Muscle dysfunction in axial spondylarthritis: the MyoSpA study

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Abstract

Objective

We aimed to investigate muscle physical properties, strength, mass, physical performance, and the prevalence of sarcopenia in patients with axial spondylarthritis (axSpA) compared to the healthy controls (HC).

Methods

We performed a cross-sectional study on 54 participants: 27 patients with axSpA and 27 HC, matched by age, gender, and level of physical activity. Muscle physical properties (stiffness, tone and elasticity), muscle strength (five-times sit-to-stand [5STS] test), muscle mass, physical performance (measured through gait speed) and sarcopenia were compared between the groups. Linear regression models were conducted allowing adjustment for relevant variables.

Results

Patients with axSpA (mean age 36.5 (SD 7.5) years, 67% males, mean disease duration 6.5 (3.2) years) had no significant difference in segmental muscle stiffness, tone or elasticity, compared with the HC, despite showing a slight numerically higher lower lumbar (L3-L4) stiffness [*median 246.5 (IQR 230.5–286.5) vs. 232.5 (211.0–293.5), p=0.38*]. *No participants presented sarcopenia. Patients with axSpA, compared to the HC, had lower total strength [B=1.88 (95% CI 0.43;3.33)], as well as lower strength in the upper (B= -17.02 (-27.33;-6.70)] and lower limbs [B= -11.14 (-18.25;-4.04)], independently of muscle physical properties. Patients had also significantly lower gait speed than the HC [B= -0.11 (-0.21;-0.01)], adjusted for muscle mass, strength and muscle physical properties.*

Conclusion

Young axSpA patients with a relatively short disease duration presented similar segmental muscle physical properties as the HC and had no sarcopenia. Patients with axSpA had reduced physical performance and lower strength compared to the HC, despite normal muscle mass, suggesting a possible muscle dysfunction. Gait characteristics may be a potential biomarker of interest in axSpA.

Key words

spondylarthritis, sarcopenia, body composition, muscle strength, physical performance

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Introduction

Axial spondylarthritis (axSpA) is an inflammatory rheumatic disease, characterised primarily by the involvement of the spine and sacroiliac joints and usually presenting as chronic back pain and stiffness (1). As the disease progresses, impaired spinal mobility and physical function may impact activities of daily living (2).

Despite extensive research in the last decade, the precise aetiopathogenesis of axSpA remains unknown, although it is thought to likely result from a complex interplay of genetic and environmental factors (3). The most important known genetic risk factor is the human leukocyte antigen B27 (HLA-B27), which explains approximately 20% of the disease heritability (4). Environmental factors, such as microbiota and biomechanical stress, may also be predisposing contributors to disease susceptibility (3). In particular, the link between biomechanical stress and axSpA has been suggested, as enthesitis is a hallmark of the disease, and entheses are sites of high mechanical stress due to repetitive forces of contracting muscles applied during movement (5). Passive axial myofascial stiffness has been proposed to contribute to chronic mechanical overload and increased stress and microinjury at enthesis sites in the spine (6). Accordingly, it has also been reported that strenuous physical activities may amplify the effects of inflammation on bone formation measured through radiographic progression in patients with radiographic axSpA (r-axSpA) (7). On the other hand, regular exercise, either as an individual home-based exercise or supervised physiotherapy, has been shown to have beneficial effects on pain and physical function of patients with axSpA (1, 8).

Sarcopenia is a generalised disorder of the skeletal muscle associated with an increased risk of falls and fractures, worse quality of life, and increased mortality (9-11). According to its revised definition by the European Working Group on Sarcopenia in Older People (EWGSOP2), sarcopenia is diagnosed when there is primarily low muscle strength associated with low muscle quantity. The additional presence of poor physical performance is used to identify severe sarcopenia (11). Although frequently attributable to ageing, sarcopenia can occur in younger ages due to various causes, including inflammatory processes (12). Proinflammatory cytokines, particularly tumour necrosis factor-α (TNF-α), can hypothetically induce anorexia, resting energy expenditure and muscle loss (13). However, data on sarcopenia in axSpA are still scarce.

