

## Why is the Left Ventricular Global Longitudinal Strain Reduced in Idiopathic Inflammatory Myopathies?

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### ABSTRACT

In the study carried out by our group-first study demonstrating speckle tracking echocardiography has prognostic value in patients with idiopathic inflammatory myopathies. We demonstrated that patients with Idiopathic Inflammatory Myopathy (IIM) have lower mean Global Longitudinal Strain (GLS) of the Left Ventricle (LV) than controls, corroborating the results of two previous studies. In addition, we found that reduced LV GLS has prognostic value in the evolution of the disease. However, the reason to explain why patients with IIM have reduced LV GLS are still uncertain. We designed this small study to assess whether disease activity or duration could, in part, explain it.

**Keywords:** Left ventricle; Global longitudinal strain; Rheumatic diseases; Cardiomyopathy

### ABOUT THE STUDY

Therefore, the objectives of the current study were as follows: 1) To assess whether the measurement of LV GLS in patients with IIM is influenced by disease activity, using two of the six domains of the activity criteria of the International Myositis Assessment and Clinical Study Group (IMACS): Creatine Phosphokinase (CPK) serum level and assessment of muscle strength by Muscle Testing Manual-8 (MMT8); 2). To assess whether the measurement of LV GLS in patients with IIM is influenced by disease duration [1-4].

This study is a sub analysis of our previous study, conducted in the autoimmune rheumatic diseases sector of the rheumatology division at the Universidade Federal de São Paulo-São Paulo/Brazil (UNIFESP/Hospital São Paulo), between February/2018 and October/2021 [1]. We included sixty-one patients with IIM and all of them met the 2017 American College of Rheumatology/The European League Against Rheumatism (ACR/EULAR) criteria [5]. The most frequent IIM subtype was dermatomyositis (62.3%), followed by anti-synthetase syndrome (21.3%), PM (9.8%), and immune-mediated necrotizing myopathy (6.6%).

To assess whether the CPK level, MMT8 measurement and the duration of IIM influenced the LV GLS measurement, we transformed each of these variables into a categorical variable:

- CPK assessment: We formed two groups: One with normal CPK (level below 192 U/L) and another with higher CPK (above the upper reference value).
- MMT8 assessment: We formed two groups: With normal MMT8 (equal or higher than 80 (normal value) and another with MMT8 below 80.
- Disease duration assessment: We formed two groups: Patients with  $\leq 5$  years and patients with  $>5$  years of disease.

Comparison was made between these groups in terms of LV GLS measurement, using Student's t-test for average GLS and Fisher's exact test for categorical variables (normal LV GLS *versus* reduced LV GLS).

### CPK and LV GLS

No differences were observed between the groups: Normal CPK and high CPK, in relation to the LV GLS measurement, both quantitatively and qualitatively (Table 1).

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**Received:** 08-Sep-2023, Manuscript No. JCEC-23-26700; **Editor assigned:** 11-Sep-2023, Pre QC No. JCEC-23-26700 (PQ); **Reviewed:** 25-Sep-2023, QC No. JCEC-22-26700; **Revised:** 02-Oct-2023, Manuscript No. JCEC-23-26700 (R); **Published:** 09-Oct-2023, DOI:10.35248/2155-9880.23.14.846

**Citation:** Sato EI, Machado LSG, Oliveira ACD, Mancuso FJN (2023) Why is the Left Ventricular Global Longitudinal Strain Reduced in Idiopathic Inflammatory Myopathies? J Clin Exp Cardiol. 14:846.

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Variable	Normal CPK (n=43)	High CPK (n=18)	P
Mean LV GLS (%)*	18,6 ± 2.8	18.1 ± 3.1	0.550
Reduced LV GLS N (%)**	17 (39.5)	9 (50)	0.572

**Note:** \*Student's t-test, \*\*Fisher's exact test, Reduced LV GLS considered when <18%

**Table 1:** Creatine Phosphokinase (CPK) level and Left Ventricle Global Longitudinal Strain (LV GLS)

### MMT8 and LV GLS

No differences were observed between the groups: MMT8 ≥ 80 and MMT8 below this value, in relation to the LV GLS measurement, both quantitatively and qualitatively (Table 2).

Variable	MMT8=80 (n=41)	MMT8<80 (n=20)	P
Mean LV GLS (%)*	18.4 ± 2.9	18.7 ± 3.0	0.749
Reduced LV GLS N (%)**	18 (43.9)	8 (40)	1.000

**Note:** \*Student's t-test, \*\* Fisher's exact test, Reduced LV GLS considered when <18%

**Table 2:** MMT8 and LV GLS

### Duration of IIM and LV GLS

No differences were observed between the groups with disease duration ≤ 5 years and >5 years, regarding the LV GLS measurement, both quantitatively and qualitatively (Table 3).

Variable	Duration ≤ 5 years (n=29)	Duration >5 years (n=32)	P
Mean LV GLS (%)*	18.4 ± 3.0	18.6 ± 2.9	0.818
Reduced LV GLS (<18%) N (%)**	13 (44.8)	13 (40.6)	0.799

**Note:** \*Student's t-test, \*\*Fisher's exact test, Reduced LV GLS considered when <18%

**Table 3:** Duration of IIM and LV GLS

There was no association between LV GLS measurements and IIM activity, assessed by two of the six IMACS criteria, CPK serum level and MMT8 scores [4]. Our results corroborate the study by Guerra, which also observed no association between reduced GLS and muscle strength or involvement of different organs. Possibly showing that the reduced strain measurement in patients with IIM does not only reflect acute inflammatory changes. It is interesting to note that in our previous study, patients with reduced LV GLS followed, on average for 25 months, evolved with more activity of myositis, that is, the activity may not cause a reduction in strain, however patients with reduced strain evolves worse in relation to the disease [2].

There was also no association between disease duration and LV GLS, showing that time alone does not influence the measurement of myocardial deformation, again agreeing with the study by Guerra [2].

The cause of the reduction in strain in the IIM probably is multifactorial and cannot be explained by a single reason. Among the factors, early atherosclerosis observed in patients with inflammatory myopathy is possibly the most important and is caused by the chronic systemic inflammation inherent to the disease, by the chronic use of corticosteroids and mainly by the higher prevalence of cardiovascular disease classic risk factors, such as diabetes mellitus, dyslipidemia and systemic arterial hypertension observed in patients with inflammatory myopathies [6-8]. However, the higher prevalence of arterial hypertension and dyslipidemia alone cannot explain the reduced LV GLS in IIM, as observed in our study [9-10]. Another plausible reason for the strain reduction in these patients is the local cardiac inflammation, mediated both by the innate and adaptive immune response that leads to a cardiomyopathy, due to the direct action on the myocytes and by an endotheliopathy causing a dysfunction in the coronary microcirculation. Finally, we can still mention the use of some drugs in the treatment of myopathies, such as cyclophosphamide, which can be cardiotoxic, contributing to heart damage.

## CONCLUSION

Patients with IIM have a reduced LV GLS compared to controls, however, this reduction probably is multifactorial and is not influenced alone by disease activity, assessed by measuring muscle enzymes and muscle strength and nor the disease duration.

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