The European Research Journal 2024;10(1):118-126 Original Article

DOI: https://doi.org/10.18621/eurj.1401607 *Cardiology*

The relationship between heart functions and anemia in patients with end-stage renal disease receiving hemodialysis

Timor Omar[1], Metin Çağdaş[2], İnanç Artaç[1], Muammer Karakayalı[1], Doğan İliş[1], Ayça Arslan[1], Yavuz Karabağ[1], Mahmut Yesin[3], Mustafa Avcı[4], İbrahim Rencüzoğulları[1]

[1]Department of Cardiology, Kafkas University, Faculty of Medicine, Kars, Turkey; [2]Department of Cardiology, Kocaeli City Hospital, Kocaeli, Turkey; [3]Department of Cardiology, VM Medical Park Kocaeli Hospital, Kocaeli, Turkey; [4]Department of Internal Medicine, Balikesir Kepsut State Hospital, Balıkesir, Turkey

ABSTRACT

Objectives: We investigated the relationship between anemia and cardiac functions by conventional and speckle-tracking echocardiography (STE) in patients with end-stage renal disease (ESRD) receiving hemodialysis.

Methods: One hundred and six patients with ESRD receiving hemodialysis were included in this cross-sectional study. The conventional echocardiography and STE findings were compared between the patients with and without anemia. In addition, a comparison of the findings between the ESRD patients and healthy controls consisting of 68 participants was conducted.

Results: Compared to healthy controls, ESRD patients had lower left ventricular ejection fraction (LVEF), left ventricular global longitudinal strain (LVGLS), and left atrial reservoir strain (LASr) [53% (48-57) vs. 65% (62-68), -15.2 (-16.9- -13.6) vs. -19.7 (-16.9- -13.6), and -21.9 (-29.5- -15.3) vs. -29.9 (-35.3- -22.8), respectively, P-value <0.001 for all]. Of the ESRD patients, 70 (66%) had anemia. ESRD patients with anemia had higher interventricular septum (IVS), posterior wall (PW), and left atrial volume index (LAVi) values than patients without anemia. In addition, ESRD patients with anemia had lower LVEF, LVGLS, and LASr than patients without anemia [median (IQR), 13 (12-15) vs. 12 (11-14), P=0.004, 13 (12-15) vs. 12 (11-13.5), P<0.005, 43 (35-55) vs. 34.7 (28-50), P=0.013, 52 (48-55) vs. 56 (47.5-60), P=0.016, -14.6 (-16.4- -13.5) vs. -16 (-18.6- -14.7), P=0.003, and -21.6 (-30.5- -16.3) vs. -30.5 (-33.6- -23.3), P=0.006, respectively]. In multivariable logistic regression analysis, diabetes, PW, LASr, and LVGLS were independently associated with the presence of anemia in ESRD patients.

Conclusion: Our study confirmed impaired cardiac mechanics in ESRD hemodialysis patients and showed that anemia was associated with further worsening cardiac mechanics in this population.

Keywords: Echocardiography, end-stage renal disease, hemodialysis, anemia

End-stage renal disease (ESRD) is one of the leading causes of mortality and morbidity worldwide [1]. Cardiovascular death accounts for more than half of mortality in patients with ESRD [2-4]. On the other hand, anemia is the most common hematologic complication in ESRD, resulting in

Corresponding author: Timor Omar, MD., Assistant Professor, Phone: +90 474 225 21 05, E-mail: tbigmurad@gmail.com

How to cite this article: Omar T, Çağdaş M, Artaç İ, et al. The relationship between heart functions and anemia in patients with end-stage renal disease receiving hemodialysis. Eur Res J. 2024;10(1):118-126. doi: 10.18621/eurj.1401607

Received: December 7, 2023
Accepted: December 25, 2023
Published Online: December 26, 2023

poorer quality of life, and is reportedly a major risk factor for cardiovascular disease in this population [5, 6].

Many studies examined the cardiac characteristics by echocardiographic examination in ESRD patients [7-9]. However, data showing the association between anemia and cardiovascular mechanics in adult patients with ESRD is rare. The purpose of the present study was to address this information gap. In other words, we aimed to evaluate the relationship between anemia and cardiac mechanics using conventional two-dimensional transthoracic echocardiography (TTE) and speckle-tracking echocardiography (STE) in ESRD patients receiving hemodialysis treatment.

