients were noted. Baseline blood values taken before the HD session at the beginning of the week were recorded. The body mass index (BMI) of the patients was calculated with the formula: body weight/height in meters squared.

Echocardiography

The Philips EPIQ echocardiography instrument (EPIQ 7, Philips Medical Systems, USA) with a X5-1 probe (Q-lab digital software version 10) was used together with a Q-Lab digital software (Philips Medical Systems, USA) for offline analysis. All echocardiographic parameters were measured offline in batches by two experienced cardiologists blinded to clinical and outcome data. Echocardiography was performed immediately before and immediately after HD.

Two-dimensional echocardiography

Left ventricular ejection fraction was assessed using the biplane Simpson's method from apical four- and two-chamber views. Preserved LVEF was defined as ≥50%. Left ventricular diastolic and systolic diameters were measured from the parasternal long axis view. Peak early (E) and late (A) diastolic velocities of the mitral inflow were evaluated by pulse wave Doppler. Tricuspid regurgitation velocity (TRV) and right atrial pressure were used to estimate pulmonary artery systolic pressure (PASP). Left atrial volume index (LAVI) was measured using the biplane area length method and was indexed to body surface area.

Two-dimensional speckle-tracking echocardiography

Apical four-, three-, and two-chamber views were acquired with high frame rate (>50 fps) for 2D speckle-tracking strain analysis. Offline analyses were performed using Automated Cardiac Motion Quantification software on Q-lab version 10 (Philips Medical Systems, USA). To define the region of interest, the endocardial surface was identified by manually placing at least 15 markings in all apical views. Systolic longitudinal strain was automatically obtained from the three standard apical views (Figure 1). The average systolic longitudinal strain value from the three apical views was regarded as the GLS (Figure 2).

Statistical analysis

Statistical analysis was performed using the SPSS for Windows version 15.0 software (SPSS Inc., Chicago, IL, USA). The Kolmogorov-Smirnov test was used to check for normality of distribution for continuous variables. Continuous variables were presented in mean ± standard deviation (SD) or median (min-max), while categorical variables were presented in number and frequency. Paired samples t-test was used to compare continuous variables before and after HD. Categorical variables were compared using the Pearson chi-square and Fisher exact test. A p value of <0.05 was considered statistically significant.

RESULTS

Of a total of 38 patients included in the study, 33 (86.8%) had hypertension, 13 (34.2%) had diabetes

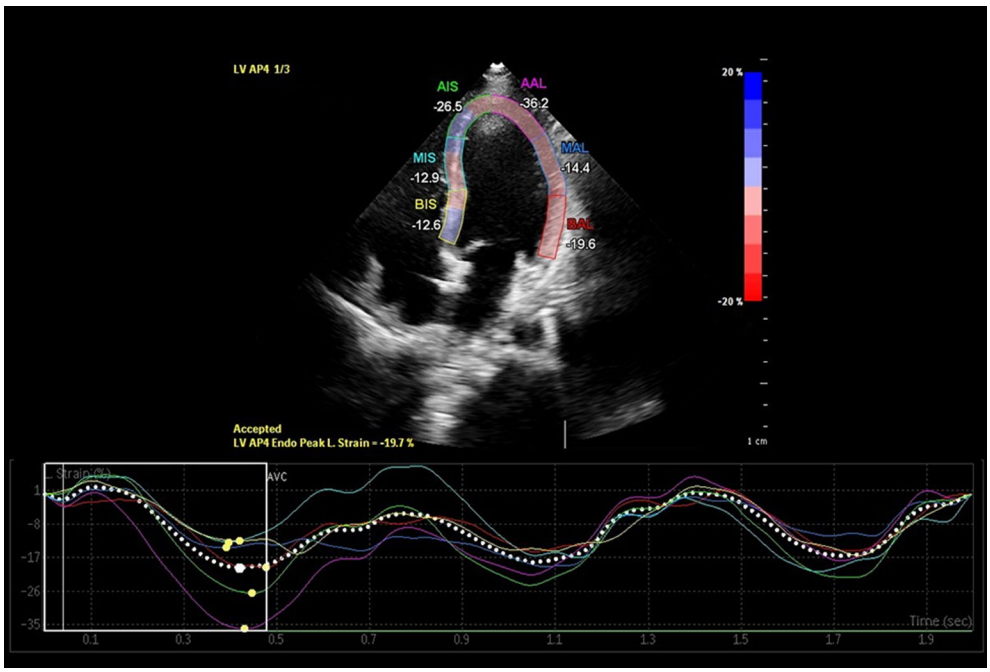

Figure 1. Two-dimensional speckle-tracking echocardiography for left ventricular 4-chamber longitudinal strain.

