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# Prevalence of subclinical systolic dysfunction in Takayasu's arteritis and its association with disease activity: a cross-sectional study

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## Abstract

**Background** Takayasu's arteritis (TA) is a vasculitis that affects the aorta and its branches and causes stenosis, occlusion, and aneurysms. Up to 60% of TA patients are associated with cardiac involvement which confers a poor prognosis. Global longitudinal strain (GLS) analysis is an echocardiographic technique that can detect the presence of subclinical systolic dysfunction. Hence, this study aimed to describe the prevalence of subclinical systolic dysfunction in patients with TA using the GLS method and to correlate this finding with disease activity using the ITAS-2010 (Indian Takayasu Activity Score).

**Methods** Thirty patients over 18 years of age who met the American College of Rheumatology (ACR) 1990 criteria for TA were included. The sample was submitted for medical record review, clinical and echocardiographic evaluation, and application of ITAS-2010. The cutoff for systolic dysfunction was  $GLS > -20\%$ .

**Results** Of the 30 patients analyzed, 25 (83.3%) were female, and the mean age was 42.6 years ( $\pm 13.2$ ). The median time since diagnosis was 7.5 years [range, 3–16.6 years], and the type V angiographic classification was the most prevalent (56.7%). Regarding echocardiographic findings, the median ejection fraction (EF) was 66% [61–71%] and the GLS was  $-19.5\%$  [ $-21.3$  to  $-15.8\%$ ]. Although half of the participants had reduced GLS, only two had reduced EF. Eleven patients (33%) met the criteria for activity. An association was found between disease activity and reduced GLS in eight patients ( $P=0.02$ ) using the chi-square test.

**Conclusion** GLS seems to be an instrument capable of the early detection of systolic dysfunction in TA. The association between GLS and disease activity in this study should be confirmed in a study with a larger sample size.

**Keywords** Takayasu's arteritis, Echocardiogram, Global longitudinal strain

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**Background**

Takayasu’s arteritis (TA) is an occlusive vasculitis of the aorta and its branches. It has a wide clinical spectrum depending on the vessels involved. Its initial phase has a nonspecific inflammatory characteristic and with progression, strictures, occlusions, aneurysms, and end-organ dysfunction are observed [1].

Cardiovascular disease is a major complication and cause of death in patients with TA. The heart is affected in up to 60% of patients with aortic insufficiency and coronary arteritis, with impaired left ventricular (LV) function being the most prevalent [2, 3].

Transthoracic echocardiography is useful for diagnosing cardiac involvement in this group of patients. However, the conventional method has low sensitivity for the early detection of myocardial dysfunction [4, 5]. In contrast, global longitudinal strain (GLS) is considered a sensitive indicator of early LV dysfunction, which measures the deformation of subendocardial fibers involved in early systolic dysfunction [5]. In previous analyses, GLS detected subclinical systolic dysfunction (SSD) in systemic autoimmune diseases [6, 7]. This is the first study to examine the association between SSD detected by GLS and disease activity in patients with TA. Therefore, our analysis may help in the early diagnosis of cardiac dysfunction and establishment of therapeutic strategies for this group.

**Table 1** Clinical, epidemiological, and angiographic profile of patients with Takayasu arteritis

Variables	n = 30 (%)
Age	42.6 ± 13.2
Sex	
Female	25 (83.3)
Time of Diagnosis	7.5 (3.0–16.6)**
<b>Immunosuppressive Drugs</b>	<b>n (%)</b>
Azathioprine	4 (13.3)
Methotrexate	4 (13.3)
Prednisone	2 (6.7)
Methotrexate/Azathioprine	1 (3.3)
Methotrexate/Prednisone	12 (40.0)
None	7 (23.3)
<b>Angiographic Classification of HATA</b>	
Type I	2 (6.7)
Type IIA	5 (16.7)
Type IIB	1 (3.3)
Type III	3 (10.0)
Type IV	2 (6.7)
Type V	17 (56.7)
<b>Cluster Classification</b>	
I	6 (20.0)
II	16 (53.3)
III	8 (26.7)

\*Mean ± standard deviation; \*\*Median with interquartile range

**Methods**

This cross-sectional study was conducted at a single center in Bahia. Data were collected between November 2021 and February 2022 through clinical and echocardiographic examinations and a review of medical records. Patients diagnosed with TA were analyzed according to the 1990 American College of Rheumatology criteria [8]. Medical history and baseline data such as sex, age, time of diagnosis, and medications prescribed were recorded. Physical examination was also performed to check for heart murmurs, pulse, and blood pressure. The patient was then referred for transthoracic echocardiography. The examination was performed by the same professional on a portable GE Vivid Lq (GE Healthcare, Zone Jiangsu, China). The GLS obtained using the two-dimensional speckle tracking technique was classified as reduced when it was > -20% [9]. After the echocardiographic assessment, the Brazilian version of Indian Takayasu Activity Score (ITAS 2010) was applied, with a score of ≥2 as the activity criterion [10, 11].