Therefore, the aims of this study were to investigate muscle physical properties, and also muscle strength, muscle mass, and physical performance (allowing to determine the prevalence of sarcopenia) in patients with axSpA contrasting them to the healthy controls (HC). We hypothesised that patients with axSpA display general changes in muscle (axial and peripheral) physical properties, namely, increased stiffness and tone. Additionally, patients with axSpA may present reduced muscle strength and/or mass and deterioration of physical performance, having criteria for sarcopenia at young ages.

Methods

Study design and population

A cross-sectional study was conducted on 54 participants: 27 patients diagnosed with axSpA according to their rheumatologists and 27 HC, matched by gender, age and level of physical activity. The patients were recruited from a Rheumatology Outpatient Clinic at Hospital de Egas Moniz in Lisbon, Portugal and the HC from the local community (mostly co-workers).

All patients with axSpA were aged between 18 and 50 years, met the Assessment of SpondyloArthritis international Society (ASAS) classification criteria and had a symptom duration of ≤10 years. Exclusion criteria were as follows: Body Mass Index (BMI) ≥35kg/m^2 (above this value, myotonometry measures are not accurate (14); previous exposure to synthetic disease-modifying anti-rheumatic drugs (DMARDs) or biological disease-modifying anti-rheumatic drugs (bDMARDs); current pregnancy or breastfeeding; infections requiring hospitalisation or intravenous antibiotics within 30 days or oral anti-

biotics within 14 days prior to screening; malignancy (except for completely treated squamous or basal cell carcinoma); any uncontrolled non-treated medical condition (*e.g.* diabetes mellitus, ischaemic heart disease); intra or peri-articular extra-axial injections within 28 days prior to screening; spine ankylosis, with syndesmophytes in all levels from the lumbar spine, on lateral spine radiograph.

This study was approved by the Ethics Committees of Centro Hospitalar Lisboa Ocidental (National Registry for Clinical Studies (RNEC), no. 20170700050), and conducted according to the Declaration of Helsinki, and written informed consent was obtained from all participants before study inclusion.

Data collection and measurements

The following information was collected from all participants: age, gender, height, weight, BMI, and level of physical activity, assessed with the International Physical Activity Questionnaire (IPAQ) (15). For patients, disease duration (defined as the time elapsed between the onset of first symptoms and study enrolment) was also registered. Disease activity and function were assessed by the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and Bath Ankylosing Spondylitis Functional Index (BASFI), respectively.

In order to obtain a detailed muscle characterisation, a set of measurements was performed on all participants by a single investigator, according to a standardised protocol.

Muscle physical properties (stiffness, tone, elasticity) were quantified using a non-invasive, hand-held myotonometer, the MyotonPRO®. The measurement with MyotonPro® consists of applying a constant pre-load by a probe to the skin surface above the muscle being measured. A mechanical impulse is then transmitted to the underlying muscle and the subsequent dampened oscillation of the muscle is recorded in the form of an acceleration signal, followed by computation of parameters of interest. This device has been previously used in other studies, to measure properties of peripheral muscles in patients with Parkinson's disease (16) or subacute stroke (17), as well as axial muscles in patients with r-axSpA (17). In our study, measurements were made in the prone position after a 10-minute resting period, in three different body segments: trunk (low lumbar myofascial/multifidus at the L3-4 level), upper (Extensor Digitorium, 5 cm below the lateral epicondyle) and lower limbs (Gastrocnemius, 10 cm below the lateral side of the knee), considering the muscle bulk. For each segment, measurement of left and right sides was performed, and the mean value calculated. Values were recorded according to the dominant and non-dominant sides of the participant reflecting the handedness. Total stiffness, tone and decrement were calculated using the sum of the values of each body segment. Decrement is the direct measure given by the myotonometer to characterise elasticity and should be interpreted as to its inverse (the lower the decrement, the higher the elasticity).

Isometric muscle strength of three different body segments (trunk, upper and lower limbs, on both sides) was quantified by a resisted hand-held dynamometer, the Lafayette Manual Muscle Tester. With the participant in a sitting position, maximal resisted lumbar spine extension (dynamometer placed in the midline over the dorsal area), leg extension (dynamometer placed proximal to the ankle joint) and forearm flexion (dynamometer placed in the middle of the anterior forearm) were performed. Thus, strength of torso extension, knee extensors and forearm flexors was registered. The mean strength of right and left, upper and lower limbs, was calculated and used in the analysis. Five-times sit-to-stand (5STS) test was used as a measure of total strength, as suggested by EWGSOP2 (12). This test measures the time a patient takes to stand five times from a sitting position, as quickly as possible, without using his/her arms (12). The longer the duration, the lower the total strength.

