

# Foot pain and disability in patients with ankylosing spondylitis is associated to disease activity

*Dor e deficiência no pé em pacientes com espondilite anquilosante estão associadas à atividade da doença*

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<https://doi.org/10.5935/2595-0118.20240028-en>

## ABSTRACT

**BACKGROUND AND OBJECTIVES:** The feet may be involved in patients with ankylosing spondylitis (AS), causing pain and walking difficulties. This research aimed to study the involvement of the foot in a sample of Brazilian patients with AS.

**METHODS:** The Brazilian version of the Foot Function Index (FFI-BR) was applied to 103 individuals (57 AS patients and 46 controls). Clinical profiles were obtained in AS patients as well as the measurement of disease activity by the ASDAS (Ankylosing Spondylitis Disease Activity Score)-ESR (erythrocyte sedimentation rate), ASDAS-CRP (C reactive protein) and BASDAI (Bath Ankylosing Spondylitis Disease Activity Index) and function by BASFI (Bath Ankylosing spondylitis functional score).

**RESULTS:** Only 19.2% of AS patients did not have any foot complaints and the FFI-BR score presented worse results than the control group ( $p = 0.02$ ). The “pain” domain of FFI-BR scored highest in AS patients, followed by “disability”. There was no association between the results of the FFI-BR and the clinical profile of patients with AS, but there was an association between the score and the disease activity indexes ( $r = 0.50$ ,  $p = 0.003$

with ASDAS-ESR;  $r = 0.44$ ,  $p = 0.005$  with ASDAS-CRP; and  $r = 0.60$ ,  $p < 0.0001$  with BASDAI). The BASFI also showed a positive correlation ( $r = 0.72$ ;  $p < 0.0001$ ).

**CONCLUSION:** Pain and disability are common in AS patients and these symptoms are associated with disease activity.

**Keywords:** Foot, Pain, Spondylitis ankylosing.

## RESUMO

**JUSTIFICATIVA E OBJETIVOS:** Os pés podem ser acometidos em pacientes com Espondilite Anquilosante (EA), causando dor e dificuldade de locomoção. O objetivo deste trabalho foi estudar o envolvimento do pé em uma amostra de pacientes brasileiros com EA.

**MÉTODOS:** A versão brasileira do *Foot Function Index* (FFI-BR) foi aplicada a 103 indivíduos (57 pacientes com EA e 46 controles). O perfil clínico foi obtido para pacientes com EA, bem como a medição da atividade da doença por meio do ASDAS (Ankylosing Spondylitis Disease Activity Score)-ESR (velocidade de hemossedimentação), ASDAS-CRP (proteína C reativa) e BASDAI (Bath Ankylosing Spondylitis Disease Activity Index) e função pelo BASFI (Bath Ankylosing Spondylitis Functional Score).

**RESULTADOS:** Apenas 19,2% dos pacientes com EA não apresentaram queixas nos pés e o escore FFI-BR apresentou resultados piores do que os do grupo controle ( $p = 0,02$ ). O domínio “dor” do FFI-BR apresentou a maior pontuação nos pacientes com EA seguido pelo domínio “disfunção”. Não se observou associação dos resultados do FFI-BR com o perfil clínico dos pacientes com EA, mas houve associação do escore com os índices de atividade da doença ( $r = 0,50$ ,  $p = 0,003$  com ASDAS-ESR;  $r = 0,44$ ,  $p = 0,005$  com ASDAS-CRP; e  $r = 0,60$ ,  $p < 0,0001$  com BASDAI). O BASFI também apresentou correlação positiva ( $r = 0,72$ ;  $p < 0,0001$ ).

**CONCLUSÃO:** Dor e disfunção são comuns em pacientes com EA e estes sintomas se associam com atividade de doença.

**Descritores:** Dor, Espondilite anquilosante, Pé.

## INTRODUCTION

Good foot function is important to preserve autonomy and quality of life of patients. Ankylosing spondylitis (AS) is a chronic

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Submitted on October 24, 2023.

Accepted for publication on April 04, 2024.

Conflict of interests: none - Sponsoring sources: none.