mellitus, and 14 (36.8%) had coronary artery disease. The mean HD time of the patients was 6.3±3.9 years. The mean ultrafiltration volume of the patients during HD was 2,428±847 mL. Seventeen of the patients were using an antiaggregant agent and two were using an oral anticoagulant. Of the patients, 26 (68.4%) were using vitamin D and 32 (84.2%) were using erythropoietin. Baseline demographic and medication features of the patients are presented in Table I and laboratory findings are presented in Table II.

While there was no significant difference in the mean heart rate before and after HD (73.1±8.6 *vs.* 74.5±8.9 bpm, p=0.194), mean systolic and diastolic

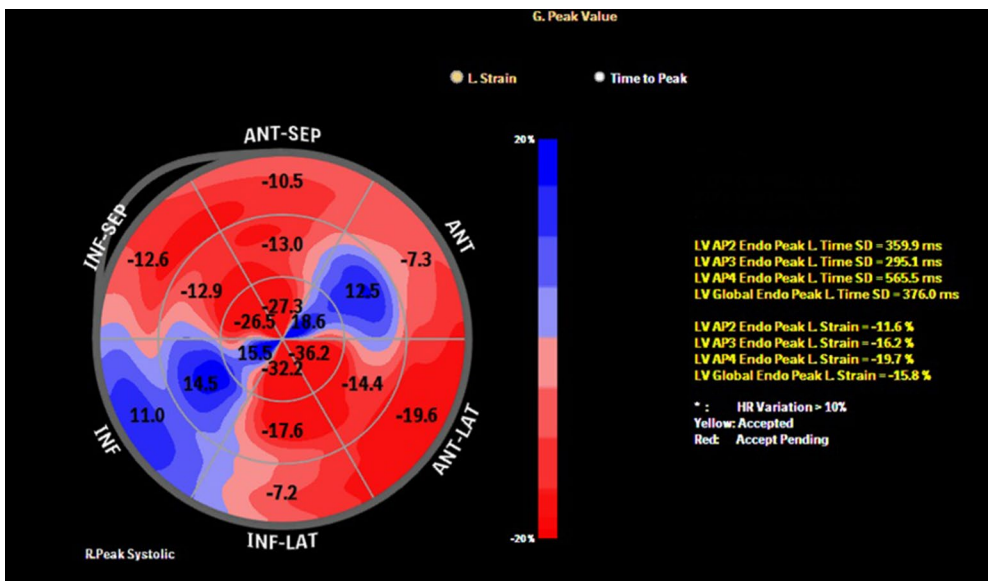

Figure 2. The average left ventricular global longitudinal strain (bull's eye plot).

Table 1
Baseline characteristics of the patients (n=38)

Variables	n	%	Mean±SD
Demographic			
Age (year)			60.8±13.8
Sex			
Male	24	63.2	
Diabetes mellitus	13	34.2	
Hypertension	33	86.8	
Hypercholesterolemia	7	18.4	
Coronary artery disease	14	36.8	
COPD	6	15.8	
Peripheral vascular disease	5	13.2	
Cerebrovascular disease	2	5.3	
Hemodialysis and ultrafiltration			
Duration of HD (year)			6.3±3.9
Ultra-filtrated volume (mL)			2428±847
Medication			
Acetylsalicylic acid	12	31.6	
ADP receptor inhibitors	5	13.2	
Oral anticoagulants	3	7.9	
Beta-blockers	12	31.6	
Calcium-channel blockers	5	13.2	
ACE-i/ARB	1	2.6	
Statin	4	10.5	
Loop diuretics	11	28.9	
Oral antidiabetic	3	7.9	
Insulin	10	26.3	
Anti-potassium	1	2.6	
Anti-acidosis	3	7.9	
Vitamin D	26	68.4	
Erythropoietin	32	84.2	

SD: Standard deviation; COPD: Chronic obstructive pulmonary disease; HD: Hemodialysis; ADP: Adenosine-diphosphate; ACE-i: Angiotensin-converting enzyme inhibitor; ARB: Angiotensin II-receptor blocker.