Body composition was measured by an octopolar multifrequency bioelectrical impedance analysis device (InBody770®). Total and segmental lean mass, fat mass, and body water were recorded.

Physical performance was measured through gait speed (12), using a 3D full-body kinematic model (Kinetikos®) fed by 15 inertial sensors placed in the head, arms, trunk, pelvis, thighs, shanks, and feet. Low physical performance was defined as gait speed ≤0.8 m/s, for both genders (12).

Sarcopenia was defined as per the EWGSOP2 definition as low muscle strength (evaluated by 5STS >15 seconds) for both genders and low skeletal muscle mass (according to the equipment's inbuilt and personalised reference values) (12).

Statistical analysis

Categorical variables are shown as frequencies and percentages. Continuous variables are presented as means and standard deviations (SD), or medians and interquartile ranges for variables with skewed distributions. Normal distribution was assessed by graphical inspection and additionally using the Kolmogorov-Smirnov test. Chi-square test or Fisher's exact test (for categorical variables), and independent t-test or Mann-Whitney U-test (for continuous variables) were used to compare differences between patients and controls, as appropriate. A completers analysis was performed without missing data imputation.

Linear regression was used to investigate differences in muscle parameters, namely muscle strength and physical performance, between the patients with axSpA and the HC. To correct for possible confounding effects, two multivariable linear regression models were developed: model 1 was adjusted for muscle mass for all outcomes, and for physical performance additionally adjusted for total strength. Model 2 was adjusted for the same covariates plus the muscle physical properties, namely stiffness, tone, and decrement. Standard assumptions for linear regression were met.

Statistical significance was defined as a p-value of less than 0.05. Statistical Package for Social Science (SPSS) version 23 was used.

Results

The participants had a mean age of 36.5 (SD 7.5) years and were predominantly males (67%). The patients with axSpA

had mean disease duration of 6.5 (3.2) years, with BASDAI and BASFI of 2.7 (2.3) and 0.9 (3.1), respectively. Subject characteristics are shown in Table I.

Regarding muscle physical properties, there was no significant difference in muscle stiffness, tone or decrement in any of the three regions between the patients with axSpA and the HC (Table II and Supplementary Tables S1-2). However, patients with axSpA showed a numerically higher trunk muscle stiffness than the HC [246.5 (230.5–286.5) *vs*. 232.5 (211.0–293.5), *p*=0.38]. This numerical difference was more pronounced in the dominant side [261.0 (232.0–312.0) *vs*. 241.0 (204.3–303.0), *p*=0.28].

Table III shows the comparison of strength, body composition, physical performance and the proportion of sarcopenia between both groups. No participants fulfilled the definition of sarcopenia, since none of the patients or controls had simultaneously low muscle strength and low muscle mass. Low muscle strength was found in 8.3% (n=2) of patients *vs*. 0% of the HC (*p*=0.15). Skeletal muscle mass was reduced in other 8.3% (n=2) of patients *vs*. 4.2% (n=1) of the HC (*p*=0.55).

Nonetheless, although patients with axSpA had significantly lower median total muscle strength, evaluated by 5STS, than the HC [7.0 (5.9–8.9) *vs*. 5.5 (5.0–6.9), *p*=0.01], these values were still in the normal range in both groups (cut-off of 15 seconds). Regarding the strength of different body segments, evaluated by dynamometry, patients with axSpA, compared to the HC, also had lower median values in the upper limbs [47.6 (40.2–73.2) *vs*. 71.8 (51.9–80.5), *p*=0.02] and lower limbs [51.0 (38.5–57.1) *vs*. 59.8 (54.6–64.5), *p*=0.01], but not in trunk.

There were no differences in total or segmental lean mass and body water, between both groups. Total fat mass was higher in the patients than in the HC [19.8 (12.1–29.1) *vs*. 15.7 (10.1–22.2), *p*=0.04], but no differences were registered in segmental body evaluation.

