Comparative study of left ventricular function in a group of asymptomatic patients with systemic sclerosis and a controls group

Authors: MÉRIEM DRISSA drissa, sana helali, marwa chebbi, habiba drissa

DOI: 10.5603/FC.a2019.0043

Article type: Original Papers

Submitted: 2018-01-05

Accepted: 2018-04-02

Published online: 2019-06-17

This article has been peer reviewed and published immediately upon acceptance. It is an open access article, which means that it can be downloaded, printed, and distributed freely, provided the work is properly cited.
Comparative study of left ventricular function in a group of asymptomatic patients with systemic sclerosis and a controls group
Meriem Drissa, Sana Helali, Marwa Chebbi, Habiba Drissa

Adress for correspondence:
Meriem Drissa, e-mail: drissameriem@yahoo.fr

Abstract
Introduction. Cardiac involvement in systemic sclerosis (SSc) and represents a major cause of morbidity and mortality and constitute an evolutionary turning point in this disease. Purpose of the work was to describe echocardiographic data in asymptomatic patients with SSc and compare them to results obtained in a control population in order to unmask subclinical cardiac involvement during systemic sclerosis.

Material and methods. Prospective study conducted between 2012 and 2017. Including 2 groups: Group A included 25 asymptomatic scleroderma patients without other comorbidities, Group B consisted of 25 control and healthy subjects. The two groups were explored by echocardiography coupled to tissue Doppler and 2D strain.

Results. The mean age of our patients was 45 ± 7 years. The sex ratio was 0.8 The control population was on the characteristic epidemiological similar to the group of patients. The anatomical data of the left ventricle, the ejection fraction normal and comparable between the two groups, the TEI index was significantly higher in the A group (0.8 ± 0.04 vs 0.28 ± 0.07, p < 0.01). Tissue Doppler velocity S peak measurement was reduced in group A compared to group B (5.6 ± 0.5 vs 9.30 ± 0.5, p < 0.01), global longitudinal strain was also altered in scleroderma patients (-11 ± 0.4 vs -18. ± 0.3 < 0.01). There was no significant difference in E / A ratio, however early LV diastolic dysfunction was revealed by a higher E / Ea and E / VP ratio in group A compared to group B with respectively (13 ± 1.8 vs 6 ± 1.6 , p < 0.01) and (2.2 ± 0.6 vs. 1.5± 0.6 p < 0.01), a longer Ap-Am duration (≥ 20 ms) and a higher volume of the left atrium was noted in groupe A. The mean value of the pulmonary pressions was 37.9 ± 9 mmHg in patients with scleroderma vs. 25 ± 3 mmHg for the control group (p < 0.01).There was no right ventricular dysfunction

Conclusions. Cardiac involvement during systemic sclerosis precede clinical expression, echocardiography coupled with tissue doppler and 2D strain are useful to detect these abnormalities at a subclinical stage of the disease.

Key words: systemic sclerosis, cardiac involvement, echocardiography, comparison
Introduction
The occurrence of cardiac involvement in systemic sclerosis (SSc) is an evolutionary turning point in this disease and represents a major cause of morbidity and mortality from this systemic pathology. It appears that a histological lesions of the heart in SSc would be much more frequent and earlier than clinical symptoms.

Purpose of study was to unmasking any signs of left ventricular dysfunction in a subclinical stage of the disease scleroderma by appreciating echocardiography systolic and diastolic function in asymptomatic patients with SSc and comparing the echocardiographic findings in these patients to those with the results obtained in a control population.

Material and methods
A prospective descriptive and comparative study was conducted in the adult cardiology department of the Rabta Hospital over a period of 5 years from 2012 to 2017. The relatively long inclusion period is due to the difficulty of recruiting patients because of the rarity of this systemic disease, to which is added the imperative that these patients must be functionally asymptomatic and free from any other comorbidity.

Inclusion criteria:
- Group A: 25 asymptomatic scleroderma patients without signs of heart failure who did not have other comorbidities that could interfere with left ventricle (LV) function.
- Group B: 25 control and healthy subjects.

