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Original Article

Left and Right Ventricular Functional Status in Patients Suffering From Scleroderma With Normal Pulmonary Arterial Pressure

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ABSTRACT

Background: The occurrence of cardiac structural and functional abnormalities in patients with scleroderma and pulmonary arterial hypertension has been clearly assessed; there are, however, only a few studies on cardiac manifestations in patients with normal pulmonary arterial pressure, which is the purpose of this study.

Methods: In this case-control study, 35 patients with known systemic sclerosis referred to the Systemic Sclerosis Clinic of Shariati Hospital in 2018 were selected. From among individuals without systemic sclerosis that had referred only for routine clinical check-ups, 35 patients were selected as the control group. All the subjects were assessed by 2D echocardiography, tissue Doppler imaging, and speckle-tracking echocardiography.

Results: Compared with the healthy control group, significant changes were observed in the left atrium, the aortic root, the interventricular septum diastolic thickness, the posterior wall diastolic thickness, the right ventricular diameter, and the right ventricular systolic motion in the patients with scleroderma. Additionally, the changes in left ventricular global circumferential strain and right ventricular global longitudinal strain in the apical 4-chamber view parameters were significant in these patients, although there was no difference between the 2 groups in terms of the left ventricular global longitudinal strain index. In the patients with scleroderma and normal pulmonary arterial pressure, there was a significant direct correlation between the age of the patients with the pulmonary artery size and an inverse correlation between age and E' septal and E' lateral.

Conclusions: Patients with scleroderma or systemic sclerosis suffer systolic and diastolic dysfunction, which can be associated with significant atrial/ventricular structural and functional changes. These changes may be independent of pulmonary arterial pressure, but the risk of these abnormalities will be increased in advanced age. ***(Iranian Heart Journal 2019; 20(4): 79-84)***

KEYWORDS: Echocardiography, Global longitudinal strain, Global circumferential strain, Scleroderma

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Scleroderma or systemic sclerosis is a chronic multi-systemic disease characterized by microangiopathy, skin and organ tissue fibrosis, and autoimmune disorders. Two subgroups of systemic sclerosis have been identified: a limited subtype, which is characterized by the thickening of the skin of the face, neck, and extremities distal to the elbows and knees, and a diffuse subtype, which is characterized by the thickening of the skin in the extremities proximal to the elbows and knees, the chest, the back, and the abdomen. The initial cardiac involvement, which is the result of the direct involvement of scleroderma, may be characterized by myocardial involvement, cardiac conduction system fibrosis, and pericardial and less commonly, cardiac valve involvement. In addition, some cardiac complications occur in the secondary form; these complications mainly include primary pulmonary hypertension, interstitial lung disease, and renal involvement. [1,2] The incidence of primary cardiac involvement following scleroderma is not well defined. [3] The use of a variety of noninvasive and semi-invasive cardiac assessment techniques has not been sufficiently sensitive to the evaluation of functional cardiac changes. [4,5] Echocardiography (especially the tissue Doppler type), cardiac computed tomography scanning, single-photon emission computed tomography, magnetic resonance imaging, positron-emission tomography, and radionuclide ventriculography are more sensitive techniques for evaluating structural and functional changes associated with scleroderma development. [1] In some reports, cardiac involvement has been reported in about 15% of patients with scleroderma, assessed on the basis of physical evaluation and echocardiography. [6] An asymptomatic reduction in the left ventricular ejection fraction, asymptomatic pericardial effusion, or asymptomatic arrhythmias have been shown as the dominant findings in the disease. One of the most important cardiovascular changes in the field of scleroderma is pulmonary arterial hypertension (PAH), which is the result of pulmonary vascular resistance. [7] The prevalence of PAH was reported to be between 10% and 12%, ranging from 4.9% to 26.7% in various studies. [8,9] This complication is associated mainly with pulmonary fibrosis, which sometimes affects up to one-third of the patients. The main reason for the occurrence of PAH and the occurrence of pulmonary fibrosis is pulmonary arterial resistance and lung vasodilation. [10,11] However, functional changes in the left and right ventricles in the background of scleroderma are not always associated with the occurrence of PAH, and these changes may occur in patients with normal pulmonary arterial pressure (PAP). The purpose of this study was to evaluate the right and left ventricular function in patients suffering from scleroderma with normal PAP.

