

Evaluation of cardiac function in patients with sickle cell disease with left ventricular global longitudinal strain

Marielle Morissens¹, Tatiana Besse-Hammer², Marie-Agnès Azerad³,
Andre Efira³, José Castro Rodriguez¹

¹Cardiology Department, Internal Medicine, CHU Brugmann, Brussels, Belgium;

²Clinical Research Department, CHU Brugmann, Brussels, Belgium;

³Hematology Department, Internal Medicine, CHU Brugmann, Brussels, Belgium

ABSTRACT

Background and Objectives: The importance of myocardial dysfunction in sickle cell disease (SCD) is currently debated. It is difficult to find a reliable index of function in patients with chronic overload as in SCD. Speckle tracking echocardiography, a new mean of evaluating cardiac function, might be a useful tool in SCD. It has been applied in many fields to detect early cardiac function deterioration, and it is less load dependent compared with other function parameters. Studies in patients with SCD are rare, and the results are conflicting. The present study aimed to determine whether left ventricular global longitudinal strain (LV-GLS) was abnormal in a population of adults with SCD and whether it was correlated with clinical or biological parameters. **Methods:** We prospectively enrolled 37 patients and 34 age- and sex-matched healthy controls. Echocardiography was performed in patients and controls. **Results:** We found that the left ventricular diameter and mass were higher and the ejection fraction and longitudinal strain were lower in patients compared with controls. Diastolic dysfunction was uncommon. LV-GLS was abnormal in 21% of the patients. No correlation was observed between strain and clinical or biological parameters. **Conclusions:** We concluded that LV-GLS could be a useful tool for evaluating these patients. However, the clinical impact of reduced LV-GLS remains to be determined.

Key words: sickle cell disease, speckle tracking, longitudinal strain, systolic function, diastolic function

INTRODUCTION

Sickle cell disease (SCD) is one of the most frequent genetic blood diseases, with a prevalence of 1/2000 birth in Europe and 1/30 birth in central Africa. SCD occurs with an autosomal mutation in the gene that encodes the β -globin chain, which leads to an abnormal form of hemoglobin (HBS). Some patients are homozygous for this recessive mutation (HB SS). HB SS polymerizes under stressful conditions and leads to sickle-shaped red blood cells with high rigidity and low deformability. This condition causes hemolysis, vaso-occlusive events, and endothelial dysfunction. These are responsible for the cardiovascular

complications of SCD mainly represented by pulmonary hypertension and also left and right ventricular dysfunctions, myocardial infarction, iron overload, arrhythmias, and sudden death.^[1]

The impact of this disease on cardiac function is currently debated. The supposed effects could arise from various mechanisms, including dilatation and hypertrophy due to chronic anemia; iron deposition in the myocardium after transfusions; ischemia due to the vaso-occlusion phenomenon; and pulmonary hypertension. All these conditions can lead to myocardial dysfunction, but the extent of dysfunction remains unclear.

Address for Correspondence:
Dr. Marielle Morissens, MD, Cardiology
Department, CHU Brugmann, Pl Van
Gehuchten 4, 1020 Bruxelles, Belgium.
E-mail: marielle.morissens@chu-
brugmann.be

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Advances in the treatment of SCD have led to extended longevity in these patients. Consequently, the prevalence of heart disease has increased in older individuals with SCD; nearly one-fourth of deaths in this population are due to cardiac involvement.^[2]

Studies on cardiac function in patients with SCD have shown conflicting results. These discrepancies reflect the difficulty in finding a reliable index of function in patients with a chronic overload due to anemia.^[3-7] Most methods for evaluating systolic function are highly dependent on volume. This is particularly true in evaluating the left ventricular ejection fraction (LVEF), which remains the most commonly used parameter for evaluating left ventricular systolic function in routine clinical practice.

Speckle tracking echocardiography is a new means of evaluating cardiac function. It is emerging in many fields as a useful tool in the detection of early cardiac function deterioration. The principle of speckle tracking is to measure myocardial strain, based on local shortening, lengthening, and thickening of the muscles. These types of strain cause the displacement of prominent speckles on images of the myocardium. The displacements allow calculations of myocardial strain. Strain can be longitudinal, radial, or circumferential; at present, longitudinal strain is the most widely available and with the more evidence of clinical applications in detecting subclinical left ventricular dysfunction.

