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Correlation of enthesitis indices with disease activity and function in axial and peripheral spondyloarthritis: a cross-sectional study comparing MASES, SPARCC and LEI

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Abstract

Background: The presence of enthesitis is associated with higher disease activity, more disability and incapacity to work and a poorer quality of life in spondyloarthritis (SpA). There is currently no consensus on which clinical score should be used to assess enthesitis in SpA. The objective of the present work was to compare the correlation of three enthesitis indices (MASES, SPARCC and LEI) with measures of disease activity and function in a heterogeneous population of patients with axial and peripheral SpA.

Methods: A cross-sectional study was conducted in three Brazilian public university hospitals; patients fulfilling ASAS classification criteria for peripheral or axial SpA were recruited and measures of disease activity and function were collected and correlated to three enthesitis indices: MASES, SPARCC and LEI using Spearman's Correlation index. ROC curves were used to determine if the the enthesitis indices were useful to discriminate patients with active disease from those with inactive disease.

Results: Two hundred four patients were included, 71.1% ($N = 145$) fulfilled ASAS criteria for axial SpA and 28.9% ($N = 59$) for peripheral SpA. In axial SpA, MASES performed better than LEI ($p = 0.018$) and equal to SPARCC ($p = 0.212$) regarding correlation with disease activity (BASDAI) and function (BASFI). In peripheral SpA, only MASES had a weak but statistical significant correlation with DAS28-ESR (r_s 0.310 $p = 0.05$) and MASES had better correlation with functional measures (HAQ) than SPARCC ($p = 0.034$).

Conclusion: In this sample composed of SpA patients with high coexistence of axial and peripheral features, MASES showed statistical significant correlation with measures of disease activity and function in both axial and peripheral SpA.

Keywords: Spondyloarthritis, Enthesitis, Disease activity, Function

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Background

A characteristic feature of the spondyloarthritis (SpA) is inflammation at tendon, fascia, capsule or ligament attachment sites, called enthesitis. Although enthesitis has traditionally been viewed as a focal abnormality, the inflammatory reaction intrinsic to enthesitis may be quite extensive [1]. In the clinical practice, the diagnosis of enthesitis is based on clinical examination, including interview (pain at the site of an enthesis that subsides following physical exercise) and observing pain in an enthesis upon compression [2]. Ultrasound and magnetic resonance image (RMI) are more direct ways to assess enthesitis although less feasible.

Recent publication comparing the clinical presentation of 2356 SpA patients from Europe (Spain and Belgium) and 1083 SpA patients from Latin America countries found a higher prevalence of peripheral arthritis and enthesitis in the Latin American patients [3].

The prevalence of enthesitis is high in Brazilian patients: among the 1505 patients included in the Brazilian Registry of Spondyloarthritis (Registro Brasileiro de Espondiloartrites - RBE), 54% had enthesitis; posterior iliac spine and Achilles tendon were the most common affected sites [4]. In this large cohort, enthesitis was found in 70.4% of the patients with undifferentiated SpA (USpA), 53.8% with psoriatic arthritis (PsA) and 53.5% with ankylosing spondylitis (AS) [4].

Patients with enthesitis present higher disease activity, disability and incapacity to work, frequently associated with a poorer quality of life [4–9]. In Brazilian patients, enthesitis was strongly associated with a more severe clinical picture, including axial as well as peripheral manifestations as well as higher Bath Ankylosing Disease Activity Index (BASDAI) [4, 7].

Although the Outcome Measures in Rheumatology (OMERACT) and the Assessment of Spondyloarthritis International Society (ASAS) recommend the assessment of enthesitis in SpA [10, 11] and besides the existence of several instruments proposed to entheseal evaluation there is no consensus on which tool should be used for subjects with axial and peripheral SpA [12–20].

There are 3 tools considered more feasible and usually employed in daily practice and clinical trials: the Maastricht Ankylosing Spondylitis Enthesitis Score (MASES), the Spondyloarthritis Research Consortium of Canada index (SPARCC), and the Leeds Enthesitis Index (LEI) [14–16]. Although there are several studies showing the correlation among one of these 3 indices with clinical variables, no single study compared the correlation among the three instruments and clinical variables in the same population [5, 8, 9, 21].