Exclusion criteria:
- Patients with high blood pressure, diabetes, valvular heart disease, ischemic heart disease.
- Patients were explored by conventional echocardiography coupled to tissue Doppler and 2D strain. Several parameters have been collected and compared between two group in particular: left ventricular anatomic measurements (diameter, septum thickness), left ventricular function (ejection fraction (EF), Tei index, S wave at Tissue Doppler, as well as global longitudinal strain) and diastolic function (mitral profile, E / E wave ratio, VP, duration of the mitral wave minus the pulmonary wave, left atrium volume).
Statistical studies: We calculated simple frequencies and relative frequencies (percentages) for qualitative variables, means, medians and standard deviations (standard deviations) for quantitative variables. We used the chi-square test and the student test respectively for the comparison of two percentages and two averages, in all the statistical tests, the significance level was fixed at 0.05.

Results
Epidemiological data of the two groups were reported in Table 1.

Both groups A and B were free from comorbidities (arterial hypertension, diabetes, ischemic heart disease). The diagnosis of SSc in our patients went back several years with an average of 6.5 years. All our patients were treated with corticosteroids; 55% of patients received calcium channel blockers due to Raynaud's syndrome.

Anatomical features and LV systolic function for both groups were reported in Table 2.

LV diameter measurements and septum thickness were normal and comparable between the two groups. The Tei index in the group of scleroderma patients was $0.6 \pm 0.08$ significantly higher than in the control group which was $0.28 \pm 0.07$ ($p < 0.01$). This therefore suggests the existence of an attributable left ventricular dysfunction during SSc that will have to be apprehended by other ultrasound methods.

The LV ejection fraction was also comparable between the 2 groups. While the peak of systolic velocities $S$ at the mitral annulus measured by the tissue Doppler mode (DTI) and the global longitudinal strain was definitely lowered in the group A compared to the group B attesting latent left ventricular systolic dysfunction in our scleroderma patients in subclinical stage.

The study of the diastolic function of the left ventricle was reported in Table 3, the analysis of the parameters of the diastolic function by the pulsed Doppler mode, shows no significant differences between the two groups with respect to velocity peaks, protodiastolic $E$, end-diastolic $A$, $E / A$ ratio. A normal or pseudo normal filling pattern was found in 82% of patients in group A and in 93% of group B. A significant difference between the two Groups was found concerning combined indices ($E / VP$, am-ap duration, $E / Ea$ ratio, and left atrial volume).

The elevation of pulmonary arterial pressures is one of the echocardiographic abnormalities found in our scleroderma patients. The mean value pulmonary pressures was $37 \pm 9$ mmHg for group A vs. $25 \pm 3$ mmHg for group B ($p < 0.01$). However, this relative
pulmonary hypertension was not important, explaining the absence of functional impairment especially in our scleroderma patients. Moreover, there was no dysfunction of the right ventricle in both groups.

**Discussion**

Systemic scleroderma (SSc) is a generalized disease of interstitial and vascular connective tissue associated with abnormalities of the immune system (autoimmune disease) leading to fibrosis. The disease usually begins between 40 and 60 years of age [1]. the average age of our patients was 45 ± 7 years old. Women are more frequently affected than men (sex ratio 8/10) [1]; this predominance was found in our study. Cardiac involvement in SSc is multiple and not very specific [2]. three tunics are interested but myocardial involvement is preponderant. It seems to be due to the combination of several mechanisms: myocardial ischemia in relation to coronary vasospasm, myocardial fibrosis, obliteration of the coronary microcirculation or an alteration of the capillary bed, all contributing to myocardial dysfunction [3].

Cardiac involvement is most often asymptomatic, which is why its prevalence is underestimated: 8 to 28% depending on the studies [4], autopsy studies have reported myocardial involvement in 50 to 89% of subjects with SSc [5]. Indeed Angelo [5], in his autopsy series including 58 patients showed myocardial fibrosis in 81% of patients, while only 16% had cardiac manifestations during their lifetime. Histological and echocardiographic cardiac involvement precedes clinical expression, hence the interest of performing echocardiography in subjects with scleroderma to detect abnormalities of systolic and diastolic function that may appear several years before causing clinical signs [6]. Several studies [7, 8] have not noted a change in the anatomical features of LV during scleroderma. In our series, the values of anatomical parameters of LV were normal and comparable between the two groups.

Myocardial involvement in SSc affected often diastolic than systolic function, indeed several studies demonstrated that scleroderma patients had a normal EF, the mean EF was 69.5% in the Candella study[9], 66.9% in the Meunes study [6] and 67.4% in the Plazak serie [10]. In our series, the ejection fraction in patients with scleroderma was normal and comparable to the control group with an average EF was 64%.