METHODS

Study Population

Between February 5, 2019, and April 30, 2019, adult patients with ESRD receiving hemodialysis were included in this cross-sectional study. Patients with congenital heart disease, severe valvular heart disease, and atrial fibrillation were excluded. Intensive-care patients were also excluded from the study. ESRD (a glomerular filtration rate of less than 15 mL/min) was defined per Kidney Disease Improving Global Outcomes (KDIGO) Chronic Kidney Disease (CKD) evaluation and management guideline [10]. Anemia is defined as hemoglobin concentration <13.0 g/dL in males and <12.0 g/dL in females, based on KDIGO anemia in CKD guidelines [11]. The patients were divided into two groups according to the presence of anemia. Findings were compared between the groups. In addition, a comparison of echocardiographic findings between the patients and age and sex-matched healthy controls of 68 participants was conducted.

The study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Ethics Committee of Kafkas University (Date: January 30, 2019/ No 80576354-050-99/30). Written informed consent was obtained from all patients or their legal representatives.

Blood Sampling

Venous blood samples were taken on the day of hemodialysis before the TTE examination. Complete blood count, renal function test (blood urea and serum creatinine), lipid profile, serum iron, serum ferritin, and transferrin saturation were done as a routine examination for CKD.

2-D Transthoracic Echocardiography Examination

TTE recordings were obtained using Philips Epiq7 (Philips Ultrasound, WA, USA), according to the American Society of Echocardiography and the European Association of Cardiovascular Imaging guidelines [12]. Diameters of the left ventricle (LV) (end-systolic and end-diastolic), interventricular septum (IVS), LV posterior wall (PW), left atrial (LA) volume, right ventricle (basal), and right atrium were measured. LA volume index (LAVi) was calculated by dividing the left atrial volume by the body surface area. Assessment of mitral inflow included the peak early (E-wave) and late (A-wave) diastolic filling velocities and calculation of the E/A ratio. The peak velocity of early diastolic mitral annular motion (e') was measured by pulse wave Doppler from the apical four-chamber view. Then, the average value was calculated from septal e' and lateral e' values. The modified Simpson's method described in the European Association of Cardiovascular Imaging (EACVI) was used to calculate the left ventricular ejection fraction (LVEF) [12].

2-D speckle-tracking Echocardiography Examination

Speckle-tracking analysis was performed according to the consensus document of the European Association of Cardiovascular Imaging Task Force [13]. Strain analyses were performed by an experienced cardiologist (T.O.) using QLAB Advanced Quantification Software. The end-diastole was regarded as the peak R wave of the electrogram, and the end-systole was estimated as aortic valve closure. LV myocardial deformation analysis was achieved from 2-dimensional gray-scale loops by automatically tracking myocardial speckles after manually selecting landmark points using apical views of the LV. Manually corrected when needed. The region of interest was the endo-myocardium (from the endocardial border to the myocardial mid-line). The left ventricular global longitudinal strain (LVGLS) calculation was obtained by averaging the negative peak of longitudinal strain from 17 ventricular segments from the apical 4-chamber, 3-cham-

ber, and 2-chamber views. The change in the percentage (%) was regarded as LVGLS. Higher negative values represent the ability of myocardial contractility (The less negative value, the worse LVGLS performance). The LA strain was measured in the reservoir phase (LASr) from the apical 4- and 2-chamber views using the QRS complex as a reference point. Then, the mean value was calculated.