The Statistical Package for the Social Science program (SPSS, Chicago II, version 21) was used for statistical analysis. The results are expressed as absolute and percentage values for the qualitative variables. For quantitative variables with a normal distribution, the means and standard deviations were reported. For asymmetric quantitative variables, median and interquartile ranges were reported. The association between quantitative variables was assessed using Pearson’s chi-squared test and Mann Whitney test. The significance level used was 5%. This study was approved by the Human Research Ethics Committee of Prof. Edgard Santos University Hospital (CAAE 51979621.1.0000.0049).

**Results**

Thirty patients with TA were included, with a mean age of 42.6 ± 3.2 years and a higher proportion of women (83.3%). Most patients (40%) were administered methotrexate and prednisone. The angiographic classifications of Hata groups V and II were the most prevalent (56.7% and 53.3%, respectively). Eleven patients (33%) had active disease according to the ITAS-2010. The results are presented in Table 1. Regarding the ITAS-2010, the most frequently observed domains were neurological (30%), cardiovascular (26%), and systemic (23%). In the cardiovascular domain, limb claudication was more frequent.

On echocardiographic assessment, valve regurgitation was the most prevalent change, detected in 53% of the patients, where the mitral and tricuspid regurgitation was the most common (26.7%), followed by aortic regurgitation (23.3%). Systolic dysfunction reduced the left ventricular ejection fraction (LVEF), and hypokinesia was found in only two patients (6.7%), while reduced GLS was found in 15 patients (50.0%). Aortic root ectasia was

common (40%), whereas pulmonary arterial hypertension was found in only one patient (3.3%) (Table 2).

Patients with reduced GLS had earlier disease, with a median duration of three years. There was no higher frequency of elevated c-reactive protein among patients with reduced GLS. The frequency of arterial hypertension was similar between groups. The frequency of Type V angiography profile and cardiovascular domain of ITAS-2010 was slightly higher in the group with GLS > -20%, but there was no statistical significance. The results are presented in Table 3.

There was a statistically significant positive association between reduced GLS and disease activity in 53.3% of the patients (P=0.02) according to ITAS 2010 and patients with ITAS≥2 was using higher doses of prednisone (Table 4).

**Discussion**

The present study revealed a high prevalence of SSD in TA patients. Assessment of SSD by echocardiography combined with the GLS technique showed higher sensitivity than the conventional method of quantifying LVEF. In addition, the study demonstrated an

**Table 2** Echocardiographic changes in patients with Takayasu arteritis

Variables	n = 30 (%)
Aortic Insufficiency	7 (23.3)
Mitral Regurgitation	11 (36.7)
Tricuspid Regurgitation	11 (36.7)
Hypokinesis	2 (6.7)
Ejection Fraction < 40%	2 (6.7)
GLS > -20%	15 (50.0)
Systolic Dysfunction	2 (6.7)
Diastolic Dysfunction	9 (30.0)
Enlarged Left Atrium	8 (26.7)
Enlarged Right Atrium	2 (6.7)
Enlarged Left Ventricle	3 (10.0)
Left Ventricular Hypertrophy	6 (20.0)
Aortic Ectasia	12 (40.0)
Pulmonary Hypertension	1 (3.3)

GLS: Global longitudinal strain

association between disease activity and early myocardial dysfunction.

Similar to TA, cardiac dysfunction has been associated with inflammatory activity in other autoimmune

**Table 3** Clinical, laboratory and angiographic profile of patients with/without GLS ≥ -20%

Variables	GLS > -20%		Total	P*
	Yes n (%)	No n (%)		
<b>Disease duration (years)**</b>	3 ± (3.0–10.0)	9 (7.0–19.0)	8 (3.0–16.0)	0.024
<b>C-reactive protein elevated (&gt; 5 mg/dL)</b>				
Yes	6 (50.0)	6 (50.0)	12 (100.0)	1.000
No	9 (52.9)	8 (47.1)	17 (100.0)	
<b>Type V (angiographic classification)</b>				
Yes	9 (52.9)	8 (47.1)	17 (100.0)	1.000
No	6 (46.2)	7 (53.8)	13 (100.0)	
<b>Hypertension</b>				
Yes	10 (50.0)	10 (50.0)	20 (100.0)	1.000
No	5 (50.0)	5 (50.0)	10 (100.0)	
<b>Cardiovascular Domain (ITAS-2010)</b>				
Yes	5 (62.5)	3 (37.5)	8 (100.0)	0.682
No	10 (45.5)	12 (54.5)	22 (100.0)	