The present study aimed to compare the correlation of these three enthesitis indices (MASES, SPARCC and LEI) with measures of disease activity and function in a heterogeneous population of Brazilian patients with axial and peripheral SpA, as well as to establish if these enthesitis indices have good power at detecting active disease in this population.

Methods

An observational, cross-sectional study was conducted in three Brazilian public university hospitals: two of them located in the South of Brazil (Hospital de Clínicas de Porto Alegre, in Porto Alegre, Rio Grande do Sul and Hospital Universitário Evangélico, in Curitiba, Paraná) and one center located in the North of Brazil (Hospital Universitário Getúlio Vargas, in Manaus, Amazonas).

Inclusion criteria

Consecutive outpatients ≥ 18 years old attending Rheumatology Clinics in these three centers and fulfilling the ASAS classification criteria for axial or peripheral SpA were invited to participate [22, 23].

Exclusion criteria

Patients not willing and able to participate in a 1-h visit, illiterate patient that were not able to fulfill self-reported questionnaires. Patients with fibromyalgia (in whom tender points could be misdiagnosed as enthesitis) were not excluded from the study but additional analysis were conducted with exclusion of this subgroup.

Data collection

Data were collected from June to December 2015; the common data collection form included demographic data (gender, age and self-reported ethnicity), information about articular and extra-articular features, family history, measures of disease activity, functional status and quality of life, past and current treatment, laboratory tests and radiographic assessment.

Disease activity was assessed in subjects with axial SpA through the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), the inflammatory markers erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) and the Ankylosing Spondylitis Disease Activity Score (ASDAS) including CRP (ASDAS-CRP) and ESR (ASDAS-ESR) [24, 25]. In subjects with peripheral SpA and PsA, disease activity was assessed by the 28-Joints Disease Activity Score using ESR (DAS28-ESR) and by the inflammatory markers CRP and ESR [26]. Functional status was assessed through the Bath Ankylosing Spondylitis Functional Index (BASFI) in patients with axial SpA and the Health Assessment Questionnaire (HAQ) in patients with peripheral SpA and PsA [27, 28].

The enthesitis were assessed on each patient through three different tools recorded in the same visit: the Maastricht Ankylosing Spondylitis Enthesitis Score (MASES), the Spondyloarthritis Research Consortium of

Canada Index (SPARCC) and the Leeds Enthesitis Index (LEI) [14–16]. These three tools record tenderness on examination as either present (1) or absent (0) on each entheseal site after a firm palpation at a pressure of approximately 4 kg/cm^2 with the pulp of the thumb (the amount of pressure required to blanch a thumbnail).

It is relevant that MASES and SPARCC were developed in AS patients while LEI was a tool developed for PsA patients [14–16]. MASES analyses 13 sites: the bilateral first and seventh costochondral joints, the anterior and posterior superior iliac spines, the iliac crests, the fifth lumbar spinous process, and the proximal insertion of Achilles tendon (overall score range 0–13). SPARCC index evaluates 16 sites: the bilateral greater trochanter, quadriceps tendon insertion into the patella, patellar ligament insertion into the patella and tibial tuberosity, Achilles tendon insertion, plantar fascia insertion, medial and lateral epicondyles, and supraspinatus insertion (overall score range 0–16). LEI evaluates 6 sites: bilateral Achilles tendon insertions, medial femoral condyles, and lateral epicondyles of the humerus (overall score range 0–6).

Statistical analysis

In patients with axial SpA, the correlation between the three enthesitis indices (MASES, SPARCC and LEI) with measures of disease activity (BASDAI, ASDAS-CRP, ASDAS-ESR and inflammatory markers) and with function (BASFI) was calculated by the Spearman's Correlation index (r_s). The classification of Dancey was used to classify variables according to the intensity of correlation, with values from 0.10 to 0.39, 0.40 to 0.69, 0.70 to 0.99 representing, respectively, a weak, moderate and strong correlation [29]. ROC curves were used to determine if the three enthesitis indices were useful to discriminate patients with active disease using a cut off ≥4 for BASDAI and ≥ 1.3 for ASDAS-CRP. The usefulness of the enthesitis score to discriminate between active and inactive disease was interpreted according to the area under the curve as following: 0.50 to 0.75, 0.75 to 0.92, 0.92 to 0.97 and 0.97 to 1.00 representing, respectively, a fair, good, very good and excellent discrimination. The DeLong's test was used to compare ROC curves [30].

