

# Skeletal and cardiac muscles involvement in systemic sclerosis

Lilian Schade<sup>1</sup>, Eduardo dos Santos Paiva<sup>2</sup>, Carolina de Souza Müller<sup>3</sup>

## ABSTRACT

Patients with systemic sclerosis (SSc) can have muscle involvement in the form of myositis or non-inflammatory myopathy. The muscle involvement can be associated with left ventricular dysfunction (LVD) in patients with SSc, resulting in worse prognosis. Eighty-seven patients of the Hospital de Clínicas of the Universidade Federal do Paraná, diagnosed with SSc, were assessed regarding the presence of skeletal muscle manifestations and their relation with LVD. A 42.5% prevalence of muscle involvement was observed in the patients studied, as well as a positive correlation with the diffuse form of the disease. Excluding other causes of LVD, three of the four patients with ejection fraction below the normal reference value had alteration of the muscle strength, atrophy and/or serum creatine phosphokinase (CPK) elevation.

**Keywords:** systemic sclerosis; myositis; left ventricular dysfunction.

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## INTRODUCTION

Systemic sclerosis (SSc) is an autoimmune disease characterized by vascular alterations and fibrosis of the skin and internal organs. It is classified as diffuse or limited, according to the extension of the skin affected.<sup>1</sup>

Patients with SSc can have muscle involvement in the form of myositis or non-inflammatory myopathy, manifesting as varied degrees of weakness, muscle atrophy and elevation in serum creatine phosphokinase (CPK), usually associated with electroneuromyographic alterations.<sup>2</sup>

The muscle involvement can be associated with left ventricular dysfunction (LVD) in patients with SSc.<sup>3,4</sup> The EUSTAR (EULAR Scleroderma Trials and Research) database, assessing 7,073 patients with SSc, has shown a 5.4% prevalence of LVD, and myositis was one of the independently associated factors. The LVD worsened the prognosis of such patients.<sup>3</sup>

The present study aimed at assessing the association of SSc with muscle manifestations, and their relation to LVD.

## MATERIAL AND METHODS

This study comprised 87 patients of the SSc outpatient clinics of the Service of Rheumatology of the Hospital de Clínicas of the UFPR diagnosed with SSc according to the American College of Rheumatology (ACR) criteria. They were assessed regarding muscle manifestations and their relation to LVD. The muscle manifestations were assessed as follows: presence of muscle weakness or atrophy, both observed on physical examination; and/or CPK elevation. Left ventricular dysfunction was assessed by use of transthoracic echocardiography by measuring the ventricular ejection fraction (EF). The muscle and cardiac findings were also correlated with the diffuse or limited presentation of SSc, and patients' age and sex. Patients

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Service of Rheumatology of the Hospital de Clínicas of the Universidade Federal do Paraná (HC-UFPR), Brazil.

1. Resident physician in Rheumatology, HC-UFPR

2. Rheumatologist; Professor of Rheumatology of the HC-UFPR

3. Rheumatologist; Assistant rheumatologist of the Systemic Sclerosis Outpatient Clinics of the HC-UFPR

Correspondence to: Lilian Schade. Serviço de Reumatologia do Departamento de Clínica Médica do Hospital de Clínicas da UFPR. Av General Carneiro, 181. Curitiba, PR, Brazil. E-mail: lilianschade@yahoo.com.br.

with alterations that could result in muscle involvement or CPK elevation due to non-SSc related causes, such as thyroid diseases or statin use, were excluded from the study.<sup>5,6</sup>

## RESULTS

Of the 87 patients with SSc assessed, 37 (42.5%) had muscle manifestations in the form of muscle weakness, muscle atrophy and/or CPK elevation (Table 1). Muscle weakness, reported by the patient and evidenced as muscle strength deficiency on physical examination, was the most common finding, present in 28 patients, associated or not with muscle atrophy and/or CPK elevation. Creatine phosphokinase elevation was observed in 11 patients, and was positively correlated with muscle atrophy ( $P = 0.04$ ), but not with muscle weakness ( $P = 0.09$ ).