## HIGHLIGHTS

- Foot pain is considered very important in spondyloarthritis (SpA)
- Patients with SpA were studied with the aim to comprehend foot function and its relationship with clinical aspects and disease activity
- This study showed that a high proportion of SpA patients have foot complaints
- The main complaint is pain and foot involvement correlate with general disease activity

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inflammatory rheumatic disease that may cause foot and ankle arthritis, foot tendonitis and enthesitis causing pain and deformities that increase the risk of falls and lead to patient's limitations in daily functioning<sup>1</sup>.

Pathophysiologic processes in AS are only partially known. While genetic and environmental factors are associated with the disease's appearance, synovial and enthesal inflammation followed by new bone formation are responsible for the observed damage<sup>1</sup>. Moreover, there is firm evidence for a role of mechanical stress that may favor lower limb involvement, including the feet<sup>2</sup>. A clinical survey in AS patients by authors<sup>3</sup> showed that the Achilles' tendon is the second most common site of enthesitis after the chondro-sternal junction and that the ankle is the second most common site for peripheral joint disease after the knee.

The foot has 31 joints, and it is divided into three main regions: forefoot (phalanges and metatarsals), mid foot (navicular, cuboid, and cuneiforms) and hind foot (talus and calcaneus). It is also rich in periarticular structures such as fascia and entheses, whose inflammatory involvement followed by new bone formation is one of the key pathophysiological aspects in spondyloarthritis<sup>4</sup>.

Together with the pelvis, the foot is the most weight bearing structure of the body and it is responsible for spreading loads through the spine, lower limbs, tarsal areas, and foot arches. This is important not only because the mechanic stress is known to induce inflammation in spondyloarthritis<sup>2</sup>, but also because gait and balance impairments, due to consequences of this lower limb involvement, were associated with imbalance and falls<sup>5-7</sup>. Studies in psoriatic arthritis patients have shown that the foot involvement shifts in the center of mass downward and forward with respect to the supporting base and may further increase patient's instability, already impaired because of spinal stiffness<sup>4</sup>.

Although involvement of the foot is important in spondyloarthritis, few studies address this issue in AS. Knowing the impact of the involvement of the foot in patients' daily lives and its association with disease variables is important for identifying these problems and formulating strategies to minimize them.

The present work studied a sample of Brazilian patients with AS aiming to know if pain and disability are associated with epidemiological and clinical aspects, as well as disease activity.

## METHODS

This study was approved by the local Committee of Ethics in Research under protocol 4.377.879. All participants signed the Free and Informed Consent Term (FICT).

A convenience sample of AS patients was recruited from a single Rheumatology outpatient clinic with individuals that came for regular consultations during a period of one year. They were included according to appointment order and willingness to participate in the study. Individuals with disease onset prior to 16 years of age (juvenile spondyloarthritis), any other associated rheumatic disease, neurologic or orthopedic problems were excluded. All included participants should have been diagnosed with AS, according to the 1984 modified New York criteria, and older than 18 years. Patient's companions were used as controls.

Data collection included:

a) Epidemiological data: age, gender, ethnic background, age at disease onset.

b) Clinical data: peripheral arthritis, uveitis, presence of HLA B27, comorbidities, disease activity measured by BASDAI (Bath Ankylosing Spondylitis Disease Activity Index), ASDAS (Ankylosing Spondylitis Disease Activity Score) ESR (erythrocyte sedimentation rate) and ASDAS CRP (C reactive protein).

c) BASDAI is a 6 items instrument that ranges from 0 (no disease activity) to 10 (worst scenario) that considers pain in the spine, peripheral pain, and pain in the entheses, fatigue and morning stiffness<sup>8</sup>.

d) ASDAS is a composite measurement of disease activity that uses either ESR or CRP and total back pain, patient's global score of disease activity, peripheral pain/swelling and duration of morning stiffness. Values under 1.3 are considered as disease inactivity; between 1.3 and under 2.1 as low disease activity, between 2.1 and lower than 3.5 as high disease activity and 3.5 or more as very high disease activity<sup>8</sup>.

e) Foot function questionnaire: The Brazilian version of the Foot Function Index or FFI-BR was used to evaluate foot functionality<sup>9</sup>. The FFI-BR questionnaire is divided into three domains: disability, difficulty, and pain. The answers are given on a numerical scale, from 0 to 10. The total score is obtained for each patient as the arithmetic mean of the three domains that is multiplied by 100 to obtain a percentage. The final score of zero means absence of foot problems and 100% is the worst scenario<sup>9</sup>.

f) BASFI (Bath Ankylosing spondylitis functional index): Measures the general function of the patient with AS through 10 self-applicable visual scales (0-10 cm) anchored by the descriptors "easy" and "impossible." All questions are related to the patient's ability to perform daily activities in the last week. The total score is calculated by the arithmetic mean of the individual scores. The final score of zero means absence of functional impairment and 10 the worst scenario<sup>8</sup>.