Strain is calculated regionally in each myocardial segment. The mean of all regional strains is called the global longitudinal strain (GLS). By convention, when two speckles draw apart from each other, the value is positive; and when two speckles draw towards each other, the value is negative. Therefore, normal systolic longitudinal strain is negative. The GLS calculation is currently available with the most recent-generation echocardiography machines. Although uniformity might be lacking among different vendors, it has been proposed that the GLS could be a useful tool for the detection of early systolic dysfunction in patients under cardiotoxic chemotherapy.^[8] Moreover, the high reproducibility of GLS measured in the left ventricle (LV-GLS) represents an advantage over the LVEF.^[9-10] Moreover, compared with LVEF, LV-GLS is less affected by changes in loading conditions, which makes it a potentially useful tool in patients with SCD due to the chronic overload associated with SCD. However, in this population, studies are rare and results are conflicting.^[11-16] More recently, the GLS was found to be altered in a population of patients with β -thalassemia,^[17,18] a hemoglobinopathy that can, in some respects, be compared with SCD.

Study aims

The primary aim of the present study was to determine whether GLS was abnormal in a monocentric population of adults with SCD, compared with a matched population of healthy individuals. The secondary aim was to investigate correlations between the echocardiographic parameters and the biological and clinical evaluations of patients with SCD.

MATERIALS AND METHODS

Between September 2014 and September 2015, we prospectively included consecutive patients diagnosed with SCD who were regularly followed at the adult hematology clinic of our institution. The patients were almost all homozygous for SCD, except for one patient who is heterozygous HbS/ β -thalassemia. One patient had a hereditary persistence of fetal hemoglobin (HbF). The Institutional Ethics Committee approved the protocol. All patients provided informed consent. The control group consisted of healthy individuals from the medical community and their relatives. Controls were matched for age and sex with the patients. One patient was excluded because of poor echocardiographic windows.

A single operator with a Philips IE 33 sonograph conducted echocardiographic examinations. We used qlab 9 software for the strain calculations. All echocardiographic examinations in SCD patients were made during steady state (no acute crisis for at least 45 days).

All echocardiographic measurements were made according to the recommendations of the European Society of Cardiology.^[19] The following measurements were performed for patients and controls: left ventricle (LV) diameter (measured by TM when beam orientation is good, or 2D-guided linear measurement when beam orientation is not good); LVEF, based on the Teichholz and Simpson biplane methods; LV mass measured by Cube formula by linear measurement; LV myocardial performance index (MPI) measured with spectral Doppler; GLS, measured with speckle tracking method; diastolic function, based on the current recommended algorithm^[20] (diastolic function is considered normal if normal left atrium and/or $e' > 8$ cm/s, diastolic dysfunction if dilated left atrium and $e' \leq 8$ cm/s, further graded to grades 1 to 3 depending on E/A ratio, deceleration time, and e/e' ratio); and the tricuspid regurgitation velocity (TRV), with usual echocardiographic evaluation of pulmonary pressure based on TRV and inferior vena cava (IVC) dimension.

Next, the patient records were reviewed, and the following parameters were recorded: total hemoglobin (Hb), HbF, ferritin, NTproBNP, the number of crises during the

past year, walking distance test results, the presence of cerebral lesions on MRIs, the presence of ocular lesions on eye fundus examinations, proteinuria, hypertension, and compliance with treatment.

Statistical analysis

Statistical analyses were performed using SPSS software, version 24. Descriptive data are expressed as the mean \pm standard deviation (SD). Univariate analyses of continuous data were compared between groups with the independent T-test or one-way ANOVA. Comparisons between discrete values were performed with the Chi-square test. The results were considered statistically significant when *P*-values were <0.05 . The multivariate analysis was performed with a regressive ANOVA analysis. Correlations between continuous data were analyzed with a bivariate correlation test (Pearson correlation coefficients).

RESULTS

This study included 37 patients with SCD and 34 healthy age- and sex-matched controls. The patient and control groups were similar in age (31 ± 10 years *vs.* 32 ± 10 years, respectively). The sex ratio was similar in the patient and control groups (57% female patients *vs.* 61% female patients, respectively). Most (92%) patients are treated with hydroxyurea, and 70% were considered by their hematologist to be compliant with their treatment. Five patients were treated with chronic transfusions and none

were exchanged. Comparison between transfused and non-transfused patient is presented in Table 4. Four patients had hypertension in the patient group, which was well controlled under treatment (no beta-blocker). No patients had clinical signs of heart failure.