Table 2
Laboratory characteristics of the patients (n=38)

Variables	Mean±SD
Fasting blood glucose (mg/dL)	128.1±48.2
Urea (mg/dL)	120.8±35.3
Creatinine (mg/dL)	8.2±2.2
Uric acid (mg/dL)	5.5±1.1
Sodium (mEq/L)	138.1±3.1
Potassium (mg/dL)	4.9±0.6
Calcium (mg/dL)	8.9±0.6
Phosphorus (mg/dL)	4.7±1.4
Ferritin (ml/ng)	525.4±548.4
TSH (mU)	2.3±1.3
Parathormone (pg/mL	520.7±733.5
Total cholesterol (mg/dL)	162.2±39.2
HDL-cholesterol (mg/dL)	38.8±11.1
LDL-cholesterol (mg/dL)	95.8±34.1
Plasma triglycerides (mg/dL)	136.5±67.3
White blood cell count ($\times 10^9$ /L)	6.5±1.8
Hemoglobin (g/dL)	10.5±1.5
Hematocrit (%)	32.5±4.4
Platelet count (10^9 /L)	220.8±68.4

SD: Standard deviation; TSH: Thyroid stimulating hormone; HDL: High-density lipoprotein; LDL: Low-density lipoprotein.

blood pressures were significantly lower after HD (136.1±29.1 *vs.* 111.9±20.6 mmHg, p<0.001 and 77.1±14.7 *vs.* 69±12.8 mmHg, p<0.001, respectively). The clinical parameters of the patients before and after HD are presented in Table III.

Of the echocardiographic parameters, the mean LV end-diastolic volume and end-systolic volume were significantly decreased after HD (97.02±20.19 *vs.*

Table 3
Clinical parameters before and after hemodialysis

	Before HD	After HD	
Variables	Mean±SD	Mean±SD	*p*
Systolic blood pressure (mmHg)	136.1±29.1	111.9±20.6	<0.001
Diastolic blood pressure (mmHg)	77.1±14.7	69±12.8	<0.001
Heart rate (bpm)	73.1±8.6	74.5±8.9	0.194
Weight (kg)	74.3±18.4	72.2±18.2	<0.001
Body mass index (kg/m^2)	27.2±7.5	26.4±7.4	<0.001

HD: Hemodialysis; SD: Standard deviation.

Table 4
Echocardiographic parameters before and after hemodialysis

Variables	Before HD Mean±SD	After HD Mean±SD	*p*
LV end-diastolic internal diameter (cm)	47.7±3.8	47.1±3.3	0.081
LV end-systolic internal diameter (cm)	28.9±3.3	28.5±2.9	0.058
LV end-diastolic volume (mL)	97.0±20.2	92.0±17.9	0.002
LV end-systolic volume (mL)	40.1±11.1	37.9±10.5	0.008
LV ejection fraction (%)	59.6±4.1	59.4±3.9	0.208
PASP (mmHg)	23.5±7.4	23.1±6.0	0.286
LA area (4-chamber view) (cm^2)	17.7±4.5	16.5±3.5	0.001
LA volume (mL)	54.7±17.1	49.7±15.5	0.002
LA volume index (mL/m^2)	30.1±10.0	27.5±8.2	0.005
E (cm/s)	99.3±38.2	80.4±27.8	0.001
A (cm/s)	99.4±23.2	90.4±25.5	0.022
E/A	1.1±0.5	1±0.6	0.660
LV GLS (%)	-17.3±2.6	-16.9±2.6	0.088

HD: Hemodialysis; SD: Standard deviation; LV: Left ventricle; PASP: Pulmonary artery systolic pressure; LA: Left atrium; E: Peak early diastolic trans-mitral flow velocity; A: Peak late diastolic trans-mitral flow velocity; GLS: Global longitudinal strain.