## Statistical analysis

Mann Whitney tests were used to analyze values of FFI-BR according to epidemiological and clinical variables. Correlation studies of numerical variables (age, disease duration, activities indexes and BASFI) with FFI-BR were done using the Spearman test. To judge data distribution, the Shapiro-Wilk test was used. The adopted significance was 5%. Tests were performed using GraphPad Prism version 8.0.0 for Windows, GraphPad Software, San Diego, California USA, www.graphpad.com.

## RESULTS

The sample included 57 AS patients and 46 controls. Table 1 shows the epidemiological and clinical characteristics and activity indexes of the AS sample. According to the median values of ASDAS (but not BASDAI), the sample had moderate to high disease activity.

Controls (n=46) were paired with AS patients for gender (p = 0.11) and age (p = 0.83). In the AS sample the FFI-BR went

from 0 to 75% (median of 16%; IQR = 2.0-37.5) and in the controls it went from 0- 48.6% (median of 7.2%; IQR =0-12.6) with p = 0.03.

In the AS sample only 11/57 (19.2%) have no feet complaints (scored zero at FFI-BR).

**Study of FFI-BR in relation to AS clinical variables**

The results of FFI-BR study according to AS clinical variables are on table 2; no relationships were found.

**Table 1.** Main characteristics of 57 patients with ankylosing spondylitis.

Male/female gender	33 (57.8%) /24 (42.1%)
Mean age - (years ± SD)	50.13 ±10.98
Mean age at diagnosis - (years ± SD)	37.97 ± 11.14
Mean disease duration - (years ± SD)	10.46 ± 7.46
Ethnic background	
European descendants	37 (64.9%)
Afro descendants	20 (35.0%)
Positive HLA B27(*) (n)	37 (75.5%)
Uveitis	26 (45.6%)
Enthesitis	28 (49.1%)
Dactylitis	8 (14.0%)
Peripheral arthritis	19 (33.3%)
Lower limb arthritis	16 (28.0%)
Comorbidities	
Arterial hypertension	16 (28.0%)
Dyslipidemia	13 (22.8%)
Diabetes	6 (10.5%)
Activity index (in points)	
Median ASDAS VHS (IQR)	2.2 (1.72-3.6)
Median ASDAS PCR (IQR)	2.1 (1.5-2.9)
Median BASDAI (IQR)	3.8 (2.0-5.35)
Median BASFI (IQR)	3.7 (1.42-6.25)

(\*) data on 49 patients. ASDAS = Ankylosing Spondylitis Disease Activity Score; ESR = erythrocyte sedimentation rate; CRP = C reactive protein; BASDAI = Bath Ankylosing Spondylitis Disease Activity Index; BASFI = Bath Ankylosing Spondylitis Functional Index; n = number; IQR = interquartile range.

**Table 2.** Study of FFI-BR (Foot Function Index Brazilian version) according to clinical and epidemiological variables in 57 patients with Ankylosing spondylitis.

	FFI median values with the variable	FFI median values without the variable	p-value
Male gender	9.0 (1.0-25.5)	21.0 (4.0-75)	0.22
Euro descendants	8.0 (2.0-37.0)	20.0 (2.7-38.7)	0.54
Positive HLA-B27	9.0 (2.0-37.5)	18.0 (4.3-37.7)	0.39
Uveitis	7.0 (0-24.2)	19.0 (4.0-41.0)	0.15
Enthesitis	20.0 (3-39.5)	8.5 (2.0-31.5)	0.49
Dactylitis	21.5 (6.7-37.0)	9.0 (2.0-37.5)	0.45
Peripheral arthritis	24.0 (9.0-38.0)	7.0 (2.0-37.2)	0.16
Lower limb arthritis	19.0 (6.0-38.0)	8.0 (2.0-36.5)	0.35

FFI values range from 0-100% with 0 meaning good performance. Values are expressed in %. Between brackets- interquartile range.