Echocardiographic data in the univariate analysis

LVEF was significantly lower in the SCD group than in the control group (Teichholz: 61.8% *vs.* 67.6%, *P*0.05; biplane Simpson: 61.9% *vs.* 69.3%, *P* <0.05 ; Table 1). However, only one patient had a Simpson LVEF $<50\%$. MPI was higher (higher values indicate impaired LV function) in the patient group compared with the control group (0.38 *vs.* 0.27; *P* <0.05), with 14 patients having an altered MPI (> 0.39). LV mass and left ventricle end diastolic diameter (LVEDD) were higher in the patient group compared with those in the control group (LV mass: 107 g/m² *vs.* 70 g/m², *P* <0.05 ; LVEDD: 53 mm *vs.* 46 mm, *P* <0.05). LV-GLS was significantly lower in the SCD group than in the control group (-19.4% *vs.* -22.4% ; *P* <0.05).

LV-GLS was normal (a cutoff value of $>-18\%$ for normal GLS was used based on the proposed cutoff of the vendor and several publications,^[21,22] although clearly established cutoff are not available) in all individuals in the control group, but it was abnormal in eight (21%) patients of the SCD group. Diastolic function was abnormal (type 1 diastole) in three patients (8%) of the SCD group, but

Table 1: Univariate analysis results show differences between patients with sickle cell disease (SCD) and healthy controls

Parameters	Control	SCD	<i>P</i>
LVEF-Teicholz (%)	67.6 \pm 6.9	61.8 \pm 6.2	0.0004
LVEF-Simpson (%)	69.3 \pm 5.3	61.9 \pm 7.2	0.00006
LVEF $< 50\%$	0	1 (2.7 %)	
MPI	0.27 \pm 0.08	0.38 \pm 0.16	0.0005
LV-GLS (%)	-22.4 \pm 2.8	-19.4 \pm 2.4	0.00007
LV-GLS $< 18\%$	0	8 (21%)	
TRV (m/s)	1.96 \pm 0.21	2.24 \pm 0.25	0.003
E/A	1.63 \pm 0.35	1.57 \pm 0.4	0.499
E' (m/s)	0.16 \pm 0.03	0.15 \pm 0.04	0.252
E/E'	5.64 \pm 1.34	6.44 \pm 1.76	0.054
DT (ms)	187 \pm 36	194 \pm 37	0.400
Diastolic dysfunction	0	3 (8%)	0.136
LVEDD (mm)	46 \pm 4.9	53 \pm 5.1	0.00000012
LV mass (g/m ²)	70 \pm 2.8	107 \pm 4.5	0.00000049
LVH	0	18 (48%)	0.033

The results are expressed as the mean \pm standard deviation.

LVEF: left ventricular ejection fraction; MPI: myocardial performance index; LV-GLS: left ventricle global longitudinal strain; TRV: maximal tricuspid regurgitation velocity; E/A: early peak diastolic velocity of the mitral inflow/late peak diastolic velocity of the mitral inflow; E': early diastolic mitral annular tissue Doppler velocity; E/E': ratio between peak velocities of mitral E wave and early diastolic mitral annulus; DT: deceleration time of E mitral wave; LVEDD: left ventricular end-diastolic diameter; LV mass: left ventricular mass; LVH: left ventricular hypertrophy.

normal in the entire control group. The three patients with type 1 diastole were more than 50 years old. One of these patients had iron overload.

TRV was higher in the SCD group than in the control group (2.24 m/s *vs.* 1.96 m/s, $P < 0.05$). However, no patient had pulmonary hypertension (defined as TRV > 2.8 m/s or systolic pulmonary pressure < 36 mm Hg if IVC is normal).

No difference in echocardiographic parameters was observed between transfused and non-transfused patients, except for MPI (Table 4).

Echocardiographic data in multivariate analysis

The multivariate analysis results (Table 2) showed that only the LV-GLS, LVEDD, and LV mass remained significantly different between groups.

Biological and clinical parameters in patients with SCD

Among patients with SCD, the mean Hb was 9.4 g/dL (range: 6.1–12.2 g/dL) and the mean HbF was 12.7% (range: 1–28.6%). After exclusion of the patient with heterozygous HbS/ β -thalassemia and one patient with a hereditary persistence of HbF, the mean Hb was 9.27 g/dL (range: 6.1–12.2 g/dL). The mean Hb of the 5 transfused patients was 9.53 g/dL, non-significantly different from the mean Hb of the non-transfused patients ($P = 0.125$). Mean ferritin level was 644 μ g/L (range: 13–7,267 μ g/L) and was higher in the transfused patients ($P < 0.05$). Iron overload, defined as a ferritin level > 1,000 μ g/L, was observed in five patients. The mean NTproBNP level was 154 pg/mL (range: 12–1,685 pg/mL).

