



ORIGINAL RESEARCH

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## Evaluation of left ventricular functions before and after iron therapy in patients with iron deficiency anemia

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### Abstract

The aim of present study is to evaluate left ventricular (LV) functions using speckle tracking echocardiography (STE) after iron therapy in patients with iron deficiency anemia (IDA). We consecutively enrolled 92 patients with IDA who needed iron therapy and 82 age- and gender-matched healthy volunteers in our study. Their clinical, laboratory, conventional two-dimensional echocardiography (2DE), and STE examinations were performed to all patients before and after iron therapy. Echocardiographic measurements were compared with healthy controls. The hemoglobin level increased after iron therapy ( $7.2 \pm 2.9$  vs.  $12.1 \pm 2.0$ ,  $p < 0.001$ ). There was no statistically difference in conventional echocardiographic measurements of patients before and after iron therapy. The LV global longitudinal strain (GLS:  $19.3 \pm 4.0$  vs.  $23.2 \pm 3.6$ ,  $p < 0.001$ ), but it was still statistically lower than the LV GLS of the healthy controls ( $23.2 \pm 3.6$  vs.  $25.9 \pm 3.1$ ,  $p < 0.001$ ). The LV global systolic strain rate increased after iron therapy ( $1.7 \pm 0.1$  vs.  $2.2 \pm 0.3$ ,  $p < 0.03$ ). IDA might be associated with impairment in LV longitudinal myocardial function. STE might be useful both for early identification of LV subclinical impairment in patients with IDA and also improvement in myocardial deformation indices after iron therapy.

**Keywords:** Iron deficiency anemia, left ventricle, speckle tracking echocardiography

### Introduction

Iron deficiency is a major cause of anemia, even though there are numerous other reasons [1]. Recent studies showed that iron deficiency anemia (IDA) affects multiple organ systems such as the cardiovascular system, nervous system, and immune system [2-4]. Moreover, anemia is considered to be an independent risk factor for cardiovascular disease (CVD) adverse outcomes [5,6]. Anemia is correlated with increased morbidity and mortality in patients with heart failure [7]. The heart failure studies demonstrated the relationship between anemia and adverse outcomes in patients with IDA [8]. Thereby, the assessment of left ventricle mechanical function is an important point in diagnosis and management of patients with IDA.

Although two-dimensional echocardiography is a major method to evaluate LV dysfunction in daily practice, it has some limitations

when compared to speckle tracking echocardiography (STE) [9].

First of all, STE a comparatively Doppler beam angle independent method. Moreover, it can evaluate the global and regional LV systolic functions in longitudinal, circumferential, and radial directions [10,11].

The aim of present study is to evaluate LV functions using both conventional echocardiography and STE after iron therapy in patients with IDA.

### Material and Methods

#### Study population

Overall, 92 patients with IDA who required iron therapy and 82 age and gender matched healthy volunteers were consecutively enrolled in our study. The mean hemoglobin value of the patients was  $7.2 \pm 2.9$  g/dL. The patients received daily 3–4 mg/kg oral iron therapy for 8–10 weeks based on IDA diagnosis and treatment guideline [12]. Clinical, laboratory, and echocardiographic evaluations were performed after a month of iron therapy. None of the patients had signs and symptoms of congestive

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heart failure before, during and after iron therapy. Patients with history of coronary heart disease, atrial fibrillation, congestive heart failure, rheumatological disease, congenital heart disease, diabetes mellitus, atrioventricular conduction disturbance, malign arrhythmia, thyroid disease, and moderate or high grade of valvular stenosis or valvular insufficiency were excluded.

Our study was approved from the Ethical Committee based on the Declaration of Helsinki and informed consent was obtained from the each participant after the process of the study was obviously explained.

### Clinical and laboratory examination

All patients had completed a physical examination, from which height and weight were measured, and body mass index (BMI, kg/m<sup>2</sup>) and body surface area (BSA, m<sup>2</sup>) were calculated. Blood pressure and blood glucose were measured before echocardiographic examination.