Statistical Analysis

Statistical analysis was performed using SPSS software version 20.0 (SPSS, Inc., Chicago, IL, USA). The continuous variables were presented as mean values and standard deviation (SD). Categorical variables were expressed as frequencies and percentages. Kolmogorov–Smirnov test was used to investigate the distribution of the data. While the independent t-test was

Table 1. Demographic, clinical, and laboratory characteristics of the patients

	Overall (n=106)	Anemia (+) (n=70)	Anemia (-) (n=36)	P value
Male sex, n (%)	66 (62.3)	44 (62.9)	22 (61.1)	0.861
Age (years), median [IQR]	71 [60-77]	68 [59-78]	72 [66-77]	0.285
BMI (kg/m^2) mean±SD	25.5±4.2	24.9±3.9	26.8±4.5	**0.027**
Laboratory				
Hemoglobin (g/dL), median [IQR]	10.7 [9.8-12.5]	10.3 [9.3-10.6]	13.1 [12.3-13.7]	**<0.001**
Hematocrit (%)	32.9 [30.4-38]	31.9 [28.7-32.9]	39 [38-41]	**<0.001**
MCV, mean±SD	89.7±6.5	90.4±5.3	89.3± 7	0.402
RDW (fL)	14.9 [14-16.2]	14.6 [13.8-16]	15.5 [14.5-16.5]	0.053
WBC (× 10^3/µL), median [IQR]	6.73 [5.49-9.22]	6.55 [5.3-9.05]	7.06 [5.49-9.22]	0.395
Lymphocyte (× 10^3/µL), median [IQR]	1.4 [1-1.81]	1.27 [1-1.63]	1.65 [1.05-1.96]	**0.039**
Neutrophil (× 10^3/µL), median [IQR]	4.34 [3.48-6.13]	4.3 [3.31-6.13]	4.83 [3.88-5.94]	0.431
Platelet (× 10^3/µL), median [IQR]	198 [156-251]	208 [158-256]	190 [154-223]	0.327
MPV (fL)	9.4 [8.8-10.5]	9.4 [8.8-10.3]	9.3 [8.6-10.8]	0.805
Total cholesterol, (mg/dL) median [IQR]	139 [120-170]	139 [113-166]	139 [128-177]	0.314
Triglyceride, (mg/dL) median [IQR]	113 [85-161]	112 [86-161]	114 [78-167]	0.878
LDL, (mg/dL) median [IQR]	75 [57-100]	75 [53-1008]	76 [60-100]	0.568
HDL, (mg/dL) median [IQR]	36 [26-42]	35 [25-40]	37 [28-44]	0.315
Creatinine (mg/dL), mean±SD	7.24±3.27	7.42±2.73	6.90±4.14	0.442
CRP (mg/L), median [IQR]	9.87 [3.92-32.3]	10 [4.46-30]	7.2 [3.8-31.3]	0.422
Albumin (g/dL), median [IQR]	37.9 [33.2-41.2]	37.6 [33-40.5]	38.1 [35.9-42]	0.454
Hs-TnT (ng/L), median [IQR]	72.9 [29.8-131.2]	66.7 [31-131.3]	91.3 [15.7-123]	0.915
Comorbidities, n (%)				
Hypertension	79 (74.5)	53 (75.7)	26 (2.2)	0.696
Diabetes	47 (44.3)	36 (51.4)	11 (30.6)	**0.040**
Smoking	20 (19.2)	11 (15.9)	9 (25.7)	0.232
Hyperlipidemia	35 (33)	25 (35.)	10 (27.8)	0.411
Coronary artery disease	25 (23.6)	17 (24.3)	8 (22.2)	0.813

BMI=body mass index, CRP=C-reactive protein, fL=femtoliters, HDL=high-density lipoprotein, Hs-TnT=high-sensitive troponin T, IQR=interquartile range, MCV=mean cell volume, MPV=mean platelet volume, LDL=low-density lipoprotein, RDW=red cell distribution width, SD=standard deviation, WBC=white blood count

used to analyze normally distributed continuous data, the Mann-Whitney U test was used to analyze non-normally distributed variables. Categorical variables were compared with the Chi-squared or Fisher exact test. Univariate regression analysis was carried out to find the variables related to the presence of anemia. Moreover, a multivariate logistic regression analysis with a backward conditional method, including body mass index (BMI), diabetes, IVS, PW, LAVi, E/A, TAPSE, LASr, and LVGLS, was used to describe the independently associated variables with the presence of anemia. Data are displayed as odds ratios (95% confidence intervals). Also, spearman correlation analysis was conducted between hemoglobin value and echocardiographic parameters, including LVEF, LVGLS, LASr, and LAVi. The statistical significance level was accepted as two-tailed P values <0.05.