92.0±17.9 mL, p=0.002 and 40.1±11.1 *vs.* 37.9±10.5 mL, p=0.008, respectively). Similarly, left atrial area, left atrial volume, and LAVI were significantly lower after HD than before (17.7±4.5 *vs.* 16.5±3.5 cm^2, p=0.001, 54.7±17.1 *vs.* 49.7±15.5 mL, p=0.002, and 30.1±10.0 *vs.* 27.5±8.2 mL/m^2, p=0.005, respectively). Pulsed Doppler echocardiography showed significantly decreased E and A wave peak velocity (99.3±38.2 *vs.* 80.4±27.8 cm/s, p=0.001 and 99.4±23.2 *vs.* 90.4±25.5 cm/s, p=0.022), but no significant change in the E/A ratio (1.1±0.5 *vs.* 1±0.6, p=0.660). There was no significant change on the LV GLS between before and after HD (-17.3±2.6% *vs.* -16.9±2.6%, p=0.088). The echocardiographic parameters of the patients are presented in Table IV.

DISCUSSION

The present study showed that HD did not significantly affect LV GLS, LVEF, and E/A ratio in the acute phase in patients with chronic ESRD.

Chronic kidney disease is a unique risk factor for cardiac remodeling. An experiment in mice showed that early subendocardial changes were worse in those with CKD than in those without.[11] The LVEF measures predominantly radial contraction, while GLS represents the function of subendocardial longitudinal myocardial fibers, which are more sensitive to decreased coronary perfusion and increased wall stress.[12,13] The GLS reflects the longitudinal contraction of the myocardium and its accuracy has been validated against tagged magnetic resonance imaging.[14] The GLS not only provides a quantitative assessment of myocardial function, but also reflects changes in the myocardial interstitium, including myocardial fibrosis.[15] Compared to the general population, the incidence of cardiovascular death in HD patients is 10 to 20 times higher.[1,16] In the general population, GLS was shown to be a superior predictor of cardiac events and all-cause mortality compared to LVEF.[17] Kramann et al.[15] showed that strain parameters were independent risk factors for cardiovascular and all-cause mortality.

Many previous studies have reported that HD adversely affects LV GLS and LVEF.[7,18,19] Indeed, LV functions are expected to improve after HD due to reduced preload and afterload, but there are different mechanisms that affect LV GLS. In addition, hemodynamic changes experienced during HD may worsen LV function by causing myocardial ischemia, myocardial damage or stunning. In a study conducted by Unlu et al.,[9] troponin-T increased with the decline

of GLS after HD. In contrast, Liu et al.[10] found that patients with ESRD who received HD had better LV GLS than those who did not. It was stated that the reason for this was the elimination of the negative effects of renal failure on LV functions by HD.

In some studies similar to our study results, it has been shown that HD does not have a significant effect on LV systolic functions.[20,21] In a different study, Amoozgar et al.[22] found no notable change in LV GLS after HD in children receiving HD, and believed that children's LV GLS was preload independent. The most important cause of deterioration in LV functions during HD is rapid intravascular volume changes. Other possible causes that increase this deterioration are changes in ionized calcium concentration, sympathetic hyperactivity, increased oxidative stress during HD, and low-resistant vessels. In our study, the mean dialysis time was 4 h and controlled ultrafiltration was performed without causing sudden hypotension. This is the most important reason why there was no significant change in LV GLS before and after HD in our study.

In the current study, a decrease in left atrial and ventricular volumes, which are indicators of preload, was found after HD, similar to the findings of Wang et al.[7] However, there was no significant change in LVEF. Furthermore, we found that HD-associated volume reduction changed mitral valve inflow parameters. Both E-wave and A-wave decreased significantly after HD, but there was no significant decrease in E/A ratio. The E/A ratio is an important indicator of LV filling and diastolic function. There was no significant change in the E/A ratio reflecting diastolic functions after HD, just as in LV GLS reflecting systolic functions.

This study has some limitations. The study has a single-center design with a relatively small sample size, and its results need to be further confirmed by a more rigorous and large-sample prospective study. In addition, LV GLS changes after HD according to the ultrafiltration volumes of the patients were not examined separately, which may have affected the LV GLS results.

In conclusion, HD has no significant effect on LV systolic and diastolic functions in the acute phase in patients with chronic ESRD. Avoiding rapid blood volume changes with controlled ultrafiltration during HD may prevent deterioration of LV functions.

Declaration of conflicting interests

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