As a surrogate marker of physical performance, low gait speed was found in 55% of the patients *versus* 22% of the HC (*p*=0.02). In addition, median gait speed values were lower in patients compared to the HC [0.8 (0.7–0.9) *vs*. 0.9 (0.8–1.0), *p*=0.02].

In model 1 of multivariable analysis (table 4), *i.e*. without muscle physical properties, patients with axSpA, compared to the HC, had lower total strength, reflected by a higher 5STS (B=2.00, 95% CI 0.59–3.42), as well as lower strength in the upper [B= -14.85, 95% CI -25.05–(-4.66)] and lower limbs [B=-11.83, 95% CI -18.67–(-4.98)], independently of muscle mass. Likewise, patients had significantly lower gait speed than the HC [B= -0.1, 95% CI -0.212–(-0.006)], adjusted for muscle mass and strength. When muscle physical properties (stiffness, tonus and decrement) were added to the model (model 2), the same results were found.

Table I. Demographic and clinical characteristics of patients with axSpA and healthy controls.

	Patients (n=27)	Controls (n=27)	*p*-value
Age (years)*	37 (7)	36 (8)	0.79
Gender (male), n (%)§	18 (67)	18 (67)	0.99
Body height (cm)	170 (164 – 177)	173 (165 – 178)	0.52
Body weight (kg)	73 (67 – 86)	70 (65 – 80)	0.35
BMI (kg/m^2)	25 (23 – 30)	24 (23 – 26)	0.30
IPAQ (%)§			
Low	29	21	
Moderate	38	42	0.80
High	33	38	
BASDAI*	3 (2)	-	-
BASFI*	1 (3)	-	-
Disease duration* (years)	7 (3)	-	-
HLA-B27 positivity, n (%)§	22 (81.5)	-	-

Values are presented as median (25th –75th percentiles), assessed by Mann-Whitney U-test, except otherwise indicated.
*Mean (SD), assessed by independent t-test, § Chi-square test or Fisher's exact test.
BMI: Body Mass Index. IPAQ: International Physical Activity Questionnaire. BASDAI: Bath Ankylosing Spondylitis Activity Index. BASFI: Bath Ankylosing Spondylitis Functional Index.

Table II. Muscle stiffness (expressed in Nm) in patients with axSpA and control subjects, stratified for body segment.

	Patients (n=27)	Controls (n=27)	*p*-value
Trunk			
Average	246.5 (230.5–286.5)	232.5 (211.0–293.5)	0.38
Dominant side	261.0 (232.0–312.0)	241.0 (204.3–303.0)	0.28
Non-dominant side	242.0 (219.0–291.0)	232.0 (209.3–288.0)	0.32
Upper limb			
Average	288.0 (266.0–320.0)	292.0 (265.0–307.5)	0.60
Dominant side	282.0 (266.0–334.0)	292.0 (254.8–311.8)	0.80
Non-dominant side	283.0 (267.0–313.0)	290.0 (266.0–313.0)	0.96
Lower Limb			
Average	293.5 (277.0–329.5)	289.0 (265.0–325.0)	0.75
Dominant side	299.0 (257.0–349.0)	298.0 (271.0–325.0)	0.91
Non-dominant side	295.0 (269.0–321.0)	290.0 (263.5–314.3)	0.81
Total	859.5 (774.0-904.5)	847.0 (778.0-884.0)	0.32

Values are presented as median (25th-75th percentile). Mann-Whitney U-test was used in the analysis. "Average" refers to the mean of right and left sides of each segment, while "dominant" and "non-dominant" sides refer to the handedness of individuals.

Discussion

In our study, relatively young patients with axSpA, with mean disease duration of 6.5 years, presented similar segmental muscle stiffness, tone and elasticity as healthy subjects. There was, however, an asymmetry in muscle stiffness between lumbar and appendicular muscles. Although the underlying mechanism for the numerically higher trunk stiffness in axSpA patients (even though the difference does not reach statistical

Table III. Comparison of sarcopenia, muscle strength, body composition and physical performance between patients with axSpA and healthy controls.