RESULTS

A total of 106 patients were included in the study. The demographical and laboratory findings of the patients are presented in Table 1. The median age was 71 (IQR, 60-77) years. Of the patients, 70 (66%) had anemia. The hemoglobin value in the global patient population was 10.7 gr/dL (IQR, 9.8-12.5). It was 10.3 g/dL (IQR, 9.3-10.6) in the patients with anemia and 13.1 g/dL (IQR, 12.3-13.7) in the patients without anemia (P<0.001). The BMI of the patients with anemia was

Table 2. Comparison of the echocardiographic findings based on anemia in ESRD patients receiving hemodialysis

	Overall (n=106)	Anemia (+) (n=70)	Anemia (-) (n=36)	P value
LVDD (mm), median [IQR]	48 [44-50]	48 [45-50]	47.5 [44-50]	0.469
LVSD (mm), mean±SD	33.4±6.5	34.3±6.8	31.8±5.5	0.068
IVS (mm), median [IQR]	13 [12-15]	13 [12-15]	12 [11-14]	0.004
PW (mm), median [IQR]	13 [12-14]	13 [12-15]	12 [11-13.5]	<0.001
LA volume index, median [IQR]	39 [29.5-51]	43 [35-55]	34.7 [28-50]	0.013
Right ventricle(mm), median [IQR]	42 [36-46]	42 [36-46]	40 [35-46]	0.194
Right atrium (mm), median [IQR]	44 [36-49]	45 [37-49]	42 [35-47]	0.057
LVEF (%), median [IQR]	53 [48-57]	52 [48-55]	56 [47.5-60]	0.016
E, median [IQR]	84 [66.7-95]	83.5 [65-100]	85.5 [72-93]	0.947
A, median [IQR]	89.5 [72.8-104.8]	91 [75-115]	85.5 [68-90.5]	0.010
e', median [IQR]	14.65 [11-17.9]	14.5 [10.4-17.2]	15.7 [12.7-20]	0.0450
E/A, median [IQR]	0.88 [0.73-1.18]	0.85 [0.69-1.03]	1.01 [0.85-1.22]	0.027
E/e', median [IQR]	5.86 [4.10-7.56]	6.40 [4.10-7.72]	4.72 [4.35-6.47]	0.106
TAPSE, median [IQR]	16.2 [13.8-18.4]	15.2 [13.2-18.2]	18 [15.2-19]	0.004
S', median [IQR]	11.5 [10-12.9]	11 [9.9-12]	12 [11-13]	0.047
PASB, mean±SD	24.8±2.1	26.7±2.7	23.9±4.4	0.001
LASr, median [IQR]	-24 [-33- -16.8]	-21.6 [-30.5- -16.3]	-30.5 [-33.6- -23.3]	0.006
LVGLS, median [IQR]	-15.2 [-16.9- -13.6]	-14.6 [-16.4- -13.5]	-16 [-18.6- -14.7]	0.003

A=late diastolic filling mitral velocity, E=early diastolic filling mitral velocity, E/A=E to A raito, IVS=interventricular septum thickness, IQR=interquartile range, LA=left atrium, LASr=left atrial reservoir strain, LVDD=left ventricle end-diastolic diameter, LVEF=left ventricular ejection fraction, LVGLS=left ventricle global longitudinal strain, LVSD=left ventricle end-systolic diameter, RA=right atrium diameter, RV=right ventricle diameter, PASP=pulmonary arterial systolic pressure, SD=standard deviation, TAPSE=tricuspid annular plane systolic excursion, PW=left ventricular posterior wall thickness, e'=the peak early diastolic velocity of the mitral annulus by tissue Doppler, S'=tissue Doppler velocity of the basal free lateral wall of the right ventricle

significantly lower than those without anemia (mean±SD, 24.9±3.9 vs. 26.8±4.5, P=0.027). Lymphocyte was also significantly lower in patients with anemia [median (IQR), 1.27 (1-1.63) vs. 1.65 (1.05-1.96), P=0.039]. The remaining laboratory findings were similar between the two groups. Regarding comorbidities, the proportion of diabetes was significantly higher in patients with anemia than those without anemia (51% vs. 30.6%, P=0.040).

