Increased modifiable cardiovascular risk factors in patients with Takayasu arteritis: a multicenter cross-sectional study

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Abstract

Background: Modifiable cardiovascular risk factors (MCRFs), such as those related to aerobic capacity, muscle strength, physical activity, and body composition, have been poorly studied in Takayasu arteritis (TAK). Therefore, the aim of the study was to investigate MCRFs and their relationships with disease status and comorbidities among patients with TAK.

Methods: A multicenter cross-sectional study was conducted between 2019 and 2020, in which 20 adult women with TAK were compared with 16 healthy controls matched by gender, age, and body mass index. The following parameters were analyzed: aerobic capacity by cardiopulmonary test; muscle function by timed-stands test, timed up-and-go test, and handgrip test; muscle strength by one-repetition maximum test and handgrip test; body composition by densitometry; physical activity and metabolic equivalent by IPAQ, quality of life by HAQ and SF-36; disease activity by ITAS2010 and NIH score; and presence of comorbidities.

Results: Patients with TAK had a mean age of 41.5 (38.0–46.3) years, disease duration of 16.0 (9.5–20.0) years, and a mean BMI of 27.7 ± 4.5 kg/m^2. Three out of the 20 patients with TAK had active disease. Regarding comorbidities, 16 patients had systemic arterial hypertension, 11 had dyslipidemia, and two had type 2 diabetes mellitus, while the control group had no comorbidities. TAK had a significant reduction in aerobic capacity (absolute and relative VO$_2$ peak), muscle strength in the lower limbs, increased visceral adipose tissue, waist-to-hip ratio, reduced walking capacity, decreased weekly metabolic equivalent, and quality of life ($P < 0.05$) as compared to controls. However, there were no correlations between these MCRFs parameters and disease activity.

Conclusions: TAK show impairment in MCRFs; therefore, strategies able to improve MCRF should be considered in this disease.

Keywords: Aerobic capacity, Cardiovascular diseases, Muscle strength, Vasculitis

Introduction

Takayasu arteritis (TAK) is a primary systemic vasculitis characterized mainly by large-diameter vessels involvement, such as the aorta and major branches. Epidemiological studies have shown that the disease mainly affects women under the age of 40 years of age [1, 2].

Patients with TAK have a high prevalence of cardiovascular disease (CVD) and its risk factors. Additionally, 60–70% of patients present dyslipidemia [3, 4]. During follow-up, approximately 85% of patients developed systemic arterial hypertension [5, 6], and an increased prevalence of metabolic syndrome in TAK [6]; altogether, these factors may lead to increased morbidity and mortality in TAK.

CVD risk factors, morbidity, and mortality rate can be divided into modifiable and non-modifiable. Modifiable cardiovascular risk factors (MCRFs) include impairment

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in aerobic capacity [7, 8], muscle strength [9, 10], physical activity levels [11, 12], and body composition [13], among others. MCRFs may be relevant for predicting traditional CVD risk factors in healthy individuals and those patients with rheumatic diseases.

Furthermore, MCRFs are closely interconnected, and the alteration of one of the factors may worsen one or more other factors. Moreover, they seem to have additive responses in morbidity and mortality [14, 15]. However, few studies have currently analyzed MCRF parameters in patients with TAK [16, 17].

For example, reduced aerobic capacity has been described in several systemic autoimmune diseases [18–20]. This reduction is accompanied by a decline in physical capacity, muscle strength, and physical activity, which can worse body composition, increase fatigue, and predispose to a higher prevalence of CVD and its risk factors in rheumatic diseases [19, 21].

Oliveira et al. [17] showed that patients with TAK had reduced aerobic capacity. However, the authors did not evaluate other MCRFs, such as visceral adipose tissue and the waist and hip index, which are relevant CVD risk factors [3–6]. In addition, limitations may exist in the analysis of its findings regarding aerobic capacity, strength, and muscle function, due to the size of your sample.