	Patients (n=27)	Controls (n=27)	*p*-value
Sarcopenia, n (%) [§]	0	0	-
Low muscle strength (5-times sit-to-stand >15s), n (%)	2 (8.3%)	0	0.15
Low skeletal muscle mass, n (%)	2 (8.3%)	1 (4.2%)	0.55
Strength			
Trunk (Nm)	56.3 (37.6–67.2)	57.3 (51.2–63.0)	0.67
Upper limb (Nm)	47.6 (40.2–73.2)	71.8 (51.9–80.5)	**0.02**
Lower limb (Nm)	51.0 (38.5–57.1)	59.8 (54.6–64.5)	**0.01**
Total - 5STS (seconds)	7.0 (5.9–8.9)	5.5 (5.0–6.9)	**0.01**
Lean mass (kg)			
Trunk	24.9 (21.9–27.0)	25.3 (20.4–27.6)	0.92
Upper limb	3.1 (2.56–3.5)	3.1 (2.3–3.5)	0.81
Lower limb	8.0 (7.2–9.5)	9.2 (7.5–10.0)	0.15
Total	50.1 (44.5–57.8)	54.1 (43.2–60.2)	0.59
Fat mass (kg)			
Trunk	10.3 (6.3–15.9)	8.1 (5.1–11.1)	0.05
Upper limb	1.3 (0.6–2.2)	0.9 (0.5–1.5)	0.05
LowerlLimb	2.9 (1.9–4.0)	2.5 (1.6–3.4)	0.21
Total	19.8 (12.1–29.1)	15.7 (10.1–22.2)	**0.04**
Body water (L)			
Trunk	19.6 (17.1–21.3)	18.8 (14.4–21.1)	0.84
Upper limb	2.4 (2.0–2.7)	2.3 (1.6–2.7)	0.38
Lower limb	6.5 (5.8–7.4)	6.5 (5.1–7.5)	0.82
Total	39 (34.6–44.9)	42.1 (33.5–46.8)	0.58
Physical performance [§§]			
Gait speed (m/s)	0.8 (0.7–0.9)	0.9 (0.8–1.0)	**0.02**
Low gait speed, n (%)	12 (54.5%)	5 (21.7%)	**0.02**

Values are median (25th –75th percentiles). Mann-Whitney U-test was used for continuous variables and Fisher's exact test or the chi-square test were used for categorical variables.
[§]Available for 48 subjects (24 patients and 24 HC).
[§§]Available for 45 subjects (22 patients and 23 HC).

significance) is unknown, we hypothesise that it may result from the local effect of inflammation. These data are in line with a previous study conducted by Andonian *et al.,* in which 24 patients with r-axSpA presented higher lumbar myofascial stiffness than 24 age- and sex-matched control subjects (this difference being statistically significant), measured by the same myotonometry device as ours (18). Importantly, these results may also support the hypothesis that abnormalities in biomechanical pathways might be implied in the course of axSpA, as these patients had established disease with a mean disease duration 12.7 years. However, it is difficult to speculate whether these changes are the cause or consequence of the disease. Furthermore, we did not show a higher prevalence of sarcopenia in these relatively young patients according to the revised EWGSOP2 definition. The low scores for BASDAI and BASFI in our patients, which reflect low disease activity and functional impairment, might explain the absence of sarcopenia. Nonetheless, we examined the three determinants of sarcopenia in detail: muscle strength, muscle mass, and physical performance.

In our study, all patients except 8% (2 out of 27), had values of general muscle strength and muscle mass in the range of the normality, but presented low levels of physical performance, which suggests a possible muscle dysfunction. Although we cannot fully explain this observation, we can hypothesise that a possible genetic determinism may be evoked and should be further investigated in future research.

Despite the normal values for total strength in patients, a deeper analysis showed a significant reduction of general and appendicular (but not in the trunk) muscle strength in the patients with axSpA patients compared to the HC. These results also raise questions about the existing reference values for strength and their applicability to our population, for whom they have not been validated. However, previous studies have also reported lower appendicular strength in patients with r-axSpA (19-21), even in the absence of peripheral joint involvement (19, 20). Various potential factors may justify a decrease in muscle strength, including systemic inflammation or fatigue (19). Inactivity or disuse is also associated with loss of strength, but in our study, the patients were matched with the HC also according to the levels of physical exercise to control for this influential effect.