In subjects with peripheral SpA and in those patients fulfilling the CASPAR criteria for PsA [31], the correlation between the three enthesitis indices (MASES, SPARCC and LEI) and the disease activity measured by the DAS28-ESR and inflammatory markers was calculated using the Spearman's Correlation index. The correlation between the three enthesitis scores and function (HAQ) was also calculated.

In patients with peripheral SpA, the ROC curve analysis was conducted to investigate if the enthesitis indices could discriminate active disease using a DAS28-ESR ≥ 2.6 cut off.

Since the diagnosis of fibromyalgia could interfere in the assessment of entheseal sites (with tender points being misdiagnosed as enthesitis), all analysis conducted in the three groups (axial SpA, peripheral SpA and PsA) were repeated with the exclusion of patients who fulfilled the American College of Rheumatology 1990 criteria for the classification of fibromyalgia [32, 33].

Although the presence of peripheral involvement is quite common in Brazilian patients with axial SpA, it was considered as "axial SpA" all patients fulfilling ASAS classification criteria for axial SpA despite the peripheral involvement, and as "peripheral SpA" those fulfilling ASAS classification criteria for peripheral SpA (and not fulfilling criteria for "axial SpA"). Patients fulfilling both ASAS criteria for "axial SpA" and "peripheral SpA" were analyzed as "axial SpA".

The Win Pepi version 11.65 was used to calculate sample size; aiming to yield a 80% power to estimate the correlation of the enthesitis indices with disease activity scores and accepting a 5% margin of error, 109 subjects (55 with axial SpA and 54 with peripheral SpA) were deemed necessary [34]. The mean of the correlation coefficient (0,372) from previous work which studied correlation of MASES and SPARCC with BASDAI in AS was used to estimate the sample size of axial SpA since AS is the prototype of axial SpA [5, 8, 14, 15]. The mean of the correlation coefficients obtained by Healey et al. in their work which studied correlation of DAS 28 ESR with MASES and LEI (0.374) was used to estimate the number of subjects with peripheral SpA [16].

Ethics Committee approvals have been obtained by all participating centers prior to the start of the study and an informed consent form was obtained from all participants prior to enrollment.

Results

Characteristics of the population

The characteristics of patients included in the analysis are shown in Table 1.

Ankylosing Spondylitis was the most prevalent disease in this sample ($N = 124$, 60.8%), followed by psoriatic arthritis ($N = 58$, 28.4%), enteropathic arthritis (N = 9, 4.4%), undifferentiated SpA ($N = 7$, 3.4%), non-radiographic axial SpA ($N = 5$, 2.5%) and reactive arthritis ($N = 1$, 0.5%). The prevalence of subjects fulfilling ASAS criteria for axial SpA was 71.1% ($N = 145$) and for peripheral SpA was 28.9% ($N = 59$). Eighty-four patients (41.2% of the total sample) fulfilled criteria for both axial and peripheral criteria and these patients were analyzed in the group of "axial SpA".

About 54.4% of patients ($N = 111/204$) were treated with biological therapy. The 111 patients on biologic