METHODS

In this case-control study, 35 patients with known systemic sclerosis who were referred to the Systemic Sclerosis Clinic of Shariati Hospital in 2018 were selected. The selection of patients was done after they had been provided with a complete explanation as to the importance of the investigation and the process of the evaluations. Patients were recruited if they provided written informed consent. Patients with systemic or other cardiovascular conditions such as heart valve diseases, a history of thromboembolism, arrhythmias, heart failure, coronary heart disease, PAH, and a history of previous cardiac surgery were excluded. From among individuals without systemic sclerosis that had referred only for routine clinical check-ups, 35 patients were selected as the control group. The demographic characteristics were recorded, and then the subjects were referred to the Echocardiography Department of Shariati Hospital. Initially, the subjects underwent 2D echocardiography,

aimed at assessing the atrial and ventricular dimensions and functional parameters. Thereafter, supplementary studies were performed using tissue Doppler imaging and speckle-tracking echocardiography. The right ventricular function was measured based on the global longitudinal strain (GLS) index, right ventricular systolic motion, tricuspid annular plane systolic excursion, and right ventricular fractional area change indices. The study endpoint was to assess the left and right ventricular functional status in patients suffering from scleroderma and also to compare the findings with those in healthy conditions.

RESULTS

Table 1 summarizes the echocardiographic findings in the patients with scleroderma. Comparison of the structural and functional ventricular parameters between the scleroderma and healthy subgroups showed significant differences in some cardiac parameters—including the left atrium, the aortic root, the interventricular septum diastolic thickness, the posterior wall diastolic thickness, the right ventricular diameter, and right ventricular systolic motion (Table 2).

Table 1. Cardiac parameters in the scleroderma and control groups

Parameter	Scleroderma Group	Control Group	*P* value
LA	31.71 ± 3.48	34.07 ± 3.31	0.003
AO	27.74 ± 3.01	29.64 ± 3.86	0.003
IVSD	8.66 ± 1.45	7.64 ± 1.00	0.001
PWD	8.54 ± 1.29	7.42 ± 0.94	0.001
LVEF	64.14 ± 4.59	64.98 ± 3.50	0.211
RVD	27.46 ± 1.93	26.89 ± 3.02	0.001
RVSM	12.09 ± 2.05	13.96 ± 1.44	0.001
TAPSE	22.69 ± 2.92	22.60 ± 1.84	0.872
LV GLS	-21.25 ± 2.50	-20.42 ± 3.06	0.186
LV GCS	-18.56 ± 3.23	-20.20 ± 1.41	0.001
RV GLS-A4C	-20.72 ± 5.32	-21.87± 13.99	0.028

LA, Left atrium; AO, Aorta; IVSD, Interventricular septum; PWD, Posterior wall diameter; LVEF, Left ventricular ejection fraction; RVD, Right ventricular dimension; RVSM, Right ventricular systolic motion; RV GLS-A4C, Right ventricular global longitudinal strain in the apical 4-chamber view; TAPSE, Tricuspid annular plane systolic excursion; LV GLS, Left ventricular global longitudinal strain; LV GCS, Left ventricular global circumferential strain

Table 2. Association between age and cardiac parameters in scleroderma

Parameter	Scleroderma Group	*P* value
LA	0.089	0.613
AO	0.300	0.080
IVSD	0.298	0.082
PWD	0.251	0.145
LVEF	0.080	0.647
RVD	0.181	0.297
RVSM	0.072	0.686
TAPSE	0.036	0.838
GLS	0.239	0.167
GCS	0.043	0.806
PA	0.435	0.011
E' septal	-0.386	0.022
E' lateral	-0.418	0.014
EDV	0.008	0.964
ESV	0.035	0.842
PAP	0.136	0.438

LA, Left atrium; AO, Aorta; IVSD, Interventricular septum; PWD, Posterior wall diameter; LVEF, Left ventricular ejection fraction; RVD, Right ventricular dimension; RVSM, Right ventricular systolic motion; TAPSE, Tricuspid annular plane systolic excursion; GLS, Global longitudinal strain; GCS, Global circumferential strain; EDV, End-diastolic volume; ESV, End-systolic volume; PAP, Pulmonary arterial pressure

There was also a significant difference in left ventricular global circumferential strain (GCS), but not in left ventricular global longitudinal strain between the scleroderma and control groups. The overall prevalence of diastolic dysfunction in the scleroderma group was 28.6%. Regarding the association between the patients' age and the cardiac parameters (Table 2), there was a positive correlation between age and PA (r = 0.435, P = 0.011), as well as an adverse association between age and E' septal (r = −0.386, P = 0.022) and E' lateral (r = −0.418, P = 0.014).