The comparison of echocardiographic findings in the patients based on the presence of anemia is presented in Table 2. Values of IVS, PW, and LAVi were significantly higher in patients with anemia than those without, while the LVEF was significantly lower. [median (IQR), 13 (12-15) vs. 12 (11-14), P=0.004, 13 (12-15) vs. 12 (11-13.5), P<0.005, 43 (35-55) vs. 34.7 (28-50), P=0.013, and 52 (48-55) vs. 56 (47.5-60), P=0.016, respectively]. Also, the A-wave was significantly higher in patients with anemia, and the E-wave was significantly lower [median (IQR), 91 (75-115) vs. 85.5 (68-90.5), P=0.010 and 6 (4.6-8.1) vs. 6.8 (5.2-9.9), P=0.024, respectively]. Respecting STE analysis, both LVGLS and LASr were significantly lower (less negative, which indicates worse function) the patients with anemia than those without anemia [median (IQR), -14.6 (-16.4- -13.5) vs. -16 (-18.6- -14.7, P=0.003 and -21.6 (-30.5- -16.3) vs. -30.5 (-33.6- -23.3), P=0.006, respectively]. Considering the right ventricular function, both TAPSE and S' were significantly lower in patients with anemia than in patients without anemia [median (IQR), 15.2 (13.2-18.2) vs. 18 (15.2-19), P=0.004 and 11 (9.9-12) vs. 12 (11-13), P=0.047, respectively]. The PASB was significantly higher in patients with anemia (mean ±SD 26.7±2.7 vs. 23.9±4.4, P=0.001). According to correlation analysis, hemoglobin level was significantly correlated with LVEF, LVGLS, LASr, and LAVi (r=0.019, P=0.041, r=0.139, P=0.001, r=0.121, and r=116, P<0.001, respectively) (Fig. 1).

In univariable logistic regression analysis, the fol-

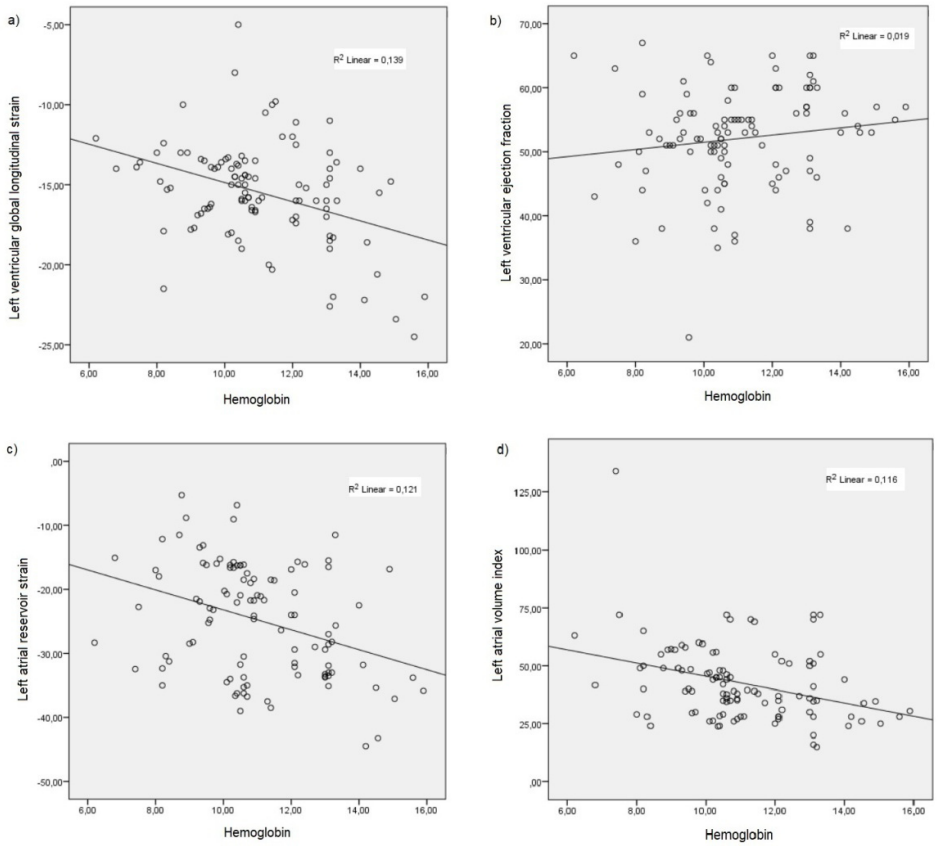

Fig. 1. The correlation between hemoglobin value and (a) LVGLS, (b) LVEF, (c) LASr, and (d) LAVi.LVEF=left ventricular ejection fraction, LVGLS=left ventricular global longitudinal strain, LASr=left atrial reservoir strain,LAVi=left atrial volume index