Reduced appendicular strength has been associated with loss of appendicular lean mass in patients with longstanding r-axSpA (21). A major known determinant of strength loss is indeed the loss of muscle mass (22). However, in our study, the reduced appendicular strength was independent of muscle mass. Since our patients had a mean disease duration of 6.5 years, we can consider that muscle mass loss may still occur in a later phase of the disease. Despite being a different age group, in older people, the strength decline has been proved to be faster than the concomitant loss of muscle mass (22). An intriguing result was the absence of decreased muscle strength in the axial muscles. The distinct physiological role of axial and peripheral muscles, the former being responsible for maintaining posture and the latter for generating strength, may represent a possible explanation to be explored.

Several studies on body composition in axSpA have found inconsistent results that may be explained by differences in the disease duration and levels of physical activity, and also, by discrepancies in the methods used to estimate muscle mass. In agreement with our data, two previous studies did not observe differences in total lean mass or even skeletal muscle mass index, as measured by dual-energy x-ray absorptiometry or bioelectrical impedance, between patients with axSpA (disease duration 6–10 years) and controls (23, 24).

Table IV. Differences in muscle strength and physical performance between patients with axSpA and HC.

Predictors	Univariable analysis	Multivariable analysis	
	Regression coefficient (95% CI)	Model 1 (without muscle physical properties) Regression coefficient (95% CI)	Model 2 (adjusted for muscle physical properties) Regression coefficient (95% CI)
Outcome: Upper limb strength			
AxSpA *vs*. controls	**-14.8 (-25.8; -3.8)**	**-14.9 (-25.1; -4.7)**	**-17.0 (-27.3; -6.7)**
Muscle mass of UL	**14.7 (6.4; 23.0)**	**14.0 (6.3; 21.7)**	**13.1 (5.4; 20.9)**
Stiffness of UL	0.1 (-0.1; 0.2)	-	0.1 (-0.1; 0.3)
Tonus of UL	1.9 (-3.1; 6.9)	-	0.1 (-6.0; 6.2)
Decrement of UL	-3.8 (-11.9; 4.3)	-	-6.0 (-12.9; 0.8)
Outcome: Lower limb strength			
AxSpA *vs*. controls	**-11.2 (-17.9; -4.5)**	**-11.8 (-18.7; -5.0)**	**-11.1 (-18.3; -4.0)**
Muscle mass of LL	0.9 (-1.5; 3.2)	0.0 (-2.1; 2.2)	0.2 (-2.0; 2.5)
Stiffness of LL	-0.0 (-0.1; 0.0)	-	-0.1 (-0.2; 0.1)
Tonus of LL	-0.6 (-2.4; 1.1)	-	0.3 (-4.1; 4.8)
Decrement of LL	3.3 (-8.0; 14.6)	-	2.4 (-8.6; 13.4)
Outcome: Trunk strength			
AxSpA *vs*. controls	-4.3 (-12.0; 3.5)	-4.2 (-12.2; 3.8)	-6.1 (-14.2; 2.1)
Muscle mass of T	0.9 (-0.2; 1.9)	0.8 (-0.2; 1.8)	0.8 (-0.2; 1.8)
Stiffness of T	-0.0 (-0.1; 0.1)	-	-0.1 (-0.3; 0.0)
Tonus of T	-0.0 (-2.3; 2.2)	-	4.3 (-1.1; 9.6)
Decrement of T	5.0 (-8.3; 18.3)	-	17.3 (-0.5; 35.1)
Outcome: Total strength (5STS)			
AxSpA *vs*. controls	**1.8 (0.5; 3.1)**	**2.0 (0.6; 3.4)**	**1.9 (0.4; 3.3)**
Muscle mass (total)	0.0 (-0.1; 0.0)	0.0 (-0.1; 0.1)	0.0 (-0.1; 0.1)
Total stiffness	0.0 (-0.0; 0.0)	-	0.0 (-0.0; 0.0)
Total tonus	0.1 (-0.2; 0.3)	-	-0.2 (-0.7; 0.3)
Total decrement	0.3 (-0.4; 1.0)	-	0.3 (-0.5; 1.1)
Outcome: Physical performance			
AxSpA *vs*. controls	-0.1 (-0.2; 0.0)	**-0.1 (-0.2; -0.1)**	**-0.1 (-0.2; -0.0)**
Muscle mass (total)	-0.0 (-0.0; 0.0)	-0.0 (-0.0; 0.0)	-0.0 (-0.0; 0.0)
Total strength	-0.0 (-0.0; 0.0)	0.0 (-0.0; 0.0)	0.0 (-0.0; 0.0)
Total stiffness	0.0 (-0.0; 0.00)	-	0.0 (-0.0; 0.0)
Total tonus	-0.0 (-0.0; 0.0)	-	0.0 (-0.0; 0.0)
Total decrement	0.0 (-0.0; 0.1)	-	0.0 (-0.0; 0.0)