Tissue Doppler by studying systolic velocities S at the mitral annulus is more reliable than EF for the detection of early LV systolic dysfunction [11]. It therefore appears much more sensitive than conventional ultrasound [12]. This notion has been reported in
several studies that have shown that despite a normal found ejection fraction, there is a decrease in LV contractility in scleroderma patients detected by the study of tissue Doppler velocities thus attesting to the existence of an early systolic dysfunction underestimated by echocardiography. In our series, although LV EF was normal in patients with SSc, early systolic dysfunction was detected by a low value of the peak velocity of S measurement at the tissue Doppler.

Interesting studies on the contribution of D2 strain, in scleroderma patients are very rare. However, some authors have shown by an analysis of radial or longitudinal myocardial function its performance in the detection of systolic and early dysfunction of LV. This method was used by Coucelo [13], who studied the segments reflecting displacement of longitudinal fibers in scleroderma patients. He found a correlation between the deterioration of systolic and diastolic function in the studied segments and the degree of fibrosis, and Edoardo Rosato [14] similarly noted in his study of 76 scleroderma patients abnormalities in Longitudinal fibers 23% vs in function of radial fibers 8%. In our series, GLS was altered in our scleroderma patients.

Myocardial involvement is much more often a diastolic lesion than a systolic one. It constitutes the essential manifestation of the primary cardiomyopathy of the SSc [4]. The transmural profile usually described in the scleroderma patients is type anomaly of relaxation. A mitral profile type I was found in 42% of the sclerodermic patients in the study of Valentini [8]. A restrictive profile has also been reported in the literature but its frequency was lower; Fernandes [15] in a study with endomyocardial biopsies in asymptomatic patients without evidence of heart failure and excluding patients with hypertension, LV hypertrophy, LV systolic dysfunction found abnormality in the disposition of the patient collagen in 94%, indicating the almost constant myocardial involvement due to this fibrosis. Candella [9] supports this view, noting in his study that diastolic dysfunction found in scleroderma patients persisted after adjustment for blood pressure, heart rate, age, valvulopathy, pericardial effusion [16] confirming primary myocardial involvement in SSc.

In our study, the 25 patients were completely asymptomatic without any clinical signs of heart failure and were free from any comorbidity that could interfere with the function of LV, we did not notice anomalies in the mitral profile. It can be concluded that diastolic dysfunction is certainly common, but may simply be due to associated comorbidities and not to primary myocardial involvement. and that diastolic alteration specifically related to scleroderma can only be discussed once other possible causes of diastolic dysfunction have been ruled out.
All studies highlight the limitations of evaluating diastolic function on transmitral flow alone, hence the contribution of tissue pulsed Doppler as a non-invasive method in the study of diastolic function at a subclinical stage. Indeed, by the Ea peak measurement on the septal side of the mitral annulus to the tissue Doppler, Ilknur Can [17] noted in patients with scleroderma a decrease in Ea compared to a control group, thus signaling early diastolic dysfunction. In our series, the tissue Doppler attest a decrease in the value of Ea in scleroderma patients comparing to the control group and confirm eventual diastolic dysfunction. Another indice to evaluate LV pressure was the E/Ea ratio in fact Ilknur [17] calculated this ratio in a group of sclérodérmia patients and a healthy group, this ratio was higher in the group of patients attesting a rise in LV filling pressure our results are similar to those reported in our series.

The study of the duration Ap-Am, E/ vp, the volume of the left atrium have not been the subject of several studies in the various series published in the literature, most studies were based on mitral flow analysis, velocity peak Ea measurement at the mitral annulus to tissue Doppler, and E/Ea ratio calculation. The values of these parameters were altered in our series attesting a rise in filling pressure.

The exact prevalence of pulmonary artery hypertension (PAH) during SSc is debated is in the range of 8 to 12% [18]. According to the new classification proposed at the Third World Congress, pulmonary hypertension during the SSc can be either a PAH associated with systemic sclerosis or pulmonary arterial hypertension secondary to pulmonary fibrosis [19]. PAH was observed in our patients and it was not important, which also explains the lack of functional impairment especially in our scleroderma patients.

Although diastolic dysfunction of the left ventricle, and to a lesser extent systolic dysfunction, was well studied in scleroderma patients, the study of right ventricular function has not been studied extensively [20].

Limitations of our work
The small size of our population is the main limitation of our work, and other single or multicenter studies, including a larger number, will improve the validity of our results.