Therefore, the aim of this study was to evaluate MCRFs and their relations with the disease status and comorbidities in patients with TAK.

Patients and methods

This is a multicenter cross-sectional study, conducted between 2019 and 2020, in which adult women with TAK. Patients had an age between 18 and 50 years and fulfilled at least three of the six items of classification criteria for TAK [22]. The study was approved by the local ethics committee and registered with ClinicalTrials (#NCT03750929).

The following exclusion criteria were adopted: patients with severe or decompensated diseases (e.g., endocrinopathies) that could interfere with the results interpretation and the physical testing safety; presence or history of critical/symptomatic aortic stenosis, congestive heart failure, arrhythmias or electrocardiographic changes in the ST segment, coronary artery disease; presence or history of peripheral atherosclerosis disease; sciatica or neurogenic claudication; with impaired walking (osteoarticular disorders in limbs), precluding exercise testing; pregnancy or lactation; and smoking in the previous 6 months of the study.

Interviews were conducted with eligible TAK patients, and medical records were systematically reviewed. In the control group, the volunteers were matched for age,

gender, and body mass index (BMI) to patients with TAK. The following data were collected:

- Demographic data: age and ethnicity;
- Quality of life: Health Assessment Questionnaire (HAQ) [23], Short Form Health Survey (SF-36) [24]
- Clinical data: age at disease diagnosis, duration of disease, the Edinburgh Claudication Questionnaire (ECQ) [25], Walking Impairment Questionnaire (WIQ) [26], Indian Takayasu's Arteritis Activity Score (ITAS2010) [27];
- Laboratory data: serum levels of C-reactive protein (CRP) and an erythrocyte sedimentation rate (ESR), total cholesterol, high-density lipoprotein (HDL), low-density lipoprotein (LDL), triglycerides;
- Pharmacological therapy: previous and current (glucocorticoids, immunosuppressive, immunomodulator and/or immunobiologicals drugs);
- Disease activity: ITAS 2010 [27], and National Institute of Health (NIH) score [28] (only in TAK);
- Comorbidities and their risk factors for CVD: type 2 diabetes mellitus was defined when the fasting glycemic test ≥ 126 mg/dL and/or the result of the oral glucose tolerance test ≥ 200 mg/dL [29]; systemic arterial hypertension was considered when blood pressure had systolic values ≥ 130 mmHg and/or diastolic values ≥ 85 mmHg [30]; dyslipidemia was defined when total plasma cholesterol ≥ 200 mg/dL, HDL-cholesterol ≤ 50 mg/dL, LDL-cholesterol ≥ 130 mg/dL and/or triglycerides ≥ 150 mg/dL [31]; or previously medical diagnosis and drug treatment for these comorbidities.
- Vascular images taken routinely and recently in the outpatient clinic (< 6 months after the inclusion of patients in the present study): data referring to vascular lesions in the aorta and the major branches (magnetic resonance-angiography and/or computed tomography-angiography) (only in TAK).

Physical activity level and weekly caloric expenditure

These parameters were obtained from the International Physical Activity Questionnaire (IPAQ, short version eight), translated into Portuguese and validated for the Brazilian population [32].

Anthropometry and body composition

The following parameters were collected: body mass (using a digital scale), height (using stadiometer), hip, waist and abdominal circumference, BMI, and waist-to-hip ratio. Dual X-ray absorptiometry was used to assess body composition, including lean mass, fat mass, and visceral adipose tissue, through iDXA equipment (GE Lunar Medical Systems, Madison, WI).

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Aerobic capacity

A treadmill cardiopulmonary test was conducted. The test was carried out according to the previous description [33].

Muscle strength

Maximum repetition test (1RM) was performed to determine muscle strength. The 1RM test was performed using the bench press and the 45° leg press. A familiarization trial was carried out, and it was followed by a 48 h-interval, followed by two tests performed on non-consecutive days, in which reproducibility was accepted as soon as the coefficient of variation was < 0.5%. The warm-up consisted of eight repetitions at 50% of 1RM with an interval of 2 min of rest. After that, three repetitions were performed at 70% of 1RM between 3-min intervals. To determine the 1RM, five attempts were made, and the highest recorded value was regarded as the maximum load. The interval between each attempt was 3 min [34].