Lesions were observed on the cerebral MRIs in 51% of patients. Ocular lesions were observed on the eye fundus examinations in 62% of patients. Proteinuria was observed in 27% of patients. The mean patient walking distance was 66% of the predicted value (range: 33–88%).

Correlations

LVEF and LV-GLS are correlated ($P = 0.027$). No correlation was observed between NTproBNP level and LVEF ($P = 0.569$), NTproBNP and LV-GLS ($P = 0.859$), walking distance test and LVEF ($P = 0.2$), and walking distance test and LV-GLS ($P = 0.106$). No correlation was observed between LVEF or LV-GLS and age or total Hb (even after exclusion of the two patients with slightly different genotype). LV-GLS and MPI were not correlated ($P = 0.130$). A correlation was observed between ferritin levels and LVEF, but this correlation is certainly due to the outlier with a very high ferritin level; thus, we will not consider it.

DISCUSSION

Our study showed that the echocardiographic parameters of cardiac systolic function were altered in patients with SCD. We showed that GLS was a powerful index of systolic function. Indeed, the GLS was abnormal in 8 (21%) of 37 patients; in contrast, the LVEF was abnormal in only one of these patients. Thus, the GLS appeared to be an effective tool for the detection of early systolic dysfunction in patients with SCD.

Our results were consistent with the results reported by Hammoudi.^[14] However, Barbosa *et al*^[13] did not find a

Table 2: Multivariate analysis results show factors significantly related to sickle cell disease (SCD)

Factors	Control	SCD	P Multivariate
LVEF-Teicholz (%)	67.6 \pm 6.9	61.8 \pm 6.2	0.221
LVEF-Simpson (%)	69.3 \pm 5.3	61.9 \pm 7.2	0.125
MPI	0.27 \pm 0.08	0.38 \pm 0.16	0.471
LV-GLS (%)	-22.4 \pm 2.8	-19.4 \pm 2.4	0.008
TRV (m/s)	1.96 \pm 0.21	2.24 \pm 0.25	0.148
E/A	1.63 \pm 0.35	1.57 \pm 0.4	0.518
E' (m/s)	0.16 \pm 0.03	0.15 \pm 0.04	0.406
E/E'	5.64 \pm 1.34	6.44 \pm 1.76	0.236
DT (ms)	187 \pm 36	194 \pm 37	0.456
LVEDD (mm)	46 \pm 4.9	53 \pm 5.1	0.004
LV mass (g/m ²)	70 \pm 2.8	107 \pm 4.5	0.008

The results are expressed as the mean \pm standard deviation.

LVEF: left ventricular ejection fraction; MPI: myocardial performance index; LV-GLS: left ventricle global longitudinal strain; TRV: maximal tricuspid regurgitation velocity; E/A: early peak diastolic velocity of the mitral inflow/late peak diastolic velocity of the mitral inflow; E': early diastolic mitral annular tissue Doppler velocity; E/E': ratio between peak velocities of mitral E wave and early diastolic mitral annulus; DT: deceleration time of E mitral wave; LVEDD: left ventricular end-diastolic diameter; LV mass: left ventricular mass; LVH: left ventricular hypertrophy.

similar alteration in longitudinal strain in a comparable population of patients. In our study, the mean GLS value in the study group was within the normal range; nevertheless, 21% of patients had an abnormal GLS (GLS < -18%). The GLS of our control group was higher than that reported by Barbosa,^[13] and it was also higher than the normal range defined by Yingchoncharoen *et al.* in a meta-analysis.^[21] Our

control group comprised healthy young individuals from the medical community. The healthy state of our controls might explain the higher strain displayed in our group compared with the more heterogeneous group analyzed by Yingchoncharoen *et al.*^[21] and perhaps the control group analyzed by Barbosa *et al.*^[13]; both those groups could have included some individuals with latent dysfunction.