**Table 3.** Correlation studies of FFI-BR (Foot Function Index Brazilian version) with activities index, BASFI, age and disease duration.

	R	95% Confidence interval	p-value
Age	0.21	-0.06 to 0.46	0.12
Disease duration	-0.09	-0.36 to 0.18	0.49
ASDAS ESR	0.50	0.23 to 0.69	0.003
ASDAS CRP	0.44	0.15 to 0.66	0.0005
BASDAI	0.60	0.39 to 0.74	< 0.0001
BASFI	0.72	0.56 to 0.83	< 0.0001

ASDAS = Ankylosing Spondylitis Disease Activity Score, ESR = erythrocyte sedimentation rate, CRP = C reactive protein, BASDAI= Bath Ankylosing Spondylitis Disease Activity Index; BASFI = Bath Ankylosing Spondylitis Functional Index.

Correlation studies of FFI-BR with activity indexes, BASFI, age and disease duration are on table 3; there it is possible to observe a good correlation of feet function with disease activity and patients’ general function measured by BASFI.

When the FFI-BR domains were studied, it was possible to observe that pain (median value of 20; IQR = 0-43) scored highest, followed by difficulties (median value of 8; IQR = 0-42).

**DISCUSSION**

This study showed that a high proportion of AS patients have foot complaints. It also showed that these complaints correlated with disease activity indexes but not with the disease clinical profile. The foot is a structure that is in contact with the ground and is responsible for impact absorption, distribution of plantar pressure, balance (adjusting the posture in the upright position) and weight support. In AS, the involvement of the mid foot, also known as tarsitis, is common<sup>1,10</sup>.

Tarsitis presents pain and swelling and often swollen ankles, inflammation of the plantar fascia, and Achilles tendon enthesitis<sup>1</sup>, and may progress to ankylosis characterized by a partial or complete fusion of the tarsal bones and by the formation of bone bridges, like certain aspects of the long-term changes of the sacroiliac and the spine of AS patients<sup>11</sup>, bringing important restriction to movements.

Interestingly, tarsitis is more common in Latin American spondylarthritis patients<sup>11</sup> but it is unknown if foot function is worse in this population than in individuals from other geographical regions. The present study did not individualize the involved foot structure, and this is one limitation of the research.

Pain was the most common complaint in the current study. A study<sup>4</sup> in AS patients from Turkey also using the FFI questionnaire observed that disability scored more than pain in their sample; they also verified correlation of foot function impairment with inflammatory activity measured by the BASDAI, similarly to the present study. Cultural aspects valuing pain may have played a role in this difference<sup>12</sup>.

The present study showed the correlation of inflammatory activity with foot complaints, as opposed to age and disease duration. In order to treat inflammation efficiently and

to reduce foot problems in AS, it should be considered that the pathophysiologic mechanism of enthesal involvement has some particularities. The finding of IL-23-responsive population of T cells and the report of a group of cytokine-dependent lymphoid cells (ILCs) points to a participation of the innate immune cells in this context<sup>12,13</sup>. Conventional DMARDs such as sulphasalazine and methotrexate are not effective<sup>14</sup>; NSAIDs remain the first-line therapy. Other options considered effective are local injection of glucocorticoids, TNF blockade, anti-IL 17, and JAK inhibitors<sup>12,14-16</sup>. However, enthesitis management remains a challenge. In addition, this study is limited by its cross-sectional design, low number of included patients and lack of image studies that would allow an individualization of involved structures. Advantages were showing that foot involvement is common in AS and that it causes pain and difficulties in daily living. It also shows a good correlation of foot involvement with disease's activity by the three used instruments (ASDAS -ESR, ASDAS -CRP and BASDAI) showing that the inflammatory control is a key measure to be taken to lessen this problem.

## CONCLUSION

This sample of Brazilian patients shows that foot pain and dysfunction are common in AS. In this context, the main complaint was pain associated with general disease activity. None of the clinical or epidemiological variables were associated with worsened foot pain or dysfunction in the studied patients.

## AUTHORS' CONTRIBUTIONS

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Data Collection, Conceptualization, Research, Writing - Review and Editing

### Ynaray Brandão-dos-Santos

Data Collection, Conceptualization, Research, Writing - Review and Editing

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Statistical analysis, Conceptualization, Project Management, Research, Methodology, Writing - Review and Editing, Supervision

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