Table 1 Characteristics of the 204 patients included in the analysis

	All Centers	Hospital de Clínicas de Porto Alegre, Porto Alegre (South Brazil)	Hospital Universitário Evangélico, Curitiba (South Brazil)	Hospital Universitário Getúlio Vargas, Manaus (North Brazil)	*P* value
Number of patients	204	54	84	66	
Male N (%)	131 (64.2)	28 (51.9)	55 (65.5)	48 (72.7)	0.057
Age in years (Mean ± SD, range)	48.6 ± 12.8 (18–87)	51.3 ± 12.2 (22–77)	47.8 ± 13.2 (18–87)	47.5 ± 12.7 (18–72)	0.213
Disease duration in years (Mean ± SD, range)	17.2 ± 10.6 (2–58)	17.4 ± 9.2 (4–44)	15.9 ± 10.9 (2–55)	18.5 ± 11.2 (2–58)	0.209
Self-reported ethnicity: white N (%)	126 (61.8)	41 (75.9)	67 (79.8)	18 (27.3)	< 0.001
Patients fulfilling ASAS classification criteria for Peripheral SpA N (%)	59 (28.9)	17 (31.5)	29 (34.5)	13 (19.7)	0.123
Patients fulfilling ASAS classification criteria for Axial SpA N (%)	145 (71.1)	37 (68.5)	55 (65.5)	53 (80.3)	0.123
Patients with at least one enthesitis N(%)	124 (60.8)	44 (81.5)	43 (51.2)	37 (56.1)	0.001
Composite activity index (mean ± SD)					
BASDAI*	3.5 (2.3)	4.7 (2.6)	3.1 (2.0)	3.0 (2.2)	0.002
ASDAS CRP*	2.3 (1.2)	2.8 (1.2)	2.4 (1.0)	1.8 (1.2)	0.001
ASDAS ESR*	2.6 (1.0)	2.8 (1.2)	2.6 (1.0)	2.5 (1.0)	0.610
DAS- 28 **	3.6 (1.4)	3.9 (1.4)	3.7 (1.5)	3.2 (1.2)	0.460
Enthesitis indices: Median (P25%, P75%), range / Mean ± SD					
MASES	1 (0, 5), 0–13/ 2.8 ± 3.9	3 (0, 7), 0–13/ 4.4 ± 4.3	0 (0, 3), 0–13/ 2.2 ± 3.5	0 (0, 3), 0–13/ 2.3 ± 3.6	< 0.001
SPARCC	0 (0, 3), 0–16/ 2.4 ± 3.9	2 (0, 6), 0–16/ 3.7 ± 4.6	0 (0, 3), 0–13/ 1.8 ± 3.0	0 (0, 2), 0–16/ 2.1 ± 4.0	0.005
LEI	0 (0, 2), 0–6/ 1.0 ± 1.6	0 (0, 2), 0–6/ 1.5 ± 2.0	0 (0, 1), 0–6/ 0.8 ± 1.5	0 (0, 1), 0–6/ 0.7 ± 1.4	0.016

SD: standard deviation; SpA: Spondyloarthritis; ASAS: Assessment of Spondyloarthritis International Society; MASES: Maastricht Ankylosing Spondylitis Enthesitis Score; SPARCC: Spondyloarthritis Research Consortium of Canada Index; LEI: Leeds Enthesitis Index * Reported only for the 145 patients fulfilling ASAS criteria for axial spondyloarthritis ** Reported only for the 59 patients fulfilling ASAS criteria for peripheral spondyloarthritis

therapy were receiving infliximab (21.6%, $N = 24$), adalimumab (36.9%, $N = 41$), etanercept (36.9%, N = 41), IL12/23 antagonists (1.8%, N = 2) and IL-17 antagonists (2.7%, $N = 3$). No patient was receiving golimumab or certolizumab. Furthermore, 54.4% (N = 111/204) were taking NSAIDs.

Among patients with axial SpA, that represented the majority of patients (N = 145), 57.2% ($N = 83$) had good disease control according to BASDAI score i.e., a BASDAI < 4. When the composite score ASDAS-CRP was considered to stablish the level of disease, 20% had inactive disease ($N = 29$), 21.3% had low disease activity ($N = 31$), 40.7% had high disease activity ($N = 59$) and 17.9% had very high disease activity ($N = 26$).

Enthesitis were common in all centers, 60.8% of Brazilian patients had at least one entheseal site with tenderness documented at physical exam, and the prevalence of enthesitis among the three centers ranged from 51.2 to 81.5%. The most prevalent site of tenderness on examination was the fifth lumbar spinous process, affected in 25% ($N = 51$) of the total sample, followed by the bilateral first and seventh costochondral joints, the right posterior superior iliac spine, and the left proximal insertion of Achilles tendon (each one affected in 24% / $N = 49$ of the total sample).

A comparison between patients < 60 years old and those ≥ 60 years old (who were expected to present lower disease activity) found no statistical difference in the distribution of MASES, SPARCC and LEI (p-value 0.222, 0.379 and 0.644 respectively). There was also no difference in the values of BASDAI, ASDAS CRP, ASDAS ESR and DAS28 between patients < 60 years old and those ≥ 60 years old (p-value 0.630, 0.851, 0.615, 0.820 respectively).