Muscle function

Timed-Stands test (TST) [35], and Timed Up-and-Go (TUG) test [36] were applied beyond the handgrip test [37]. We performed a familiarization that was preceded by at least 48 h of interval before the tests. The coefficient of variation for all tests was < 0.5%.

As a control group (CTR), healthy volunteers were matched for age, gender, and BMI to patients with TAK. In addition, individuals in the CTR group had no systemic autoimmune diseases and were not smokers in the previous 6 months of the study.

Statistical analysis

Data distribution was evaluated using the Shapiro-Wilk test. Data with normal distribution were expressed as mean ± standard deviation, while data with asymmetric distribution were expressed as the median and the interquartile range (25–75%). The existence of differences between quantitative variables and normal distribution was analyzed using the Student's *t*-test. For the quantitative variables with asymmetric distribution, the Mann-Whitney U test was used. The categorical data were expressed as a percentage (%), and the differences were analyzed using Fisher's exact test. The correlation between variables with symmetric distribution was analyzed using the Pearson correlation coefficient, while that with asymmetric distribution was analyzed using the Spearman coefficient ρ [38]. Furthermore, the correlations were classified as poor (< 0.3), fair (0.3–0.5), moderately strong (0.6–0.8), and very strong (> 0.8) [39]. The differences were considered statistically significant when values of $P < 0.05$. The analyzes were performed

with the GraphPad Prism® software, version 6.01 for Windows (San Diego, California, USA).

Results

One hundred eight patients with TAK were interviewed. Of these patients, 56 did not meet the inclusion criteria, and 32 refused to participate for various personal reasons (e.g., lack of time, a long distance from home, and lack of interest); therefore, 20 patients were included in the study (Fig. 1).

TAK and 16 CTR were comparable regarding age, ethnicity distribution, and BMI parameters (Table 1). There no evidence of any chronic disease and comorbidities in the CTR group (Table 2).

Half of the patients with TAK had a type V angiographic classification by Hata et al. [40], followed by four type III patients, three type IV patients, two type IIb patients, and one type I patient (Table 1).
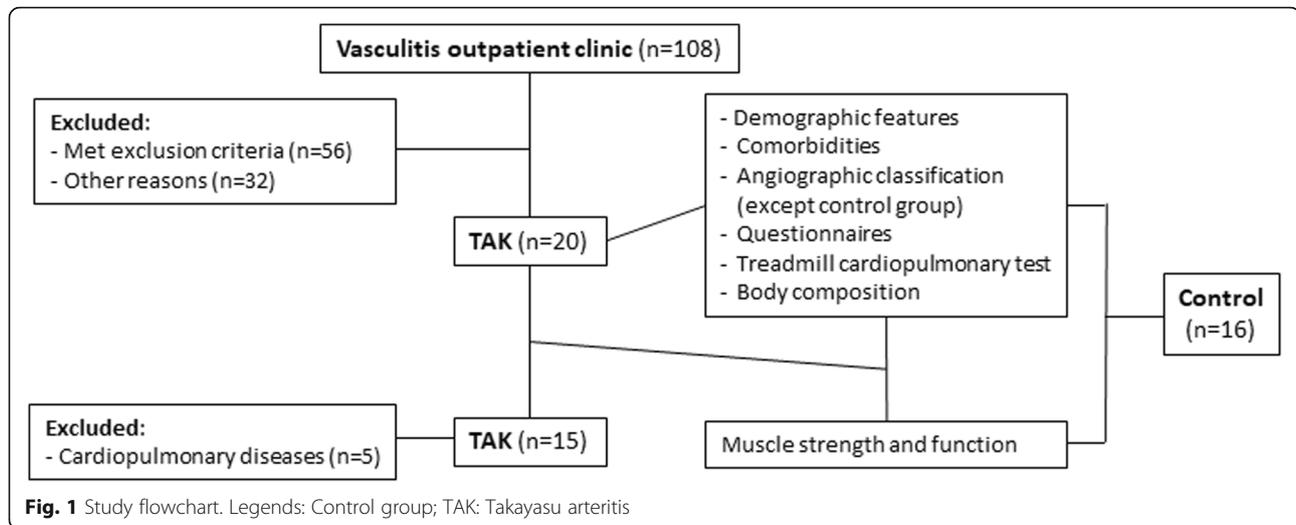
Regarding the drug treatment, only two patients were treated with prednisone at the time of data collection (doses were 10 mg/day and 5 mg/day over the past 3 months). Eleven (55.0%) patients used one or more immunosuppressive and/or immunobiological drugs: six used methotrexate, two azathioprine, and one leflunomide. Moreover, two patients were treated with infliximab, and one was treated with tocilizumab. Moreover, according to the ITAS2010 and NIH questionnaires, three (15.0%) patients were classified as presenting active disease (Table 1).