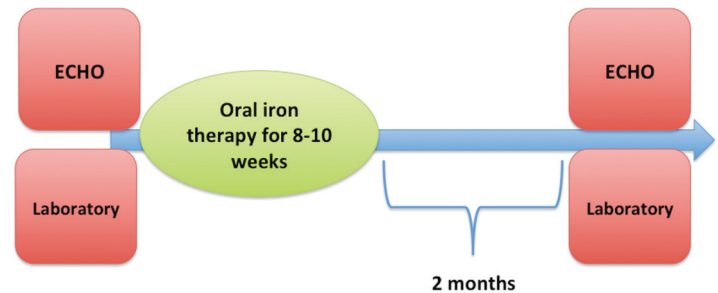
Diagnosis of IDA include the following based on based on IDA diagnosis and treatment guideline [12]: Hemoglobin values were lower than <12 g/dL for adult women, <11 g/dL for pregnant women, and <13 g/dL for adult men were included in the study. The microcytic hypochromic anemia was described as mean corpuscular volume (MCV) <80 fL. Moreover, the patients' serum iron and ferritin concentrations, total iron binding capacity, and serum transferrin saturation were evaluated in the diagnosis of IRA. We also excluded other cause of microcytic hypochromic and macrocytic anemia. Eleven patients who could not response to oral iron therapy were excluded from study.

### Echocardiographic Evaluation

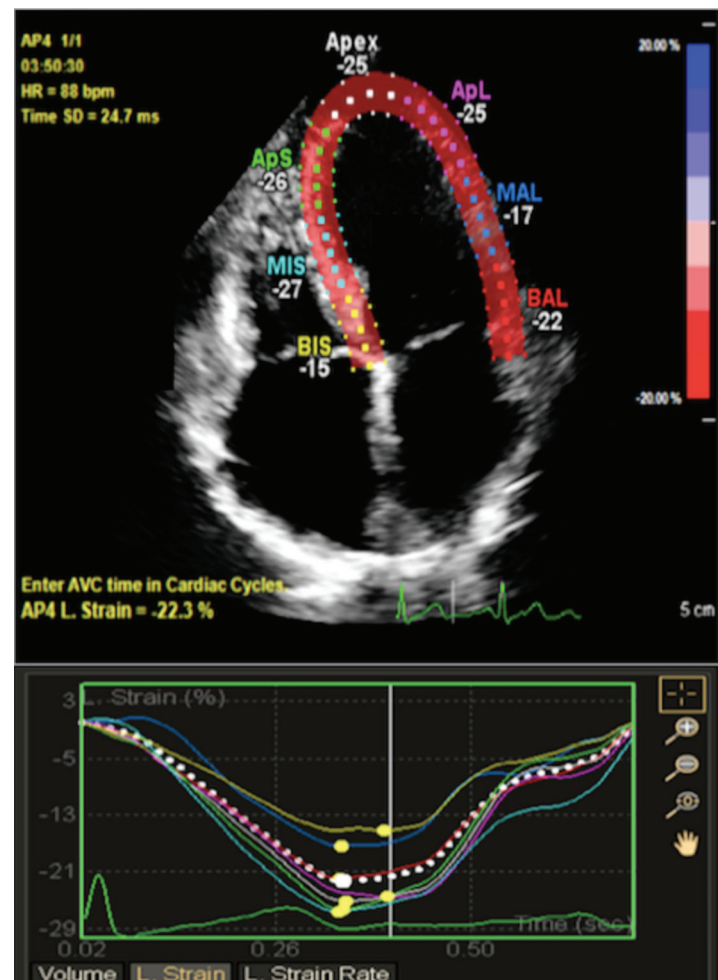
The two-dimensional (2D) echocardiographic evaluations of the LV's systolic and diastolic functions were performed with an ultrasound system (Epic, Philips Healthcare Medical Systems, Andover, Massachusetts, USA) in accordance with the guidelines of the American and European Societies of Echocardiography for cardiac chamber quantification and diastolic dysfunction evaluation [13,14]. Standard echocardiographic views were obtained with a 3.5 MHz transducer in all participants.

