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Original Article

Assessment of Global Longitudinal Strain via Speckle-Tracking Echocardiography in Patients With Rheumatoid Arthritis

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ABSTRACT

Background: The inflammatory nature of rheumatoid arthritis presents a hypothesis on the increase in the likelihood of cardiovascular diseases in patients with rheumatoid arthritis. Recently, the use of speckle-tracking echocardiography to evaluate ventricular strain, especially the global longitudinal strain (GLS), has provided more comprehensive information on ventricular dysfunction in these patients. In the present study, we evaluated changes in the GLS index along with other left and right ventricular parameters in patients with rheumatoid arthritis compared with healthy controls.

Methods: The study population was comprised of a case group (patients with rheumatoid arthritis in the active phase during the first 5 years of diagnosis referred to Shariati Hospital without a history of any other diseases) and a control group (individuals without a history of rheumatoid arthritis or cardiac abnormalities referred for clinical check-ups). In both groups, 2D and 3D echocardiographic examinations were performed by a single cardiologist to assess cardiac functional parameters.

Results: Comparisons of the echocardiographic indices between the 2 groups showed significantly lower LA (Left Atrium), AO (Aorta), interventricular septal end-diastole (IVSD), Posterior wall diastolic diameter (PWD), and RVsm (Right Ventricular systolic celocity) in the group suffering from rheumatoid arthritis than in the control group. The GLS parameter was significantly lower in the rheumatoid arthritis group than in the healthy group (-19.5 ± 2.34 vs -20.42 ± 3.07; P = 0.042); however, there was no difference in the global circumferential strain parameter between the 2 groups (-19.69 ± 3.55 vs -20.49 ± 1.79; P = 0.566). In contrast, the mean right ventricular GLS was -18.77 ± 5.34 in the case group versus -21.87 ± 13.99 in the control group, indicating a significant difference (P = 0.008).

Conclusions: In the echocardiographic assessment of patients with rheumatoid arthritis, a decrease in the ventricular function parameters, especially the GLS, is expected, which may be due to the effect of inflammatory factors on the cardiac ventricular strain. ***(Iranian Heart Journal 2020; 21(1): 103-109)***

KEYWORDS: Rheumatoid arthritis, Global longitudinal strain, Speckle-tracking echocardiography

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Patients with rheumatoid arthritis are about 1.5 to 2 times more likely to be at risk of coronary heart disease. [1,2] This is almost identical to the risk of heart disease among patients with diabetes mellitus. [3] This increase in the risk of heart disease occurs even before the onset of rheumatoid arthritis manifestations. [4] In the Framingham Heart Study, a 1.5-fold increase in the risk of heart disease among patients with rheumatoid arthritis was noted. [4] Patients with rheumatoid arthritis also have a high risk of heart failure. [5] This increase in risk is mainly seen in patients with positive rheumatoid factors. [6] Most importantly, patients with heart failure and simultaneous rheumatoid arthritis also experience a progressive reduction in the left ventricular (LV) systolic function manifested by a drop in the left ventricular ejection fraction (LVEF). [7] The set of these statements reflects the fact that patients with rheumatoid arthritis encounter heart failure with systolic and diastolic dysfunction of the LV, the underlying cause of which is systemic inflammation associated with the disease. Patients with rheumatoid arthritis face an increased risk of LV systolic and diastolic dysfunction; therefore, echocardiographic evaluations in these patients are of utmost importance. Because rheumatoid arthritis is a type of connective tissue inflammatory disease, this involvement in the connective and muscular components of the heart is also contagious; thus, myocardial and endocardial disturbances can also be expected in such patients. Nonetheless, in some patients, and with regard to the severity of the disease, heart disease is sometimes asymptomatic and because patients are not physically active, changes in the cardiac function may not be detected until the end stages of the disease. Echocardiography is very useful in evaluating and detecting cardiac disturbances in patients with rheumatoid arthritis, especially in the early stages of the disease. Various studies have been conducted on echocardiographic impairment in rheumatoid arthritis. Overall, it appears that the prevalence of valvular involvement in patients with rheumatoid arthritis, not least mitral valve regurgitation, followed by pericardial effusion, is a common and prevalent finding. [8,9] In addition to pericardial and valve involvement, what is revealed in patients with rheumatoid arthritis is systolic and diastolic dysfunction and what is predictable in rheumatoid arthritis is systolic dysfunction (with a reduction in the LVEF), diastolic dysfunction (accompanied by changes in the E (E velocity in mitral inflow), E/A (E velocity/A velocity), IVRT (Isuvolomic Relaxation time), and myocardial performance indices), valve involvement, mitral insufficiency, and mild pericardial effusion, especially in nodular types.