Systemic arterial hypertension and claudication of lower limbs were respectively present in 80.0 and 65.0% of patients with TAK, and two patients had type 2 diabetes mellitus. In addition, 11 (55.0%) of the patients had dyslipidemia under treatment, with two (10.0%) patients having diabetes mellitus. No individuals from the CTR group had systemic arterial hypertension, dyslipidemia, limb claudication or type 2 diabetes mellitus, and none of them used any type of medication other than contraceptives. No smokers were reported in the TAK and control groups (Table 2).

In the treadmill cardiopulmonary test, there were no differences between the TAK and CTR groups with respect to estimated maximum heart rate, anaerobic threshold, respiratory compensation point, and time-to-exhaustion (Table 3).

However, in comparison with the CTR group, patients achieved a lower maximum heart rate during the test, as well as a significant decrease in the absolute and relative VO_2 peak (Table 3).

Five out of 20 patients with TAK were excluded due to possible cardiopulmonary diseases; therefore, 15 patients participated in muscle strength and function tests (Table 3).

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Fig. 1 Study flowchart. Legends: Control group; TAK: Takayasu arteritis

Regarding muscle strength, the TAK group did not show significant reductions in the muscle strength of the upper limbs, assessed via the bench press. However, compared to the CTR group, a significant decrease in the strength of the lower limbs, assessed via leg press, was found in the TAK group (Table 3).

The TST, TUG, and handgrip strength in both hands were similar between the TAK and CTR groups (Table 3). Concerning the CTR group, patients with TAK presented a significant reduction in the ability to perform activities of daily living, assessed using the HAQ questionnaire (Table 4).

In the domains of the SF-36 questionnaire, in comparison with the CTR, the TAK group showed more

significant impairment, in terms of functional capacity, physical function, pain, general health, and mental health. In the walking impairment questionnaire (WIQ), compared to CTR, patients showed a reduction in all the variables evaluated ($P < 0.05$) (Table 4).

Regarding the level of physical activity assessed through the IPAQ, 14 (60%) patients in the TAK group had lower levels of physical activity than CTR. In the TAK group, six (30%) patients had moderate physical activity levels, with no difference compared to CTR, and none of the patients was classified as having a high level of physical activity. Additionally, in comparison with CTR, the weekly caloric expenditure values of the TAK group were lower (Table 4).

In comparison with the CTR group, the body composition and anthropometric measurements were similar between the TAK and CTR groups (Table 5), except for the higher volume and mass of visceral adipose tissue, and the waist-hip ratio in patients with TAK.

Based on reduced responses in both lower limb strength and aerobic capacity, we investigated possible correlations between these two variables and variables related to functional capacity. However, no correlations were found between any of the evaluated variables (Table 6).

Discussion

The present study showed patients with TAK present worse MCRF than controls. Moreover, the patients showed impaired walking capacity and increased visceral adipose tissue and waist-to-hip ratio. However, no correlations were observed between MCRF parameters or disease activity.