Two independent cardiologists performed STE post-processing analysis using the Philips QLAB off-line software program (Philips Healthcare Medical Imaging System, Andover, MA, USA). They recorded three consecutive cardiac cycles in the DICOM format for each view, with a frame rate above 50 per second, which seems to be the best compromise between appropriate spatial and temporal resolutions of the heart chambers. The region of interest (ROI) was obtained by tracing the endocardial border of the LV in a still frame at end-systole in STE post-processing analyses [15]. The ROI was adjusted to cover at least 90% of the myocardial wall thickness. If the first tracking was considered suboptimal, other retracings were performed either manually or semi-automatically. The longitudinal strain curves of 6 LV segments (the basal, mid, and apical segments of the LV lateral wall and inter ventricular septum [IVS]), and the longitudinal strain curves of the LV lateral wall were analyzed using the same method. LV longitudinal strain analysis measured the global longitudinal strain (GLS), systolic strain rate (SRS), early diastolic strain rate (SRE), and late diastolic strain rate (SRA) using the apical views (4-, 3-, and 2-chamber).

In addition, global circumferential strain (GCS) and global radial strain (GRS) were analyzed using short-axis views at the basal, midpapillary, and apical levels as recommended [10,16]. Systolic Strain is the systolic displacement of the tracking segment of the myocardium as a percentage (figure 2). It is negative values; the more negative the value is, the greater the deformation and LV function are [17]. The LV GLS analysis revealed the intraobserver variability as 6.6% and the interobserver variability 11.5%.



**Figure 1.** Study protocol. Figure shows the design of the study. Before oral iron therapy for 8-10 weeks, the echocardiography, laboratory and clinical examinations were performed. All examinations were repeated after two months end of the oral iron therapy



**Figure 2.** Representative two-dimensional left ventricular strain images. Speckle-tracking apical four chamber view showing global and regional left ventricular longitudinal strain

### Statistical analysis

All statistical variables were analyzed with the Statistical Package for the Social Sciences (SPSS 22.0 for Mac; Inc., Chicago, IL, USA) software. The disturbances of variables were examined with analytic Kolmogorov–Smirnov or Shapiro–Wilk’s tests. Continuous variables are presented as mean  $\pm$  standard deviation and categorical variables as numbers and percentages. Statistical analysis of the quantitative data was conducted using unpaired and paired samples Student t tests because all variables were normally distributed. Binary post-hoc analyses were performed using Tukey’s test when an overall statistically significance was determined. In sample size calculation, we calculated that we would need 92 patients with IDA and 82 healthy subjects in each group to detect a 2 point difference in DAN scale with 80% power and at 1% significance. ‘Kappa coefficients were calculated to estimate interobserver as well as intraobserver correlations in the STE analysis [18]. A p value of  $< 0.05$  was considered statistically significant. Intra- and interobserver variabilities were evaluated using the intraclass correlation coefficient.

### Results

Overall, we enrolled 92 patients (28.5 $\pm$ 12.1 years and 77.1% female) with IDA and healthy controls (29.4 $\pm$ 9.3 years and 71.9%

female). Patients and healthy controls clinical, demographic, and laboratory characteristics showed in Table 1. Patients with IDA had higher heart rate (98.7 $\pm$ 34.7 vs. 72.8 $\pm$ 27.5,  $p<0.001$ ) and had lower hemoglobin level (7.2 $\pm$ 2.9 vs. 14.1 $\pm$ 3.1,  $p<0.001$ ) when compared to healthy controls.

The laboratory characteristics of patients with IDA before and after iron therapy showed in Table 2. The hemoglobin (7.2 $\pm$ 2.9 vs. 12.1 $\pm$ 2.0,  $p<0.001$ ), MCV, serum iron, transferrin saturation, ferritin levels increased and iron binding capacity decreased after iron therapy.

The conventional echocardiographic measurements of patients before and after iron therapy and healthy controls showed in Table 3. There was no statistically significant difference among three groups.