Myocardial strain imaging is one of the advanced echocardiographic methods aimed at evaluating myocardial deformities during ventricular contraction and relaxation. [10] The evaluation of the strain index is reported as the percentage change in myocardial dystonia at a point from another point and can be analyzed and reported through speckle-tracking echocardiography (STE). [11-13] Accordingly, strain abnormalities for a wide range of cardiovascular diseases [14] and strain imaging are accurate and sensitive in the diagnosis and prediction of systolic dysfunction. [15-17] The disruption of myocardial strain can be a symptom of coronary heart disease, even in the early and subclinical stages. Given the importance of identifying cardiovascular and myocardial infarction in patients with rheumatoid arthritis, the imaging of myocardial strain in the early stages of the disease is very beneficial. [18] In this regard, some studies

have identified the sensitivity and specificity of the global longitudinal strain (GLS) index in assessing the infarct size and the severity of myocardial involvement in coronary heart disease. [19-21] The GLS index is valuable for the evaluation of systolic dysfunction compared with other indicators such as the LVEF. Indeed, the GLS index can be drawn upon to assess the severity of myocardial dysfunction in patients with rheumatoid arthritis. The present study aimed to assess and compare the GLS along with other parameters for cardiac systolic dysfunction in patients with rheumatoid arthritis.

METHODS

This is a descriptive-analytical case-control study conducted in Shariati Hospital in Tehran in 2018. The study population was comprised of a case group (patients with rheumatoid arthritis in the active phase during the first 5 years of diagnosis referred to Shariati Hospital without a history of any other diseases except rheumatoid arthritis) and a control group (individuals without a history of rheumatoid arthritis or cardiac abnormalities referred for clinical check-ups). The American College of Rheumatology (ACR) diagnostic criteria for rheumatoid arthritis include 1) morning stiffness more than an hour, 2) arthritis in 3 or more joints, 3) arthritis in the hand joints (≥ 1 swollen joint), 4) symmetric arthritis, 5) the presence of rheumatoid nodules, 6) positive serum rheumatic factor, and 7) radiographic X-ray changes of the hands as the erosion. In both groups, 2D and 3D echocardiographic examinations were performed by a single cardiologist to assess the cardiac functional parameters including the Left Atrium (LA), the Aorta (AO), the interventricular septal end-diastole (IVSD), the Posterior Wall Diastolic Diameter (PWD), the Posterior Wall Diastolic Diameter (RVD), the Right Ventricular systolic velocity (RVsm), the tricuspid annular plane systolic excursion (TAPSE), and the 2 strain-related indices of the GLS and the global circumferential strain (GCS).

For the description of the data, descriptive analysis was used, including the mean ± the standard deviation (SD) for the quantitative variables and frequencies (percentages) for the categorical variables. The χ^2 test, the *t*-test, or the Mann–Whitney *U* test was used for the comparison of the variables. The correlations between the quantitative variables were assessed using the Pearson or Spearman correlation test. For the statistical analyses, the statistical software IBM SPSS Statistics for Windows, version 23.0 (IBM Corp, released 2013, Armonk, NY) was used. A *P* value < 0.05 was considered statistically significant.

RESULTS

In this study, 35 patients with active rheumatoid arthritis (mean age = 43.33 ± 22.9 y) and 35 healthy controls (mean age = 34.27 ± 9.10 y) were evaluated for echocardiographic parameters.

Comparisons of the echocardiographic indices between the 2 groups (Table 1) showed significantly lower LA, AO, IVSD, PWD, and RVSm in the group suffering from rheumatoid arthritis than in the control group. The GLS parameter was significantly lower in the rheumatoid arthritis group than in the healthy group (-19.5 ± 2.34 vs -20.42 ± 3.07; *P* = 0.042); however, there was no difference in the GCS parameter between the 2 groups (-19.69 ± 3.55 vs -20.49 ± 1.79; *P* = 0.566). In contrast, the mean RV-GLS was -18.77 ± 5.34 in the case group versus -21.87 ± 13.99 in the control group, indicating a significant difference (*P* = 0.008). With respect to the association between age and the echocardiographic parameters (Table 2), the patients' age was adversely correlated with the RVSm (*r* = -0.616, *P* = 0.001) and with the TAPSE (*r* = -0.496, *P* = 0.005), but not with the other cardiac parameters.