Despite being a rare disease, this study evaluated a sample of patients with well-characterized TAK, which were compared with well-matched healthy individuals.

Table 1 General features of patients with Takayasu arteritis

	N=20
Age (years)	41.5 (38.0–46.3)
Caucasian ethnicity	11 (55.0)
Disease duration (years)	16.0 (9.5–20.0)
Angiographic classification	
Hata I	1 (5.0)
Hata IIa	0
Hata IIb	2 (10.0)
Hata III	4 (20.0)
Hata IV	3 (15.0)
Hata V	10 (50.0)
Disease activity - NIH	3 (15.0)
Disease activity - ITAS2010	3 (15.0)
Erythrocyte sedimentation rate (mm/1st hour)	12.0 (9.5–21.5)
C-reactive protein (mg/L)	3.4 (0.9–6.8)

Data are presented in median (25–75%) or percentage (%)
ITAS2010 Indian Takayasu Activity Index, *NIH* National Institute of Health score

Table 2 Comorbidities and traditional risk factors for cardiovascular diseases

	TAK (*n*=20)	CTR (*n*=16)	*P* value
SAH or drug treatment	16 (80)	—	—
Dyslipidemia or drug treatment	11 (55)	—	—
Type 2 diabetes mellitus or drug treatment	2 (10)	—	—
Smoker	—	—	—
Total cholesterol (mg/dL)	167.0 (143.5–188.5)	177.0 (148.0–208.0)	0.335
HDL-cholesterol (mg/dL)	60.0 (48.5–74.0)	50.0 (48.0–81.0)	0.899
LDL-cholesterol (mg/dL)	93.0 (78.5–107.0)	109.0 (109.0–120.0)	0.089
Triglycerides (mg/dL)	100.0 (74.5–114.5)	83.0 (53.0–87.0)	0.279
Fasting glucose test (mg/dL)	83.5 (80.25–92.0)	85.0 (81.0–89.0)	0.832

Data are presented as median (25–75%) or percentage (%)
CTR Control group, *SAH* Systemic arterial hypertension, *TAK* Takayasu arteritis

Furthermore, the demographic, clinical, and laboratory data, as well as imaging conditions, pharmacological treatment, comorbidities, and disease status of patients with TAK were comprehensively described.

In the present study, only women were selected due to the higher prevalence of this gender in TAK [1, 2]. Individuals over 50 years of age were excluded to minimize the inclusion of individuals with comorbidities inherent in older age groups, as well as patients with atherosclerosis and peripheral arterial disease [41], or other vasculitis such as giant cell arteritis [42]. The inclusion of such group of patients would have undermined the accuracy of the diagnosis and symptoms.

Even with rigorous selection criteria, it was necessary to exclude five out of 20 TAK patients who had already been recruited to the study. The exclusion of these patients was due to arrhythmias, severe systemic arterial hypertension, or decompensated increase in heart rate observed during maximum stress in the cardiopulmonary test. Hence, we were unable to proceed with a cardiopulmonary test protocol. Therefore, these patients were excluded from muscle strength and function tests because they may pose a risk to personal safety and health.

A large gap exists in the literature regarding the assessment of MCRFs in TAK, specifically in the assessment of VO$_2$ peak. However, our study obtained

Table 3 Parameters of aerobic capacity, strength and functional capacity of patients with Takayasu arteritis and the control group