The speckle tracking echocardiographic measurements of patients before and after iron therapy and healthy control showed in Table 4. The LV GLS increased after iron therapy (19.3 $\pm$ 4.0 vs. 23.2 $\pm$ 3.6,  $p<0.001$ ), but it was still statistically lower than the LV GLS of the healthy controls (23.2 $\pm$ 3.6 vs. 25.9 $\pm$ 3.1,  $p<0.001$ ). The LV global SRS increased after iron therapy (1.7 $\pm$ 0.1 vs. 2.2 $\pm$ 0.3,  $p<0.03$ ).

**Table 1.** Clinical, demographic, and laboratory characteristics of patients with iron deficiency anemia and control group

	Patients with IDA (n=92)	Healthy control group (n=82)	p value
Age (years)	28.5 $\pm$ 12.1	29.4 $\pm$ 9.3	0.37
Sex (female/male)	71/21	59/20	0.33
Body mass index (kg/m <sup>2</sup> )	26.9 $\pm$ 5.1	27.0 $\pm$ 4.8	0.21
Systolic BP (mmHg)	122.3 $\pm$ 25.3	121.5 $\pm$ 19.0	0.22
Diastolic BP (mmHg)	77.4 $\pm$ 14.0	77.2 $\pm$ 12.6	0.30
Heart rate (rates/min)	98.7 $\pm$ 34.7	72.8 $\pm$ 27.5	$<0.001$
Smoking (%)	27(29.3%)	22(26.8%)	0.14
Hemoglobin (g/dL)	7.2 $\pm$ 2.9	14.1 $\pm$ 3.1	$<0.001$
Creatinine (mg/dL)	0.88 $\pm$ 0.7	0.91 $\pm$ 0.9	0.38

Data are presented as mean  $\pm$  standard. Bold values indicate statistical significance. Abbreviations: BP: blood pressure

**Table 2.** Laboratory characteristics of patients with iron deficiency anemia before and after iron therapy

	Patients before iron therapy (n=92)	Patients after iron therapy (n=92)	p value
Hemoglobin (g/dL)	7.2 $\pm$ 2.9	12.1 $\pm$ 2.0	$<0.001$
Mean corpuscular volume (fL)	74.1 $\pm$ 3.8	82.1 $\pm$ 3.2	$<0.001$
Serum iron ( $\mu$ g/dL)	53.1 $\pm$ 28.2	71.1 $\pm$ 33.7	$<0.001$
Iron binding capacity ( $\mu$ g/dL)	407.4 $\pm$ 67.5	372.3 $\pm$ 64.6	$<0.001$
Transferrin saturation (%)	10.2 $\pm$ 6.3	17.2 $\pm$ 8.1	$<0.001$
Ferritin (ng/mL)	9.8 $\pm$ 4.7	27.5 $\pm$ 9.6	$<0.001$
Creatinine (mg/dL)	0.88 $\pm$ 0.7	0.90 $\pm$ 0.9	0.41

Data are presented as mean  $\pm$  standard. Bold values indicate statistical significance

**Table 3.** Conventional echocardiographic measurements of patients with iron deficiency anemia before and after iron therapy and control groups

	Patients before iron therapy (n=92)	Patients after iron therapy (n=92)	Healthy control group (n=82)	p value
<b>LV end diastolic diameter (mm)</b>	44.0±5.4	44.7±4.3	46.1±3.0	0.26
<b>LV end systolic diameter (mm)</b>	29.2±3.1	28.2±3.5	29.3±4.3	0.20
<b>IVS thickness (mm)</b>	7.2±1.8	7.4±1.8	8.2±1.7	0.16
<b>Posterior wall thickness (mm)</b>	7.1±1.2	7.0±1.1	7.0±0.9	0.13
<b>LV Ejection fraction (%)</b>	63.5±4.1	63.3±3.8	62.8±3.2	0.34
<b>E (cm/s)</b>	0.80±0.4	0.84±0.4	0.78±0.3	0.15
<b>A (cm/s)</b>	0.62±0.3	0.64±0.3	0.57±0.2	0.19
<b>E/A ratio</b>	1.2±0.3	1.3±0.2	1.4±0.3	0.10
<b>Deceleration time (ms)</b>	118±28	121±24	110±27	0.17
<b>IVRT (ms)</b>	82±12	88±14	76±19	0.32
<b>Mean* e'</b>	9.2±2.8	8.9±2.6	9.4±2.8	0.14
<b>Mean* a'</b>	5.7±2.0	6.0±2.1	5.9±2.1	0.18
<b>Mean* s'</b>	6.4±1.9	6.1±2.1	6.5±2.2	0.07
<b>E/e' ratio</b>	8.6±2.1	9.4±2.5	8.2±2.0	0.23