Table 3: Clinical and biological parameters

Parameter	Patients with SCD	Controls
	Mean (range)	Mean (range)
Age (years)	31 (20–55)	32 (18–54)
Weight (kg)	68.5 (51–90)	66 (52–95)
Height (cm)	170 (156–192)	169 (154–188)
Body surface area	1.8 (1.51–2.14)	1.7 (1.49–2.15)
Total Hb (g/dL)	9.4 (6.1–12.2)	
HbF (%)	12.7 (1–28.6)	
Ferritin (µg/L)	644.8 (13–7267)	
NTproBNP (pg/mL)	154 (12–1685)	
% predicted WDT (%)	66 (33–88)	
Crises during last year	2 (0–6)	

Hb: hemoglobin; HbF: fetal hemoglobin; WDT: walking distance test.

Table 4: Comparison between transfused and non-transfused patients

Factors	Non-transfused	Transfused	P-Value
LVEF-Teicholz (%)	62.6 ± 5.8	57.2 ± 7.4	0.471
LVEF-Simpson (%)	62.4 ± 6.8	56.8 ± 7.9	0.538
MPI	0.37 ± 0.16	0.47 ± 0.06	0.044
LV-GLS (%)	-19.4 ± 2.3	-19 ± 3.4	0.441
TRV (m/s)	2.24 ± 0.26	2.2 ± 0.14	0.316
E/A	1.53 ± 0.39	1.77 ± 0.5	0.165
E' (m/s)	0.14 ± 0.04	0.18 ± 0.02	0.453
E/E'	6.58 ± 1.73	5.12 ± 1.34	0.204
DT (ms)	196 ± 41	182 ± 29	0.238
LVEDD (mm)	51.7 ± 5.3	55 ± 2.7	0.07
LV mass (g/m ²)	99.2 ± 29	95 ± 16	0.299
Age (years)	31.6 ± 10.9	29 ± 5.9	0.048
Body surface area	1.78 ± 0.16	1.89 ± 0.25	0.177
Total Hb (g/dL)	9.38 ± 1.54	9.53 ± 0.89	0.125
Ferritin (µg/L)	492 ± 724	1636 ± 3164	0.00009

The results are expressed as the mean ± standard deviation.

LVEF: left ventricular ejection fraction; MPI: myocardial performance index; LV-GLS: left ventricle global longitudinal strain; TRV: maximal tricuspid regurgitation velocity; E/A: early peak diastolic velocity of the mitral inflow/late peak diastolic velocity of the mitral inflow; E': early diastolic mitral annular tissue Doppler velocity; E/E': ratio between peak velocities of mitral E wave and early diastolic mitral annulus; DT: deceleration time of E mitral wave; LVEDD: left ventricular end-diastolic diameter; LV mass: left ventricular mass; Hb: hemoglobin.

Bedirian *et al.*,^[15] in a more recent research, found no difference in LV strain between a group of patients with SCD and a group of patients with other sickle cell diseases (OSCD). However, they found 79% of the patients with SCD to have abnormal strain, which is more than that we found but with a slightly higher cutoff for normal strain. Unlike in our study, their control group is not made of normal subjects; this can explain the absence of difference between their two groups. Another bias of this study is the fact that less than half of the patients with SCD had a LV strain measurement.

In a recent study investigating children (Whipple *et al.*^[16]), no difference in LV strain was observed between patients with SCD and controls, but this population was very young when compared with our population and we can assume that abnormalities of myocardial function are more prevalent as the patients are aging.

Similar to the Barbosa study, we found very few patients with diastolic dysfunction, in contrast to other studies.^[23-25] These conflicting results might be explained by the difficulty in defining diastolic dysfunction and the various criteria used in different studies. Diastolic function cannot be determined with a simple index, similar to that used to determine systolic function. Diastolic dysfunction has several grades and can be responsible for heart failure with preserved ejection fraction in the more severe grades. Parameters used to evaluate diastole are dependent on the loading condition, which can be highly variable over time, even in a single patient. In our series, none of the younger patients (aged <50 years) had an abnormal diastole. Therefore, the findings might reflect the effects of age-related comorbidities.

The MPI (or Tei index) is a historical parameter for evaluating function. The MPI is load independent, and it serves as a marker of both systolic and diastolic functions. It was previously shown that the MPI was impaired in patients with SCD.^[5] Consistent with that study, we found a higher MPI in patients with SCD than in controls. MPI is also found to be higher in the transfused patients, but these are in great minority so this result is to take with caution.