DISCUSSION

Primary cardiac involvement, which is the result of the direct involvement of scleroderma, may be characterized by myocardial involvement, cardiac conduction system fibrosis, and pericardial and less commonly, cardiac valve involvement. In addition, some cardiac complications occur in the secondary

form—mainly due to PAH, lung disease, or renal involvement. What has been confirmed so far is the occurrence of cardiac structural and functional abnormalities in patients with PAH; nonetheless, there is a paucity of information on cardiac manifestations in patients with normal PAP, which is the purpose of the current study. Based on echocardiographic evidence, we found significant differences in most cardiac parameters among our patients with scleroderma and healthy controls, suggesting the significant effects of the underlying pathophysiology of scleroderma on the cardiovascular function and diameters. Interestingly, according to the nature of the study (including patients with scleroderma but with normal PAP), these significant changes in the structure and function of the heart were completely independent of the effects of PAP elevation in these patients. Accordingly, the changes in the structure and function of the heart were mainly related to significant diastolic dysfunction, as well as changes in ventricular strain.

A significant change was manifest in GCS, which was not significant in terms of changes in the GLS index. About a quarter of our patients with scleroderma also had diastolic dysfunction, which was associated with normal PAP. Therefore, independent of changes in PAP, patients with scleroderma suffer not only diastolic and systolic cardiac dysfunction but also changes in ventricular strain, and will experience a change in GCS. It should be noted that these disorders in our study were affected by the age of the patients, such that increasing age was in tandem with a decrease in tissue Doppler velocities (decrease in E' septal and E' lateral).

In previous studies, such changes—in particular in the cardiac diastolic function—were clearly outlined. In a study by Saito et al, [12] the GLS and GCS values were associated with severe impairment, which was unique to the GCS index. However, in their study, patients with high PAP were evaluated. Interestingly, in this study, changes in GCS and not GLS were correlated with increased PAP. In a study by Dedeoglu et al, [13] there was a significant difference in the left ventricular end-systolic and end-diastolic diameters. The values of GLS and GCS were significantly lower in the patient group than in the control group, which is consistent with our study regarding the change in GCS. In a study by Zlatanovic et al, [14] the parameters of the interventricular septal thickness, the left ventricular mass index, and the right ventricular wall thickness were significantly higher in the patient group, which is quite similar to our study. Zlatanovic and coworkers also reported that the diastolic function (based on the E/A ratio) had a significant change in their patients and a drop in GLS and GCS was the dominant finding in the patients, which is consistent with our study. Vemulapalli et al [15] reported that 44% of their patients had left ventricular diastolic dysfunction, which is less frequent in our study perhaps because we included patients with normal PAP. Karna et al [16] observed diastolic dysfunction in the right ventricle of most of their study population; in addition, they reported right and left ventricular diastolic dysfunction in half of their patients, which chimes in with the results of our study. In a study by Meune et al, [17] significant impairments were observed in the function and structure of the right ventricle, especially the diastolic function in patients with scleroderma by comparison with the control group. Left ventricular diastolic dysfunction was also observed in those patients, which is quite similar to our findings.

Therefore, what can be mentioned as a summary of the studies is that disturbance in the left and right ventricular diastolic functions, along with increased diameters and increased ventricular septal thickness, are the consequences of scleroderma—especially in the long-term—which will ultimately lead to severe

disturbance in the cardiac diastolic function in a significant proportion of patients. The important point in the present study was that this cardiac dysfunction occurred even in the absence of PAH and, in other words, changes in the cardiac diastolic function can be completely independent of changes in PAP. However, the risk of these pathological changes in older patients will be much higher.

CONCLUSIONS

Patients with scleroderma or systemic sclerosis suffer diastolic dysfunction, which can be associated with significant atrial/ventricular structural and functional changes. These changes may be quite independent of PAP, but the risk of these abnormalities will be increased in advanced age as well as in normal cases.

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