lowing parameters demonstrated a significant relationship with the presence of anemia: BMI, diabetes, IVS, PW, LAVi, E/A, TAPSE, LVEF, LVGLS, and LASr. In multivariable logistic regression analysis, diabetes, PW, LASr, and LVGLS were independently associated with the presence of anemia in ESRD patients receiving hemodialysis (Table 3).

When the findings were compared between hemodialysis patients and the healthy controls (Table 4), the hemoglobin value was significantly lower in the patients than in the healthy controls [median (IQR), 10.7 (9.8-12.4) vs. 14.7 (13.8-15.9), P<0.001]. Echocardiographic findings, including IVS, PW, and LAVi, were significantly higher in the patients than the control group [median (IQR), 13 (12-15 vs. 11 (11-11.75), 13 (12-14 vs. 11 (11-12), and 39 (29.6-51) vs. 34 (30-44.2), respectively, the P-value for all <0.001]. The medians of LVEF, LVGLS, LASr, TAPSE, and S' were significantly lower in the hemodialysis patients [median (IQR), 53 (48-57) vs. 65 (62-68), -15.2 (-16.9- -13.6) vs. -19.7 (-16.9- -13.6), -21.9 (-29.5- -15.3) vs. -29.9 (-35.3- -22.8), 16.2 (14.-18.2) vs. 21 (20-22) and 11.5 (10-12.8) vs. 12.9 (11.9-14.5), respectively, the P-value for all <0.001]. In the patients, the diameters of cardiac chambers were also significantly higher.

DISCUSSION

This study investigated the relationship between anemia and cardiac mechanics, including systolic and diastolic LV functions and LA and RV functions, using standard TTE and STE analysis in patients with ESRD receiving hemodialysis. First, our study confirmed the previous literature findings that cardiac mechanics in patients with ESRD were impaired compared to healthy controls. Of note, for the first time, in patients with ESRD receiving hemodialysis, we found that LAVi, IVS, and PW thickness were higher in patients with anemia than those without anemia. Moreover, using both TTE and STE, we observed that left atrial, left ventricular, and right ventricular functions were further impaired in patients with anemia. Finally, LV PW thickness, LASr, and LVGLS were independently associated with the presence of anemia in ESRD patients receiving hemodialysis. Our results provided robust evidence regarding the relationship between anemia and cardiac functions, specifically in patients with ESRD receiving hemodialysis.

LV hypertrophy and increased LV mass are well-established identifiable risk factors for cardiovascular events in patients with ESRD [9]. In early reports, cardiac hypertrophy has been reported in about 2/3 of pa-

Table 3. Univariable and multivariable analysis of the variables related to ESRD patients

	Univariate analysis		Multivariate analysis	
	OR (95% CI)	P value	OR (95% CI)	P value
BMI	0.89 (0.80-0.99)	**0.031**		
Diabetes	2.40 (1.03-5.63)	**0.043**	3.6 (1.3-10.3)	**0.017**
IVS	1.37 (1.08-1.74)	**0.010**		
PW	1.57 (1.2-2.08)	**0.001**	1.4 (1.03-1.9)	**0.031**
LAVi	1.04 (1.002-1.07)	**0.032**		
E/A	0.29 (0.09-0.97)	**0.044**		
TAPSE	0.90 (0.81-0.99)	**0.047**		
LVEF	0.95 (0.89-0.99)	**0.048**		
LASr	1.08 (1.03-1.14)	**0.003**	1.09 (1.03-1.16)	**0.005**
LVGLS	1.27 (1.09-1.48)	**0.002**	1.27 (1.06-1.51)	**0.008**