Table 1. Values of echocardiographic parameters in both case and control groups

Parameter	RA Group	Healthy Group	*P* value
LA	30.83 ± 4.02	34.07 ± 3.31	0.001
AO	26.53 ± 4.84	29.64 ± 3.87	0.003
IVSD	8.57 ± 1.25	7.64 ± 1.00	0.001
PWD	8.40 ± 1.00	7.42 ± 0.94	0.001
RVD	26.21 ± 3.56	26.89 ± 3.02	0.380
RVSm	11.61 ± 1.23	13.96 ± 1.45	0.001
TAPSE	22.73 ± 3.32	22.60 ± 1.84	0.824
GLS	-19.5 ± 2.34	-20.42 ± 3.07	0.042
GCS	-19.69 ± 3.55	-20.49 ± 1.79	0.566
RV-GLS	-18.77 ± 5.34	-21.87 ± 13.99	0.008

RA, Rheumatoid arthritis; LA, Left Atrium; AO, Aorta; IVSD, Interventricular septal diastolic diameter; PWD, Posterior wall diastolic diameter; RVD, Right ventricular diastolic diameter; RVsm, Right ventricular systolic velocity ;TAPSE, Tricuspid annular plane systolic excursion; GLS, Global longitudinal strain; GCS, Global circumferential strain; RV-GLS, Right ventricular global longitudinal strain

Table 2. Correlations between the patients' age and the echocardiographic parameters in the affected group

Parameter	R Coefficient	*P* value
LA	0.299	0.108
AO	0.298	0.109
IVSD	0.139	0.465
PWD	0.201	0.286
RVD	0.293	0.123
RVSM	-0.616	0.001
TAPSE	-0.496	0.005
GLS	0.182	0.336
GCS	0.355	0.098
RV-GLS	0.122	0.884

LA, Left Atrium; AO, Aorta ; IVSD, Interventricular septal diastolic diameter; PWD, Posterior wall diastolic diameter ; RVD, Right ventricular diastolic diameter; RVsm, Right ventricular systolic velocity ;TAPSE, Tricuspid annular plane systolic excursion; GLS, Global longitudinal strain; GCS, Global circumferential strain; RV-GLS, Right ventricular global longitudinal strain

DISCUSSION

The inflammatory nature of rheumatoid arthritis and the role of inflammatory factors in the development and progression of coronary artery atherosclerosis and also the valve defects present a new hypothesis on the increase in the likelihood of cardiovascular diseases in patients with rheumatoid arthritis. This has been confirmed in clinical observations as well as heart imaging studies. Recently, the use of STE to evaluate the ventricular strain, especially the GLS, has provided more comprehensive information on ventricular dysfunction in these patients. In the current study, we aimed to assess changes in the GLS index along with other LV and RV parameters in patients with rheumatoid arthritis compared with healthy controls. We found that whereas the decrease in the GLS index in patients with rheumatoid arthritis was significant compared with the healthy controls, these changes were not significant concerning the GCS index. Additionally, among the other parameters of the ventricular function, reductions in the LA, the AO, the IVSD, the PWD, and the RVSm in these patients were evident in comparison with the healthy controls. In other words, the

consequence of rheumatoid arthritis in the first 5 years of the active phase of the disease is the involvement of the LV and the RV. In this regard, 2 important issues should also be considered. Firstly, ventricular echocardiographic changes in patients with rheumatoid arthritis may not appear in the early stages of the disease or they may be asymptomatic; consequently, after years of active disease and with the progression of inflammatory processes, changes in the ventricular function become evident. In contrast, these changes may begin to appear subclinically at the very beginning of the active period of the disease. An echocardiographic evaluation with the aim of examining the course of changes in the parameters of the heart within 5 years of the active period of the disease is necessary.

The results of the previous studies chime in with our findings concerning changes in the ventricular function parameters in rheumatoid arthritis. In a study by Naseem et al, [22] the values of the GLS in both LV and RV for patients with active rheumatoid arthritis were significantly lower than those in healthy controls. In addition, the severity of rheumatoid arthritis activity was significantly correlated with a further reduction in the GLS. Cioffi et al [23] reported reduced GLS values in 24% of their patients. In a study by Benacka et al, [24] patients with rheumatoid arthritis had a greater LV mass, a lower LVEF, and a more prolonged IVCT (Isovolumic Contraction time). Moreover, the prolongation of the IVRT and a higher E/E' ratio showed a much higher degree of diastolic ventricular dysfunction in the patients. In the STE evaluation, a significant reduction in the GLS was also reported. Benacka et al [25] reported that the active status of the disease was significantly correlated with the decrease in the GLS. In an investigation by Fine et al, [26] the mean GLS in both RV and LV showed a significant decrease compared with healthy controls. Therefore, with the development and progression of rheumatoid arthritis, the risk of developing heart disease, in particular of ventricular dysfunction, is predictable. In this regard, the efficiency of the GLS evaluation can be very important and diagnostic in predicting adverse cardiac outcomes in patients with rheumatoid arthritis, which, of course, needs to be further evaluated.

CONCLUSIONS

In the echocardiographic assessment of patients with rheumatoid arthritis, a decrease in the ventricular function parameters, especially the GLS, is expected, which may be due to the inflammatory nature of the disease and the effect of inflammatory factors on the cardiac ventricular strain.

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