Consistent with many other studies, we found that LV mass and volume were greater in patients with SCD compared with controls. This finding could be readily explained by the chronic overload associated with SCD. Moreover, it was possible that an iron overload contributed to LV enlargement, because iron overloads can lead to hypertrophy. However, we could not find a correlation between the ferritin levels and hypertrophy.

In our population, we could not find correlation between LV strain and the walking distance test or the NTproBNP

level. The small number of patients included in the study might explain these results. Furthermore, walking distance test can also be influenced by anemia, as could be NTproBNP level,^[26] although we could not find a correlation between these parameters in this study.

The clinical impact of an altered GLS has been demonstrated in some situations, such as chemotherapy.^[8] Indeed, many studies have shown that patients undergoing chemotherapy exhibited alterations in the LV-GLS before they exhibited reductions in the ejection fraction. Consequently, the GLS measurement is currently recommended for those patients. The technique of measuring the GLS, despite slight variability among vendors, is also studied in many other fields, including coronaropathy, hypertrophic cardiomyopathy, and valvular heart disease. It is currently considered a promising tool for supporting clinical decision-making.^[27]

On the basis of our results, we suggest that the LV-GLS could be a useful parameter for following patients with SCD. However, this application should be evaluated in a larger study, because the many small series on this topic have provided conflicting results. Moreover, the clinical impact of an altered LV-GLS in patients with SCD remains to be assessed; this could be the purpose of a larger study, multicentric, with a long-term follow-up in order to find if LV-GLS could have a prognostic value.

Limitations

This study had some limitations. The main limitation was that our study population was quite small; this limited the possibility of finding correlations in clinical and biological parameters. In addition, we designed the study to focus only on the LV-GLS, not radial strain, circumferential strain, or right ventricle strain. We made this choice, because our aim was to use a measure that is currently available in routine echocardiography. However, LV-GLS has no well-established cutoff for normal values and there is still intervendor variability.

CONCLUSIONS

Our study showed that GLS, an emerging sensitive reproducible parameter of systolic function, was altered in a significant proportion of patients with sickle cell anemia. Larger studies, probably multicentric, should be conducted to confirm our results and to evaluate whether LV-GLS might have prognostic implications and whether it should be recommended in routine evaluations of these patients.

Conflict of Interest

None.