The involvement of bilateral enthesis was common: among the 109 patients with axial or peripheral SpA who reported tenderness in at least 2 enthesis in one of the three enthesitis scores (MASES, SPARCC or LEI), 88.0% (96/109) had bilateral enthesis involved; bilaterality was found in 86.1, 76.1 and 89.7% of patients reporting tenderness in at least two enthesis in MASES, SPARCC and LEI, respectively.

Correlation of enthesitis indices with disease activity and function in axial SpA

Among the 145 patients who fulfilled ASAS classification criteria for axial SpA the three enthesitis indices MASES, SPARCC and LEI were moderately correlated with disease activity measured by BASDAI (r_s 0.572 for MASES, r_s 0.508 for SPARCC and r_s 0.447 for LEI) (Table 2).

The comparison of the coefficients using the 95% confidence interval showed that MASES had a better correlation with BASDAI compared to LEI ($p = 0.018$). There was no statistical difference between MASES and SPARCC ($p = 0.212$) or between SPARCC and LEI ($p = 0.14$).

In the analysis of ROC curves, the three enthesitis scores could discriminate patients with suboptimal control of disease (BASDAI ≥4) from those with BASDAI< 4, but MASES and SPARCC performed better compared to LEI (Fig. 1). The DeLong's test for two correlated ROC curves showed statistically significant difference between MASES and LEI ($p = 0.02$) as well as between SPARCC and LEI (p = 0.02), but there was no statistically significant difference between MASES and SPARCC ($p = 0.60$). All the three enthesitis scores had only weak correlation with ASDAS-CRP and ASDAS-ESR (Table 2) and the three had only fair capability to discriminate subjects with inactive disease (ASDAS-CRP < 1.3) and active disease (ASDAS-CRP ≥1.3) (Area under the curve: MASES 0.647, SPARCC 0.638 and LEI 0.595). When the analysis was repeated using 2.1 as cut-off, the result was similar: the enthesitis indices had fair capability to discriminate between low (ASDAS-CRP < 2.1) and high disease activity (ASDAS-CRP ≥ 2.1) (Area under the curve: MASES 0.625, SPARCC 0.618 and LEI 0.579).

To evaluate if the three enthesitis scores had better correlation with BASDAI than ASDAS-CRP and ASDAS-ESR due to question 4 from BASDAI (which evaluates enthesitis), the correlation with every question from BASDAI was analyzed (data not shown). Question 4 had higher correlation with the three enthesitis scores than the remaining questions from BASDAI. However, when question 4 was excluded from BASDAI, this score continued to have better correlation with enthesitis indices compared to ASDAS-CRP and ASDAS-ESR (Table 2).

There was no statistical significant correlation between enthesitis indices and the inflammatory markers ESR and CRP (Table 2).

Functional status measured by BASFI had moderate correlation with MASES (r_s 0.465 $p \leq 0.01$) but only weak correlation with SPARCC (r_s 0.371 $p \leq 0.01$) and LEI (r_s 0.314 $p \leq 0.01$) (Table 2). Although the correlation coefficient of MASES was greater than SPARCC and LEI, the comparison of coefficients using the 95% confidence interval showed statistically significant difference only between MASES and LEI ($p = 0.008$). There was no statistically difference between the correlation coefficient of MASES and SPARCC ($p = 0.094$) or between SPARCC and LEI ($p = 0.2$).

The exclusion of patients with fibromyalgia ($N = 9$) did not change the correlation of enthesitis indices with scores of disease activity and function in patients with axial SpA.

Correlation of enthesitis indices with disease activity and function in peripheral SpA

Among the 59 patients fulfilling ASAS classification criteria for peripheral SpA, only MASES had a weak but statistically significant correlation with DAS28-ESR (r_s 0.310 $p = 0.05$) (Table 3).

The three enthesitis indices had only a fair capacity to discriminate active disease (DAS28-ESR ≥ 2.6) from inactive disease (DAS28-ESR < 2.6) (AUC 0.714 for MASES, 0.738 for SPARCC and 0.666 for LEI). The comparison of ROC curves using the DeLong's test showed no statistical significant difference among the three scores regarding their ability to discriminate active from inactive disease (comparison MASES/SPARCC $p = 0.733$; MASES/LEI $p = 0.466$; SPARCC/LEI $p = 0.06$).