Of the 87 patients assessed, 19 (21.8%) had diffuse SSc. The diffuse cutaneous form of SSc showed a positive correlation with an increased number of muscle manifestations (muscle weakness, muscle atrophy and/or CPK elevation,  $P = 0.04$ ). The limited cutaneous form showed a negative correlation ( $P = 0.08$ ).

The mean age of patients with SSc and muscle manifestation was  $48 \pm 11.7$  years, similar to the mean age of all patients with SSc assessed in this study ( $48.5 \pm 11.7$  years). Only seven patients (8%) were males, of whom, three (42.8%) had muscle manifestation, one with the diffuse form and the other two with the limited form of the disease. In the female sex, the prevalence was similar (42.5%).

The transthoracic echocardiogram showed EF below the normal reference value for age in four of the 87 patients assessed (4.59%). Of those four patients, three (75%) had alterations of the muscle strength, atrophy and/or CPK elevation, and other causes of LVD were excluded. The age of those three patients ranged from 34 to 61 years.

**Table 1**

Correlation between muscle manifestations and cutaneous forms of SSc in the patients studied

Muscle manifestations	Diffuse SSc	Limited SSc
Isolated muscle weakness	4	14
Isolated muscle atrophy	1	3
Isolated CPK elevation	3	2
Weakness + atrophy	1	3
Weakness + CPK elevation	0	2
Atrophy + CPK elevation	0	0
Weakness + atrophy + CPK elevation	3	1

## DISCUSSION

In the literature, muscle involvement in SSc has been classified into two types: myositis, usually associated with more intense muscle weakness and high CPK levels; and non-inflammatory myopathy.<sup>7</sup> The latter does not have a consensual definition and usually includes muscle involvement without inflammation. The alterations found on the electroneuromyography of patients with SSc are similar to those evidenced in idiopathic inflammatory myopathies.<sup>7,8</sup> The histological findings are heterogeneous and include both the inflammatory myopathy component and specific findings of SSc in varied proportions: from inflammatory infiltrates, necrosis, and atrophy to microangiopathy and fibrosis of the perimysium and epimysium.<sup>7,8</sup> The diagnostic criteria for muscle involvement in SSc have not been well defined, and neither has the superposition SSc/polymyositis versus SSc-associated myopathy.<sup>7</sup> The myositis type of SSc has a favorable prognosis and usually responds adequately to corticoids. Although clinically less expressive, non-inflammatory myopathy responds poorly to immunosuppressant treatment.<sup>2,7</sup>

In our study, we observed a 42.5% prevalence of muscle involvement in the form of muscle weakness, atrophy and/or CPK elevation in patients with SSc. The same assessment in other studies has shown prevalence between 16% and 81%, reflecting the heterogeneity of the criteria used to define muscle involvement in SSc. The greatest prevalence was observed in patients with the diffuse cutaneous form of SSc, in accordance with the literature.<sup>2</sup> No relation to age or sex was observed.

Heart involvement in SSc, characterized by arrhythmias, conduction disorders and/or LVD, is more frequent in patients with skeletal myopathy, either inflammatory or not.<sup>4,7</sup> Thus, considering that association and the poor prognosis of heart involvement in SSc, cardiac monitoring in patients with SSc and skeletal myopathy should be performed regularly,<sup>7</sup> including the assessment of prophylactic pacemaker indication in high-risk patients.<sup>9</sup>

The association between muscle involvement and LVD was also observed in our study. Of the patients with LVD, 75% had an alteration in muscle strength, atrophy and/or CPK elevation. Because this is a cross-sectional study, the clinical outcome of those patients was not assessed regarding the prognosis of that manifestation.

Thus, the present study aimed at confirming the literature data regarding muscle involvement in SSc and its association with LVD, in addition to drawing attention to that clinical manifestation in the context of a heterogeneous, systemic, and severe disease.

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