Data are presented as mean ± standard. Bold values indicate statistical significance. Abbreviations: A: transmitral peak A velocity; E: transmitral peak E velocity; IVS: interventricular septum; IVRT: isovolumetric relaxation time; LV: left ventricle.

Mean\*: It was calculated as mean values of lateral and mitral annular tissue Doppler imaging

**Table 4.** Speckle tracking echocardiographic measurements of patients with iron deficiency anemia before and after iron therapy and control groups

	Patients before iron therapy (n=92)	Patients after iron therapy (n=92)	Healthy control group (n=82)	p value
<b>LV global longitudinal strain (-%)</b>	19.3±4.0 <sup>a</sup>	23.2±3.6 <sup>b</sup>	25.9±3.1	<0.001
<b>LV circumferential strain (%)</b>	27.2±4.0	28.2±4.3	27.9±3.2	0.41
<b>LV radial strain (%)</b>	37.8±5.0	39.4±4.8	42.1±4.1	0.06
<b>LV global SRS (-1/s)</b>	1.7±0.1 <sup>a</sup>	2.2±0.3	2.6±0.4	0.03
<b>LV global SRE (1/s)</b>	2.3±0.3	2.4±0.2	2.8±0.4	0.28
<b>LV global SRA (1/s)</b>	2.0±0.2	2.1±0.3	2.3±0.2	0.47

Data are presented as mean ± standard. Bold values indicate statistical significance. Abbreviations: LV: left ventricle; SRA: late diastolic strain rate; SRE: early diastolic strain rate; SRS = systolic strain rate.

<sup>a</sup> p < 0.05, Patients before iron therapy group versus after iron therapy group (Tukey's HSD post hoc test).

<sup>b</sup> p < 0.05, Patients after iron therapy group versus healthy controls (Tukey's HSD post hoc test).

## Discussion

At present, oral iron therapy is the major treatment method for treating IDA [12]. We conducted a prospective study to investigate LV mechanical and diastolic functions before and after iron therapy by performing conventional and advanced echocardiography techniques. The conventional 2DE did not detect any left ventricular systolic dysfunction after the iron therapy. In STE analyses, we showed that patients with IDA had significantly lower LV GLS and LV SRS values when compared to healthy controls. After iron therapy, patients LV GLS value increased but it was still lower than healthy controls. On the other hand, LV SRS increased without statistical significant differences when compared to controls.

As far as recent clinical studies are concerned, the evaluation of the LV mechanical and diastolic function was studied in a numerous study in patients with IDA. Zhou et al. showed the decrease of LV GLS, LV circumferential strain, LV radial strain based on the patients' hemoglobin levels. The lesser hemoglobin level, the lesser LV GLS, LV circumferential strain, and LV radial

strain values in the STE analyses of the patients with IDA [19]. In a STE based study, Shen et al. demonstrated the decrease of LV GLS, LV SRS, LV SRE, and LV SRA in patients with IDA [20]. Our results were in accordance with these findings. Bedirian and Hammoidi et al. explored the decrease of LV GLS in patients with sickle cell anemia [21,22]. In a STE based study, Barbosa et al. showed that there was no statistically difference between sickle cell anemia and healthy controls in the measurements of LV GLS, LV circumferential strains and LV radial strain [23]. In a conventional 2DE study, Aessopos et al. demonstrated the LV dysfunction in patients with chronic anemia [24]. To the best our knowledge, our study is the first study showed the decrease of LV GLS when compared to healthy controls and also demonstrated the improvement of LV GLS after iron therapy.