There was no statistical significant correlation between enthesitis indices and the inflammatory markers ESR and CRP in patients with peripheral SpA (Table 3).

The correlation with function measured by HAQ was moderate for MASES (r_s 0.541) and LEI (r_s 0.497) and weak for SPARCC (r_s 0.347) (Table 3). The comparison of the 95% confidence interval of the three correlation coefficients showed that MASES had a better correlation with HAQ compared to SPARCC ($p = 0.034$) but it was not statistically different from LEI ($p = 0.628$). The exclusion of patients with fibromyalgia ($N = 2$) did not change the correlation between the enthesitis scores and clinical measures of disease activity and function in peripheral SpA.

Table 2 Correlation of the enthesitis indices with disease activity and function in 145 patients fulfilling ASAS criteria for axial SpA

	BASDAI	BASDAI without question 4	ASDAS- ESR	ASDAS-CRP	ESR	CRP	BASFI
MASES	,572[b]	,495[b]	,372[b]	,368[b]	-,085	-,091	,465[b]
SPARCC	,508[b]	,440[b]	,297[b]	,342[b]	-,066	-,065	,371[b]
LEI	,447[b]	,384[b]	,288[b]	,297[b]	-,074	-,064	,314[b]

[b]correlation is significant at the 0.01 level (2-tailed)

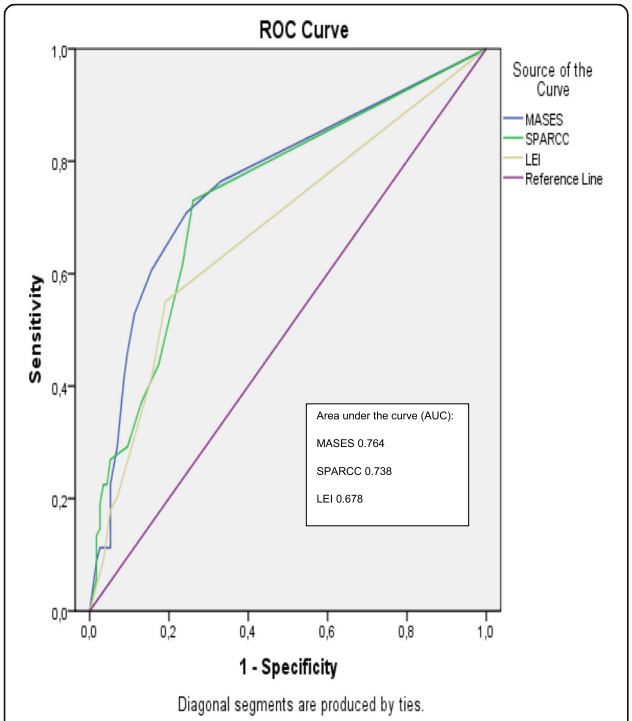

Fig. 1 Performance of MASES, SPARCC and LEI in axial SpA to discriminate between active disease (BASDAI ≥4) and inactive disease (BASDAI < 4)

Discussion

In this sample of Brazilian patients, MASES performed slightly better than SPARCC and LEI regarding correlation with disease activity and function in SpA patients. The three enthesitis scores had only fair capacity to discriminate active from inactive patients.

To the best of our knowledge, this is the first work to compare the correlation of the three indices MASES, SPARCC and LEI with disease activity and function in Brazilian patients studying their performance in categories of patients with SpA (axial x peripheral) regardless of the underlying individual disease. In the last years, the new ASAS criteria for axial and peripheral SpA emerged with the purpose to enhance design of clinical trials and allow an earlier and more effective diagnosis and treatment for patients. While previous work studied the correlation of enthesitis indices with clinical parameters in a specific entity, more frequently AS, our work incorporate the new tendency to group patients according to the pattern of manifestations and analyze the correlation of the instruments with disease activity and function among these groups rather than study their performance in a single, specific entity [5, 8, 14, 15].

Table 3 Correlation of the enthesitis indices with disease activity and function in 59 patients with peripheral SpA

	DAS28-ESR	ESR	CRP	HAQ
MASES	,318[a]	-,023	-,044	,541[b]
SPARCC	,250	-,006	-,093	,347[b]
LEI	,234	,008	-,002	,497[b]

[b]Correlation is significant at the 0.01 level (2-tailed)
[a]Correlation is significant at the 0.05 level (2-tailed)

In the present work, MASES, SPARCC and LEI were correlated to measures of disease activity in axial SpA and MASES was also correlated with DAS28-ESR in peripheral SpA. These findings are in accordance to previously published work which demonstrated that MASES index was correlated to BASDAI, patient global VAS and physician global VAS in AS patients [5, 8, 14].