REFERENCES

1. Galdwin MT, Sachdev V. Cardiovascular Abnormalities in Sickle Cell Disease. *J Am Coll Cardiol* 2012;59:1123-33.
2. Fitzhugh CD, Lauder N, Jonassaint JC, Telen MJ, Zhao X, Wright EC, *et al.* Cardiopulmonary complications leading to premature deaths in adult patients with sickle cell disease. *Am J Hematol* 2010;85:36-40.
3. Poludasu S, Ramkissoon K, Salciccioli L, Kamran H, Lazar JM. Left Ventricular Systolic Function in Sickle Cell Anemia: A Meta-Analysis. *J Card Fail* 2013;19:333-41.
4. Vasconcelos MC, Nunes MC, Barbosa MM, Fernandes BM, Passaglia LG, Silva CM, *et al.* Left ventricular remodeling in patients with sickle cell disease: determinants factors and impact on outcome. *Ann Hematol* 2015;94:1621-9.
5. AboHadeed HM, Zolaly MA, Khoshhal SQ, El-Harbi KM, Tarawah AM, Al-Hawsawi ZM, *et al.* Assessment of Cardiac Functions in Children with Sickle Cell Anemia: Doppler Tissue Imaging Study. *Arch Med Res* 2015;46:462-9.
6. Eddine AC, Alvarez O, Lipshultz SE, Kardon R, Arheart K, Swaminathan S. Ventricular Structure and Function in Children With Sickle Cell Disease Using Conventional and Tissue Doppler Echocardiography. *Am J Cardiol* 2012;109:1358-64.
7. Dabirian M, Janbabaie G, Karami H, Nabati M, Aarabi M, Namazi M, *et al.* Cardiac Structural and Functional Changes Evaluated by Transthoracic and Tissue Doppler Echocardiography in Adult Patients with Sickle Cell Disease. *Acta Inform Med* 2017;25:9-13.
8. Thavendiranathan P, Poulin F, Lim KD, Plana JC, Woo A, Marwick TH. Use of Myocardial Strain Imaging by Echocardiography for the Early Detection of Cardiotoxicity in Patients during and After Cancer Chemotherapy. A Systematic Review. *J Am Coll Cardiol* 2014;63:2751-68.
9. Medvedofsky D, Kebed K, Laffin L, Stone J, Addetia K, Lang RM, *et al.* Reproducibility and experience dependence of echocardiographic indices of left ventricular function: Side-by-side comparison of global longitudinal strain and ejection fraction. *Echocardiography* 2017;34: 365-70.
10. King A, Thambyrajah J, Leng E, Stewart MJ. Global longitudinal strain: a useful everyday measurement? *Echo Res Pract* 2016;3:85-93.
11. Sengupta SP, Jaju R, Nugurwar A, Caracciolo G, Sengupta PP. Left ventricular myocardial performance assessed by 2-dimensional speckle tracking echocardiography in patients with sickle cell crisis. *Indian Heart J* 2012;64:553-8
12. Ahmad H, Gayat E, Yodwut C, Abduch MC, Patel AR, Weinert L, *et al.* Evaluation of Myocardial Deformation in Patients with Sickle Cell Disease and Preserved Ejection Fraction Using Three- Dimensional Speckle Tracking Echocardiography. *Echocardiography* 2012;29: 962-9.
13. Barbosa MM, Vasconcelos MC, Ferrari TC, Fernandes BM, Passaglia LG, Silva CM, *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.
14. Hammoudi N, Arangalage D, Djebbar M, Stojanovic KS, Charbonnier M, Isnard R, *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.
15. Bedirian R, Soares AR, Maioli MC, de Medeiros JFF, Lopes AJ, Castier MB. 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.
16. Whipple NS, Naik RJ, Kang G, Moen J, Govindaswamy SD, Fowler JA, *et al.* Ventricular global longitudinal strain is altered in children with sickle cell disease. *Br J Haematol* 2018;183:796-806.
17. Parsaee M, Saedi S, Joghataei P, Azarkeivan A, Alizadeh Sani Z. Value of speckle tracking echocardiography for detection of clinically silent left ventricular dysfunction in patients with β -thalassemia. *Hematology* 2017;22:554-8.
18. Ari ME, Ekici F, Çetin İİ, Tavil EB, Yaralı N, Işık P, *et al.* Assessment of left ventricular functions and myocardial iron load with tissue Doppler and speckle tracking echocardiography and T2* MRI in patients with β -thalassemia major. *Echocardiography* 2017;34:383-9.
19. Lang RM, Badano LP, Mor-Avi V, Afilalo J, Armstrong A, Ernande L, *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.
20. Nagueh SF, Appleton CP, Gillebert TC, Marino PN, Oh JK, Smiseth OA, *et al.* Recommendations for the Evaluation of Left Ventricular Diastolic Function by Echocardiography. *Eur J Echocardiogr* 2009;10:165-93.
21. Yingchoncharoen T, Agarwal S, Popović ZB, Marwick TH. Normal Ranges of Left Ventricular Strain: A Meta-Analysis. *J Am Soc Echocardiogr* 2013;26:185-91.
22. Takigiku K, Takeuchi M, Izumi C, Yuda S, Sakata K, Ohte N, *et al.* Normal Range of left ventricular 2-Dimensional strain-Japanese Ultrasound Speckle Tracking of the left ventricle (JUSTICE) study. *Circ J* 2012;76:2623-32.
23. Hankins JS, McCarville MB, Hillenbrand CM, Loeffler RB, Ware RE, Song R, *et al.* Ventricular Diastolic Dysfunction in Sickle Cell Anemia Is Common But Not Associated With Myocardial Iron Deposition. *Pediatr Blood Cancer* 2010;55:495-500.
24. Kanadaşi M, Akpınar O, Caylı M, Dönmez Y, Acartürk E. Frequency of diastolic dysfunction in patients with sickle cell anemia: a tissue Doppler imaging study. *Acta Cardiol* 2005;60:471-6.
25. Sachdev V, Machado RE, Shizukuda Y, Rao YN, Sidenko S, Ernst I, *et al.* Diastolic Dysfunction Is an Independent Risk Factor for Death in Patients With Sickle Cell Disease. *J Am Coll Cardiol* 2007;49:472-9.
26. Karakoyun I, Colak A, Arslan FD, Asturk AG, Duman K. Anemia considerations when assessing natriuretic peptide levels in ED patients. *Am J Emerg Med* 2017;35:1677-81.
27. Smiseth OA, Torp H, Opdahl A, Haugaa KH, Urheim S. Myocardial strain imaging: how useful is it in clinical decision making? *Eur Heart J* 2016;37:1196-207.

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