In a STE based current study, Stokke et al. explored the interactions among different types of strain and how they compensate for early LV dysfunction [25]. Longitudinal fibers are mainly located in the subendocardium and thus are more vulnerable to wall stress and fibrosis in contrast to the midwall circumferential fibers. Stokke

et al. concluded that STE could better identify systolic function in patients with a preserved estimated LV EF. STE-derived strain might be a potential indicator of subclinical LV dysfunction in numerous diseases [26,27].

### Clinical implications

In our research, we found that STE might detect LV mechanical dysfunction earlier than 2D conventional echocardiography and tissue Doppler imaging in patients with IDA. Moreover, it could help indicate the management of the therapy in daily practice, determine the affectivity of the oral iron therapy in the follow-up, improve the quality of patients' life, and decrease the major cardiovascular risk. Therefore, the echocardiography should be used in daily practice in the management of the patients with IDA.

### Study limitations

Our present clinical research had several limitations. First of all our study population is small. Second, most of our study population included female, this situation might affect the LV mechanical function. Our results need to be supported by large scale and multi-center clinical studies. Third, our results should be compared with cardiac magnetic resonance imaging, because it is still the gold standard non-invasive imaging method to diagnosis of iron deposition in the cardiac myocytes and also the LV mechanical dysfunction with its higher spatial resolution than the echocardiography [28]. However, the echocardiography is still the most common method the evaluation of LV systolic and diastolic functions because of its cost effectiveness, easy accessibility, ability to assess more than ventricular function, and absence of radiation and contrast agent exposures. Fourth, our results might be supported with cardiac biopsy but it was not approved by our ethical committee. Fifth, we did not have the duration of the anemia before the diagnosis although it might affect the contraction of the myocardium.

### Conclusion

In this clinical work, we revealed that IDA might be associated with impairment in LV longitudinal myocardial function. STE might be useful both for early identification of LV subclinical impairment in patients with IDA and also improvement in myocardial deformation indices after iron therapy.

### Conflict of interest

*The authors declare that there are no conflicts of interest.*

### Financial Disclosure

*All authors declare no financial support.*

### Ethical approval

*Consent of ethics was approved by the local ethics committee.*

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### References

1. DeLoughery TG. Iron deficiency anemia. *Med Clin North Am.* 2017;101:319-32.
2. Lopez A, Cacoub P, Macdougall IC, et al. Iron deficiency anaemia. *Lancet.* 2016;387:907-16.