A=late diastolic filling mitral velocity, BMI=body mass index,E=early diastolic filling mitral velocity, E/A=E to A raito, IVS=interventricular septum thickness, LAVi=left atrial volume index, LASr=left atrial reservoir strain, LVGLS=left ventricle global longitudinal strain, LVEF=left ventricular ejection fraction, PW=left ventricular posterior wall thickness, TAPSE=tricuspid annular plane systolic excursion

Table 4. Comparison of the echocardiographic characteristics between hemodialysis patients and healthy controls

	Overall (n=174)	Hemodialysis (n=106)	Control (n=68)	P value
Age (years), median [IQR]	70.5 [62-77]	71 [62-77]	70 [62.5-76]	0.806
Male, sex, n (%)	105 (60.3)	66 (62.3)	39 (57.4)	0.518
BMI (kg/m^2) mean±SD	26.1+4.1	25.5+4.2]	27.1+3.9]	**0.012**
Hemoglobin (g/dL), median [IQR]	12.5 [10.5-14.4]	10.7 [9.8-12.4]	14.7 [13.8-15.9]	**<0.001**
Echocardiographic findings				
LVDD (mm), median [IQR]	47 [43-49]	48 [44-50]	44 [41-48]	**<0.001**
LVSD (mm), mean±SD	32 [29-35]	33 [30-37]	30 [28-35]	**0.001**
IVS (mm), median [IQR]	12 [11-14]	13 [12-15]	11 [11-11.75]	**<0.001**
PW (mm), median [IQR]	12 [11-13]	13 [12-14]	11 [11-12]	**<0.001**
LA volume index, median [IQR]	34 [30-44.2]	39 [29.6-51]	34 [30-44.2]	**<0.001**
RV (mm), median [IQR]	36 [33-43.3]	42 [36-46]	32 [29.5-34]	**<0.001**
RA (mm), median [IQR]	36 [34-46]	44 [36-49]	33 [31-36]	**<0.001**
LVEF (%), median [IQR]	59 [51-64.3]	53 [48-57]	65 [62-68]	**<0.001**
E/A, median [IQR]	1.1 [0.83-1.33]	0.88 [0.74-1.17]	1.3 [1.1-1.5]	**<0.001**
E/e', median [IQR]	6.2 [4.6-7.7]	5.9 [4.1-7.5]	6.4 [5.5-8]	**0.007**
TAPSE, median [IQR]	19 [15.2-21.4]	16.2 [14-18.2]	21 [20-22]	**<0.001**
S', median [IQR]	12 [11-13.7]	11.5 [10-12.8]	12.9 [11.9-14.5]	**<0.001**
LASr, median [IQR]	-24.9 [32.3- -17.7]	-21.9 [-29.5- -15.3]	-29.9 [-35.3- -22.8]	**<0.001**
LVGLS, median [IQR]	-17 [-19.8- -14.5]	-15.2 [-16.9- -13.6]	-19.7[-16.9- -13.6]	**<0.001**

A=late diastolic filling mitral velocity, BMI=body mass index, E=early diastolic filling mitral velocity, E/A=E to A raito, IVS=interventricular septum thickness, IQR=interquartile range, LA=left atrium, LASr=left atrial reservoir strain, LVDD=left ventricle end-diastolic diameter, LVEF=left ventricular ejection fraction, LVGLS=left ventricle global longitudinal strain, LVSD=left ventricle end-systolic diameter, RA=right atrium diameter, RV=right ventricle diameter, SD=standard deviation, TAPSE=tricuspid annular plane systolic excursion, PW=left ventricular posterior wall thickness,e'=the peak early diastolic velocity of the mitral annulus by tissue Doppler, S'=tissue Doppler velocity of the basal free lateral wall of the right ventricle

tients receiving renal replacement therapy [4, 14, 15]. In line with these findings, our results showed that hemodialysis patients had increased LV wall thicknesses compared to healthy controls. However, the association between anemia and hypertrophy has remained unknown in these patients. Our study observed a notable increase in LV posterior and septum thicknesses in hemodialysis patients with anemia than those without anemia. There is evidence that anemia, the most common complication of ESRD, increases the risk of cardiovascular diseases [9, 16]. Since anemia reduces the oxygen-carrying capacity of the blood, a greater cardiac output is needed to maintain a sufficient supply of oxygen. As anemia becomes severe, it leads to a hyperdynamic circulatory system and eventually may cause cardiac enlargement, hypertrophy, and dysfunction [9, 17]. These facts may explain the observed further advanced LV hypertrophy in anemic hemodialysis patients in our study.