	TAK (*n*=20)	CTR (*n*=16)	*P* value
Aerobic capacity			
Estimated maximum heart rate (bpm)	180.5±7.2	180.2±6.1	0.907
Maximum heart rate in test (bpm)	149.3±15.7	172.9±18.2	0.002
Anaerobic threshold (min)	4.5±1.6	3.8±0.6	0.111
Respiratory compensation point (min)	7.7±1,9	7.9±1,7	0.730
Time-to-exhaustion (min)	10.7±2.6	10.5±2.3	0.847
VO$_2$ peak relative (mL/kg/min)	17.4±4.6	26.3±8.0	0.004
VO$_2$ peak absolute (L/min)	1.2±0.3	1.6±0.4	0.007
Muscle strength and function			
Bench press 1RM (kg)	25.3±4.3	28.0±5.4	0.311
Leg press 1RM 45° (kg)	122.7±35.9	174.2±37.3	0.018
Handgrip test			
Right (kg)	28.4±5.4	30.0±5.4	0.543
Left (kg)	26.1±5.7	28.5±5.2	0.378
Timed-Stands test (reps)	15.5±2.4	18.8±3.4	0.068
Timed Up and Go test (s)	6.7±0.6	6.3±0.5	0.199

Data are presented as mean ± standard deviation
CTR Control group, *RM* Repetition maximum, *TAK* Takayasu arteritis, *VO$_2$* Volume of oxygen uptake

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Table 4 Ability to perform activities of daily living, quality of life and level of physical activity of patients with Takayasu arteritis and the control group

	TAK (*n*=20)	CTR (*n*=16)	*P* value
HAQ (0.00–3.00)	0.56 (0.12–0.87)	0.00 (0.00–0.00)	< 0.001
SF-36 (0–100)			
Functional Capacity	62.5 (46.2–88.7)	100.0 (95.0–100.0)	< 0.001
Physical function	50.0 (0.0–100.0)	100.0 (100.0–100.0)	0.008
Pain	41.0 (34.2–63.5)	84.0 (69.2–100.0)	< 0.001
General health	61.0 (43.2–80.7)	92.0 (79.5–97.7)	< 0.001
Vitality	55.0 (35.0–72.5)	77.5 (55.0–85.0)	0.066
Social aspects	88.0 (66.0–100.0)	100.0 (84.7–100.0)	0.194
Emotional aspects	100.0 (33.0–100.0)	100.0 (67.0–100.0)	0.195
Mental health	60.0 (53.0–84.0)	82.0 (75.0–97.0)	0.034
WIQ (0–100)			
Walking distance	68.0 (37.3–100.0)	100.0 (100.0–100.0)	< 0.001
Walking speed	64.1 (38.6–79.9)	100.0 (97.3–100.0)	< 0.001
Ability to climb stairs	58.3 (42.7–85.4)	100.0 (96.7–100.0)	< 0.001
Overall score	64.4 (42.4–86.9)	100.0 (88.9–100.0)	< 0.001
IPAQ-SF (%)			
Low	14 (60.0)	3 (18.7)	0.013
Moderate	6 (30.0)	9 (56.2)	0.080
High	0	2 (12.5)	–
METs per week	453.0 (240.0–751.7)	1693 (1089.0–2206.0)	< 0.001

Data are presented as median (25–75%) or percentage (%)

CTR Control group, *HAQ* Health Assessment Questionnaire, *IPAQ-SF* International Physical Activity Questionnaire Short Version, *METs* Metabolic equivalent, *SF-36* Short Form Health Survey, *TAK* Takayasu arteritis, *WIQ* Walking Impairment Questionnaire

Table 5 Body composition of patients with Takayasu arteritis and the control group

	TAK (*n*=20)	CTR (*n*=16)	*P* value
Body mass (kg)	69.8±13.7	67.1±13.3	0.564
Height (cm)	158.3±6.1	159.7±6.7	0.508
Body mass index (kg/m2)	27.7±4.5	26.2±3.8	0.264
Fat body mass (kg)	29.4±9.4	26.0±11.5	0.347
Lean body mass (kg)	38.0±5.3	40.5±7.1	0.255
Bone mineral content (kg)	2.3±0.3	2.3±0.4	0.580
Visceral adipose tissue (cm^3)	804.0±432.5	506.4±307.8	0.022
Visceral adipose tissue (g)	760,1±408,7	477,8±290,3	0.021
Abdominal circumference (cm)	91.6±10.7	85.5±7.7	0.172
Waist circumference (cm)	83.5±9.7	77.4±5.8	0.100
Hip circumference (cm)	104.3±11.0	104.8±8.0	0.919
Waist-hip ratio	0.8±0.1	0.7±0.0	0.016