Model 1 (without muscle physical properties): adjusted for muscle mass and, in case of physical performance, also total strength.
Model 2 (with muscle physical properties): adjusted for the same covariates as model 1 plus stiffness, tonus, and decrement.
Independent variables (particularly, muscle mass, stiffness, tonus, decrement, and strength) refer to the 54 participants.
In the "axSpA *vs*. controls" variable, HC are the reference group.
p-values<0.05 are shown in bold.
UL: upper limbs. LL: lower limbs. T: trunk.

On the other hand, muscle atrophy and/or increased intramuscular fat, evaluated by CT or MRI, have been described in patients with longstanding disease or advanced radiographic changes (24, 25).

In our study, total fat mass was significantly higher in patients than in control subjects, suggesting that even if mass loss is not detected, signs of muscle degeneration may already be present. Notably, we underscore the importance of assessing not only muscle quantity, but also muscle quality, a new term that underlines the micro- and macroscopic changes in muscle architecture and composition (12). Imaging techniques and anatomopathological evaluation would be of interest to clarify the physiopathological mechanisms involved.

Regarding physical performance, gait in patients with longstanding r-axSpA has long been referred to as "walking gingerly", as they walk slower and have a shorter stride length than healthy individuals, which can be attributed to the increased rigidity of the spine (13). In our cohort, we showed that young patients with axSpA also have significantly lower gait speed than the HC, independently of muscle mass, strength or muscle physical properties. In this context, gait characterisation (including speed and other parameters) could be considered a marker with potential interest in axSpA, eventually for diagnosis and, in particular, for disease monitoring.

Limitations of our study include the small sample size and the cross-sectional design that precludes causal inferences. Also due to its small sample size should this study be seen as a pilot study, pioneer in gaining insight into muscle properties in patients with axSpA and for the first time including a segmental characterisation of different body regions, and which should be followed by larger studies to hopefully confirm and further clarify the findings. We cannot exclude the possibility of residual confounding, since other variables, such as dietary intake, were not determined and could theoretically influence the outcomes. Measurements were performed by one assessor only and future studies should consider at least 2 assessors and some reliability analyses. Furthermore, sarcopenia criteria according to the EWGSOP2 are not destined for young people. Additionally, the Myoton device is capable of measuring the biomechanical properties of muscles covered by subcutaneous fat up to a depth of 20 mm, and therefore measurements from the deeper muscles may not be as accurate [Myoton website: https://www.myoton.com/technology/]. For this reason, in our study, we have excluded patients with BMI ≥35kg/m^2. Plus, even though a 10-minute resting period was required before all muscle measurements, no surface electromyography (sEMG) was carried out to confirm the resting state of the muscle being measured.

Our study also has several strengths, such as the extensive muscle characterisation that includes, for the first time, different body segments (trunk, UL and LL) for each participant. Despite being a small study, it already allowed us to identify important differences between patients with axSpA and HC, which warrants more in-depth research in future studies.

Overall, our study suggests that muscle physical properties were not different between axSpA patients and HC, not only at axial but also at appendicular levels. These results cannot be extrapolated for patients with longstanding disease (*e.g.* superior to 10 years of disease duration). Notwithstanding, a deterioration in physical performance and muscle strength, despite normal values of muscle mass and physical properties, seems to indicate a possible muscle dysfunction. Further robust studies are needed to determine its potential causes, and a genetic aetiology should also be pursued. These findings are of utmost importance, since physical performance is a strong predictor of adverse outcomes, including mortality (27). We also provide evidence for a potential new biomarker related to gait analysis with plausible interest for disease diagnosis and monitoring.

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