Several studies have demonstrated that cardiac mechanics, including the left ventricular, right ventricular, and left atrial structural and functional characteristics, are altered in dialysis patients [18-20]. Some factors such as fluid retention, volume overload, anemia, and calcium phosphate metabolism abnormalities may provoke cardiac dysfunction and may lead to my-

ocardial changes in this population [21]. Studies using STE, which better detects subtle cardiac dysfunction, have also revealed LV systolic dysfunction in hemodialysis patients. According to previous reports, LVGLS was decreased in hemodialysis patients compared to healthy controls, although LVEF was similar [22, 23]. In parallel, our standard and STE echocardiography results showed that cardiac functions in hemodialysis patients were more impaired than in the healthy controls. Of note, previous works have not investigated the relationship between anemia and cardiac functions in the hemodialysis population. Our study addressed this important knowledge gap. Our study revealed that hemodialysis patients with anemia had further deteriorated cardiac functions than those without anemia. Notably, our study identified LASr, and LVGLS as independent markers for association with the presence of anemia in hemodialysis patients but not LVEF. This may be because strain measurement better reflects cardiac mechanics by directly assessing myocardial motion [24]. LVEF is more volume and cardiac-filling dependent. Thus, strain measurement may be a more accurate parameter for hemodialysis patients to follow-up cardiac mechanics, particularly in anemic patients. To our knowledge, only Bhagat *et al*.[25] investigated the association between anemia and cardiac mechanics in children with different stages of chronic kidney disease. They found a significant adverse change in standard echocardiographic findings, including chamber diameters, left ventricular systolic and diastolic functions, and right ventricular function in the anemic group. Unlike ours, their study performed cardiac function analysis using only conventional echocardiographic parameters such as LVEF and did not include the STE technique.

In patients receiving hemodialysis, due to pressure and volume overload, the left atrium is repeatedly subjected to abnormal filling pressure [23]. Dialysis may not be enough to prevent morphological and functional changes in atriums alongside ventricles. It was shown that LA characteristics, including maximum LA volume and LA active and passive emptying volumes, were higher in dialysis patients than in healthy subjects [26, 27]. Some studies showed subclinical LA dysfunction by STE in individuals with ESRF [28]. Our study found that conventional LV diastolic function parameters, including E/A and A wave and LA strain parameters, were more impaired in ESRD patients with anemia.

Our findings align with the literature regarding impaired cardiac mechanics in patients. Furthermore, our results by conventional and myocardial motion tracking techniques showed that cardiac mechanics were even further impaired in hemodialysis patients with anemia. Therefore, anemia may have a further pathophysiological adverse impact on the cardiac structures and functions in ESRD adult patients receiving hemodialysis.

Limitations

Our study had some limitations. Our study had a relatively small sample size. Because our research was a cross-sectional study, we cannot draw cause-and-effect connections from our results. Multicenter prospective analyses should verify the generalizability of these results. Other speckle tracking parameters to evaluate LV systolic function, such as global circumferential and radial strain, were not obtained.

CONCLUSION

Our study confirmed impaired cardiac mechanics in hemodialysis patients and showed that anemia was associated with further worsening cardiac mechanics in this population. These pathophysiological findings indicate the role of anemia in the alteration of cardiac mechanics in patients with ESRD receiving hemodialysis.

Authors' Contribution

Study Conception: TO, MA; Study Design: TO; Supervision: İR, MÇ; Funding: TO; Materials: MK; Data Collection and/or Processing, İA; Statistical Analysis and/or Data Interpretation: YK; Literature Review: MY, TO; Manuscript Preparation: TO and Critical Review: Dİ, AA.

Conflict of interest

The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

Financing

The authors disclosed that they did not receive any grant during the conduction or writing of this study.

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