Data are presented as mean ± standard deviation

CTR Control group, *TAK* Takayasu arteritis

Table 6 Correlation between functional variables, lower limb strength and peak relative VO$_2$ of patients with Takayasu arteritis

	TAK (*n*=15)	
	rho/r	*P* value
Lower limb strength (leg press)		
HAQ	−0.291	0.293
WIQ - Overall score	0.069	0.806
SF36 - Functional capacity	0.171	0.543
SF36 - Physical aspect	−0.057	0.838
IPAQ-SF - METs	0.295	0.285
VO$_2$ peak relative (mL/kg/min)	0.024	0.933
VO2 peak relative (mL/kg/min)		
HAQ	0.158	0.517
WIQ - Overall score	−0.193	0.427
SF36 - Functional capacity	−0.122	0.619
SF36 - Physical aspect	−0.114	0.641
IPAQ-SF - METs	−0.051	0.835
Lower limb strength (leg press)	0.024	0.933

HAQ Health Assessment Questionnaire, *IPAQ-SF* International Physical Activity Questionnaire Short Version, *METs* Metabolic equivalent, *SF-36* Short Form Health Survey, *TAK* Takayasu arteritis, *VO$_2$* Volume of oxygen

results similar to cardiopulmonary treadmill test by Oliveira et al. [17] Lanzi et al. [16] evaluated (even though indirectly) the 6-min walk test, finding low values. However, they did not use a control group and employed one "gold standard" test, making comparisons difficult.

Furthermore, as seen in ANCA-associated vasculitis [43] and other rheumatic diseases [20, 21], our patients showed a significant reduction in maximum oxygen consumption; that is, a reduction in the capacity to absorb, transport, and use oxygen [44]. This reduction and poor test performance can be attributed to two main purported mechanisms:

a) Impairment of the cardiopulmonary system is expected for this population with major cardiovascular impairments, such as stenosis or occlusion of the branches of the aorta, valve problems, etc.

b) The presence of vascular claudication may impair physical performance, imposing the same daily living limitation as a peripheral arterial disease [45]. Difficulty in walking produces even more impaired aerobic capacity, creating a vicious circle of reduced VO_2 peak and inactivity, as seen in peripheral arterial disease [45].

Although the disease pathogenesis is distinct, the walking capacity of TAK patients is hindered, which occurs similarly to patients with peripheral arterial disease [45].

Moreover, patients with TAK also had a reduction in functional capacity, physical strength, pain, and general and mental health, demonstrating this disease leads to impairments in multiple aspects of quality of life.

Similarly, the patients had impairments in daily living, as pointed out in the HAQ questionnaire. These findings corroborate other studies that assessed quality of life using the SF-36 and HAQ questionnaires, where a worsening was found in all domains that demonstrated a worsening of quality of life in general when compared to healthy controls [46, 47].

Another important aspect is the association between remission and improved quality of life. In our study, only 15% of patients had disease activity demonstrating regardless of activity the disease seems to deteriorate patients' quality of life [47].

As found in our patients, muscle strength is reduced due to other chronic diseases [48, 49], resulting in a significant decrease in functional capacity and quality of life. Our data are similar to outocmes found in ANCA-associated vasculitis, demonstrating a possible association between reduced strength and worsened quality of life in vasculitis patients [50].

Importantly, muscle weakness is a strong and independent risk factor for all-cause morbidity and mortality in some populations [9, 10, 48, 49].

A critical factor in our results is the reduction in the total level of weekly caloric expenditure and physical activity. As seen in other rheumatic diseases, the reduction may be associated with a worsening of quality of life [51].