\*Chi-square test; GLS: Global longitudinal strain; ITAS: Indian Takayasu Activity Score

\*\*Median ± interquartile interval. U de Mann-Whitney test

**Table 4** Association between GLS, prednisone doses and disease activity (ITAS-2010)

Variables	ITAS ≥ 2		Total	P*
	Yes n (%)	No n (%)		
<b>GLS &gt; -20%</b>				
Yes	8 (53.3)	7 (46.7)	15 (100.0)	<b>0.020</b>
No	2 (13.3)	13 (86.7)	15 (100.0)	
<b>Prednisone doses(mg/dia)**</b>	18 (6.0–40.0)	5 (5.0–13.0)	10 (5.0–25.0)	0.080

\*Chi-square test; GLS: Global longitudinal strain; ITAS: Indian Takayasu Activity Score

\*\*Median ± interquartile interval. U de Mann-Whitney test

diseases. For example, a Chinese study examining ninety-seven patients with systemic lupus erythematosus (SLE) found a positive association between SSD diagnosed using echocardiography with GLS and systemic lupus erythematosus disease activity index (SLEDAI) score  $\geq 4$  [6].

SSD in the TA is multifactorial. The high prevalence in our series, compared to the 7–20% prevalence reported in the literature, may be related to valvular insufficiency, which occurred in 53% of the patients [12]. Other factors, such as an inflammatory process in the myocardial tissue and/or conduction system, contribute to systolic dysfunction in this population, in addition to accelerated atherosclerosis [13]. Disease activity was associated with SSD. The greater the activity, the greater the damage to the myocardium. This can be explained by vasculitis activity, which leads to myocardial fibrosis and ventricular remodeling [13].

Comparing the groups with and without GLS  $> -20\%$ , it was observed that patients with reduced GLS had a shorter disease duration, which shows that subclinical cardiac damage may be present in the first years of the disease. This finding corroborates the importance of a screening method for this condition in TA, promoting rapid recognition and prevention of adverse progression.

The limitations of this study include the small sample size, as it was conducted at a single center. Therefore, our results should be validated in a multicenter cohort study. In addition, echocardiogram with GLS is a subjective test that may vary with examiners. The ITAS-2010 score is an imminent clinical index that considers the subjective assessment of recent symptoms associated with TA and has a limited ability to accurately assess disease activity.

In autoimmune diseases, a reduction in GLS may be associated with unfavorable outcomes and a negative impact on life expectancy [14]. Therefore, it is recommended to perform cardiac evaluation in patients with TA using this technique to detect early myocardial dysfunction. This would help in preventing morbidity and mortality through therapeutic optimization.

## Conclusion

GLS detected SSD in our samples and showed a positive association with disease activity. These findings highlight the importance of echocardiographic screening with GLS for early detection of myocardial involvement in patients with TA and prevention of adverse progression. Thus, our study will help in the better management of patients with TA.

## Abbreviations

TA	Takayasu's arteritis
GLS	Global longitudinal strain
ITAS	Indian Takayasu Activity Score
ACR	American College of Rheumatology

EF	ejection fraction
LV	left ventricular
SSD	subclinical systolic dysfunction
SPSS	Statistical Package for the Social Science program
LVEF	left ventricular ejection fraction
SLE	systemic lupus erythematosus
SLEDAI	systemic lupus erythematosus disease activity index

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## Authors' contributions

All the authors of the manuscript have made substantial contributions to the conception or design of the study, the acquisition, analysis, or interpretation of data, as well as the drafting of the manuscript or revising it critically concerning its intellectual content. All authors read and approved the final version of the manuscript before submission.

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## Data Availability

The datasets during and/or analysed during the current study available from the corresponding author on reasonable request.

## Declarations

### Ethics approval and consent to participate

This study was approved by the Human Research Ethics Committee of Prof. Edgard Santos University Hospital (study#5.062.633; CAAE 51979621.1.0000.0049).

### Consent for publication

Not applicable.

### Competing interests

The authors declare that they have no professional, financial, or direct or indirect benefits that may influence the results and/or placement of this study.

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