3. Lozoff B, Beard J, Connor J, Barbara F, et al. Long-lasting neural and behavioral effects of iron deficiency in infancy. *Nutr Rev.* 2006;64:34-43.
4. Das I, Saha K, Mukhopadhyay D, et al. Impact of iron deficiency anemia on cell-mediated and humoral immunity in children: A case control study. *J Nat Sci Biol Med.* 2014;5:158-63.
5. Pereira AA, Sarnak MJ. Anemia as a risk factor for cardiovascular disease. *Kidney Int Suppl.* 2003;87:S32-9.
6. Sarnak MJ, Tighiouart H, Manjunath G, et al. Anemia as a risk factor for cardiovascular disease in the atherosclerosis risk in communities (ARIC) study. *J Am Coll Cardiol.* 2002;40:27-33.
7. Mitchell JE. Emerging role of anemia in heart failure. *Am J Cardiol.* 2007;99:15-20.
8. Sullivan JL. Iron therapy and cardiovascular disease. *Kidney Int Suppl.* 1999;69:135-7.
9. Chengode S. Left ventricular global systolic function assessment by echocardiography. *Ann Card Anaesth.* 2016;19:26-34.
10. Cameli M, Mondillo S, Galderisi M, et al. Speckle tracking echocardiography: a practical guide. *G Ital Cardiol (Rome).* 2017;18:253-69.
11. Collier P, Phelan D, Klein A. A Test in context: myocardial strain measured by speckle-tracking echocardiography. *J Am Coll Cardiol.* 2017;69:1043-56.
12. Comité Nacional de Hematología. Iron deficiency anemia. Guideline for diagnosis and treatment. *Arch Argent Pediatr.* 2009;107:353-61.
13. Lang RM, Badano LP, Mor-Avi V, et al. Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American society of echocardiography and the european association of cardiovascular imaging. *Eur Heart J Cardiovasc Imaging.* 2015;16:233-70.
14. Nagueh SF, Smiseth OA, Appleton CP, et al. Recommendations for the evaluation of left ventricular diastolic function by echocardiography: an update from the American society of echocardiography and the european association of cardiovascular imaging. *Eur Heart J Cardiovasc Imaging.* 2016;17:1321-60.
15. Mądry W, Karolczak MA. Physiological basis in the assessment of myocardial mechanics using speckle-tracking echocardiography 2D. Part I. *J Ultrason.* 2016;16:135-44.
16. Voigt JU, Pedrizzetti G, Lysyansky P, et al. Definitions for a common standard for 2D speckle tracking echocardiography: consensus document of the EACVI/ASE/Industry Task Force to standardize deformation imaging. *J Am Soc Echocardiogr.* 2015;28:183-93.
17. Sugimoto T, Dulgheru R, Bernard A, et al. Echocardiographic reference ranges for normal left ventricular 2D strain: results from the EACVI NORRE study. *Eur Heart J Cardiovasc Imaging.* 2017;18:833-40.
18. Viera AJ, Garrett JM. Understanding interobserver agreement: The kappa statistic. *Fam Med.* 2005;37:360-3.
19. Zhou Q, Shen J, Liu Y, Luo R, et al. Assessment of left ventricular systolic function in patients with iron deficiency anemia by three-dimensional speckle-tracking echocardiography. *Anatol J Cardiol.* 2017;18:194-9.
20. Shen J, Zhou Q, Liu Y, et al. Evaluation of left atrial function in patients with iron-deficiency anemia by two-dimensional speckle tracking echocardiography. *Cardiovasc Ultrasound.* 2016;14:34.
21. Bedirian R, Soares AR, Maioli MC, et al. Left ventricular structural and functional changes evaluated by echocardiography and two-dimensional strain in patients with sickle cell disease. *Arch Med Sci.* 2018;14:493-9.
22. Hammoudi N, Arangalage D, Djebbar M, et al. Subclinical left ventricular systolic impairment in steady state young adult patients with sickle-cell anemia. *Int J Cardiovasc Imaging.* 2014;30:1297-304.

23. Barbosa MM, Vasconcelos MC, Ferrari TC, et al. Assessment of ventricular function in adults with sickle cell disease: role of two-dimensional speckle-tracking strain. *J Am Soc Echocardiogr.* 2014;27:1216-22.
24. Aessopos A, Deftereos S, Farmakis D, et al. Cardiovascular adaptation to chronic anemia in the elderly: an echocardiographic study. *Clin Invest Med* 2004; 27:265-73.
25. Stokke TM, Hasselberg NE, Smedsrud MK, et al. Geometry as a confounder when assessing ventricular systolic function: comparison between ejection fraction and strain. *J Am Coll Cardiol* 2017;70: 942-54.
26. Reant P, Lafitte S, Bougteb H, et al. Effect of catheter ablation for isolated paroxysmal atrial fibrillation on longitudinal and circumferential left ventricular systolic function. *Am J Cardiol.* 2009;103:232-7.
27. Demirkıran A, Albayrak N, Albayrak Y, et al. Speckle-tracking strain assessment of left ventricular dysfunction in synthetic cannabinoid and heroin users. *Anatol J Cardiol.* 2018;19:388-93.
28. Heiss R, Wiesmueller M, Treutlein C, et al. Cardiac T2 star mapping: standardized inline analysis of long and short axis at three identical 1.5 T MRI scanners. *Int J Cardiovasc Imaging.* 2018;21;1-8.