Similar to Margiotta et al.'s [52] study of paitents with systemic lupus erythematosus, our TAK patients presented low levels and intensities of physical activity that did not meet the recommendations of the World Health Organization (i.e., at least 150 min per week of moderate-intensity physical activity or 75 min of vigorous-intensity activity) [53].

Similar to outcomes in the healthy population, physical inactivity may worsen the health of patients with rheumatic diseases, which may lead to higher risk of CVD and comorbidities and increase the number and length of hospital stays [54].

Far from our findings, Akar et al. [49] demonstrated no differences in body composition in patients with rheumatoid arthritis, with the exception of bone mass density. Ours results found TAK patients showed a significant increase in waist-to-hip ratio and visceral adipose tissue compared to controls, signaling an impairment of body composition in this population.

However, patients with rheumatic diseases who present worse body composition, specifically adipose tissue, show an association with greater inflammation, disease activity, glucocorticoid use, and disease severity, but mainly increased cardiovascular risk, as seen in systemic lupus erythematosus [55].

Adipose tissue has long been related to morbidity and mortality. In addition to this traditional relationship, another important link is adipose tissue's pro-inflammatory nature, where adipokines are linked to immune response through their link with cytokines that lead to the inflammatory process in rheumatic diseases, such as interleukin-6 and tumor necrosis factor-alpha [56]. The result is the hypothetical maintenance of vicious circle of inflammation in rheumatic diseases, which can favor the process of atherosclerosis, cardiovascular risk, and mortality in this population [57].

In addition, BMI should not be the sole parameter to assess by which to assess boody composition in TAK. In our study, the BIM parameter was shown to be inaccurate, as it was in other populations, for evaluating adipose tissue and obesity [58].

Traditionally, patients with TAK have a higher risk of developing CVD and a greater presence of its risk factors. A series of studies corroborate our findings, as they observed the increase in systemic arterial hypertension and dyslipidemia in TAK [4, 6].

Markers such as LDL, total cholesterol, triglycerides were close to or within the normal range compared to

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healthy subjects, as shown in our study. These findings make it difficult to assess possible long-term risks, probably due to previous treatment of lipoproteins in patients with TAK.

The focus of this study is to assess the MCRFs, which corroborate the higher risk of morbidity and mortality [7–15, 59]. In our study, we found that most of the factors studied were deteriorating in TAK patients, such as reduced aerobic capacity, decreased muscle strength, reduced physical activity, low intensity of physical activity, and increased visceral adipose tissue.

As demonstrated by Crump et al. [14, 15], even though the analysis of these factors was conducted in studies including most men, the sum of these MCRFs seem to represent an aggravated risk, with a 2.5-fold increase in CVD.

Additionally, the MCRFs did not show significant correlations in our study, which may be, however, probably due to the sample size. In addition, drug treatment can also make it challenging to detect existing correlations between these factors. Therefore, our findings need to be analyzed with caution.

Many of the factors are modifiable with changes in habits, increased physical activity level, reduced sedentary lifestyle, and physical exercise, to ultimately improve the quality of life. However, a longitudinal study is eminently necessary to assess these changes.

Conclusions
Our patients in the TAK group have significant impairment of several MCRFs. These patients require strategies that will help change the MCFR, in order to reduce morbi-mortality and improve the quality of life.

Abbreviations
BMI: Body mass index; CRP: C-reactive protein; CTR: Control group; CVD: Cardiovascular disease; ECQ: Edinburgh Claudication Questionnaire; ESR: Erythrocyte sedimentation rate; HAQ: Health Assessment Questionnaire; HDL: High-density lipoprotein; IPAQ: International Physical Activity Questionnaire; ITAS: Indian Takayasu's Arteritis Activity Score; LDL: Low-density lipoprotein; MCRFs: Modifiable cardiovascular risk factors; NIH: National Institute of Health; RM: Maximum repetition test; SF: Short Form; TAK: Takayasu arteritis; TST: Timed-Stands test; TUG: Timed Up-and-Go; WIQ: Walking Impairment Questionnaire

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