We have not also developed the contribution of this echocardiographic study in the decision of to prescribe or not a treatment in a totally asymptomatic scleroderma patients.

Conclusion
Our patients with sclérodermie were completely asymptomatic and without any clinical signs of heart failure, but the comparative study with a healthy population has identified by echocardiography coupled with tissue Doppler and 2D strain the presence of a latent subclinical cardiac involvement in SSc. The diagnosis of its anomalies allow appropriate thérapeutique approach (the vasodilatory drugs) to early vasospastic and reversible abnormalities of the early myocardial disease observed in scleroderma.

**Competing interests**
The authors declare no competing interest.

**Authors’ contributions**
All authors had contribute to write this article

**References**


<table>
<thead>
<tr>
<th></th>
<th>Group A</th>
<th>Group B</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>45 ±7</td>
<td>43 ±7</td>
<td>NS</td>
</tr>
<tr>
<td>Sex ratio (female)</td>
<td>0.8</td>
<td>0.8</td>
<td>ns</td>
</tr>
<tr>
<td>BMI</td>
<td>22 ±1</td>
<td>24±4</td>
<td>ns</td>
</tr>
<tr>
<td>diabetes</td>
<td>5.6 ± 0.8</td>
<td>5.3 ±0.6</td>
<td>ns</td>
</tr>
<tr>
<td>Systolic BP (mmhg)</td>
<td>121±1</td>
<td>117±2</td>
<td>ns</td>
</tr>
<tr>
<td>Diastolic BP (mmhg)</td>
<td>78±5</td>
<td>72±5</td>
<td>Ns</td>
</tr>
</tbody>
</table>

**Table 1**: Epidemiological characteristics of study population.
<table>
<thead>
<tr>
<th></th>
<th>Group A (25 patients)</th>
<th>Group B (25 témoins)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVEDD (cm)</td>
<td>47±0.5</td>
<td>45±0.5</td>
<td>0.1</td>
</tr>
<tr>
<td>SIV (cm)</td>
<td>0.9±0.1</td>
<td>0.8±0.1</td>
<td>0.2</td>
</tr>
<tr>
<td>PP (cm)</td>
<td>0.9±0.15</td>
<td>0.8±0.1</td>
<td>0.6</td>
</tr>
<tr>
<td>EF %</td>
<td>63±3</td>
<td>64±1</td>
<td>0.45</td>
</tr>
<tr>
<td>Tei index</td>
<td>0.6±0.08</td>
<td>0.28±0.07</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Peak S velocity (cm/s)</td>
<td>5.6±0.5</td>
<td>9.3±0.5</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>GLS (%)</td>
<td>-11±0.4</td>
<td>-18±0.3</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

Table 2: anatomical features and LV systolic function in both groups of population

**Figure 1**: comparison TEI index

**Figure 2**: comparison Peak S velocity

Between two groups
Figure 3: comparison of GLS between two groups

GLS: global longitudinal strain

<table>
<thead>
<tr>
<th></th>
<th>Group A</th>
<th>Group B</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peak E velocity (cm/s)</td>
<td>89 ± 14</td>
<td>87± 16</td>
<td>0.6</td>
</tr>
<tr>
<td>Peak A velocity (cm/s)</td>
<td>65 ± 12</td>
<td>64 ± 16</td>
<td>0.4</td>
</tr>
<tr>
<td>E/A ratio</td>
<td>1.46± 0.3</td>
<td>1.32 ± 0.4</td>
<td>0.3</td>
</tr>
<tr>
<td>E/Vp ratio</td>
<td>2.3± 0.6</td>
<td>1.3 ± 0.6</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Am-Ap duration</td>
<td>0</td>
<td>&gt; 20ms</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Peak velocity at mitral annulus Ea (cm/s) TD</td>
<td>7.0 ± 1.2</td>
<td>11. ± 1.4</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>E/Ea ratio</td>
<td>12.71 ± 1.8</td>
<td>7.9 ± 1.4</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Volume of left atrium ml/m2</td>
<td>37±9</td>
<td>25± 3</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

Table 3: Features of diastolic LV function
**Figure 4**: comparison of E/vp between two groups

**Figure 5**: comparison of peak Ea between two groups

**Figure 6**: comparison of E/Ea between two groups

**Figure 7**: comparison of volume of left atrium between 2 groups