Maksymowych et al. also found a correlation between SPARCC and the two measures of disease activity BASDAI and physician global VAS when studying 245 AS patients, while Healy et al.demonstrated a positive correlation between LEI and DAS28, tender joint count, swollen joint count, patient global VAS, physician global VAS and patient pain VAS in PsA patients [15, 16].

In this sample of Brazilian patients with axial SpA, the three enthesitis scores had better correlation with BASDAI than with ASDAS-CRP or ASDAS-ESR. The better correlation with BASDAI could be related to the item 4 of this questionnaire which evaluates entheseal pain although MASES has also been correlated with individual BASDAI items analyzed separately [5]. The absence of correlation between enthesitis and inflammatory markers contributes to decrease the correlation of the three enthesitis indices with ASDAS and has already been remarked in other studies [5, 8, 14] We can hypothesize that clinical entheseal scores are really a measurement of "pain" in the enthesis rather than true "inflammation" at entheseal sites and therefore correlate with item 4 of BASDAI. It would be interesting to obtain the correlation between inflammatory markers and the objective signs of inflammation detected through ultrasound or RMI.

There is a controversial result in literature regarding the correlation between the three enthesitis indices evaluated in this work and measures of function. Several trials are in line with our study and showed BASFI to be correlated with MASES and SPARCC in AS patients; a positive correlation was also found between HAQ and both MASES and LEI in PsA while other authors found no statistical significant correlation between enthesitis and function [5, 6, 8, 9, 15, 16].

Since the main difference among the three scores is the number and location of entheseal sites assessed, we could hypothesize that entheseal sites evaluated by MASES but not evaluated by SPARCC and LEI could be partially responsible for the better correlation of MASES with function and disease activity in the analyzed sample. MASES differs from the other two indices by evaluating enthesis with a more axial distribution as

costochondral joints, antero and posterior iliac spines and the fifth lumbar spinous process. In the present work, the most prevalent site of entheseal tenderness was the fifth lumbar spinous process, affected in 25% ($N = 51$) of the total sample. Besides that, 24% of the 204 analyzed patients also had enthesitis in bilateral first and seventh costochondral joints and the right posterior superior iliac spine. The fact that there was a high prevalence of enthesitis in a more axial distribution could be partially responsible for the good performance of MASES in this sample.

Corroborating our findings, a high prevalence of enthesitis in a more axial location was also found when patients included in the Brazilian registry of SpA were analyzed, with posterior iliac spine and fifth lumbar spinous process being affected, respectively, in 22.8 and 19.2% of 1505 SpA patients [4]. Some sites evaluated exclusively by MASES as the iliac crests and posterior iliac spines were found to be associated with work incapacity in this large cohort of Brazilian patients, leading to the hypothesis that the enthesitis located in pelvis and lumbar spine, only evaluated by MASES, could play a significant role on functional disability [4].

Bilateral involvement of enthesis is a descriptive element suggested by the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) which can aid physicians (mainly non-rheumatologists) to recognize enthesitis. In our sample, bilaterality was found in 86.1, 76.1 and 89.7% of patients reporting tenderness in at least two enthesis in MASES, SPARCC and LEI, respectively. This result reinforces the importance of "bilaterality" in the assessment of enthesitis [35].

This study has some weaknesses: the sample did not include patients from other states of Brazil outside the South and North region and the enthesitis were characterized only clinically, without imaging methods to confirm the diagnosis. More than 50% of patients were receiving biologic therapy and NSAIDs, therapies that could decrease the number of enthesitis. Despite the high prevalence of patients receiving biologic therapy in our sample (54.4%), the majority of axial SpA included in the study (58.6%) had high or very high disease activity. So, the probability to find enthesitis in the sample, in our opinion, was high.

We did not assess the University of California San Francisco (UCSF) Enthesitis Index which was specifically developed for AS and found to be slightly more sensitive than MASES in a previous study [18, 36]. Many clinical scores to assess enthesitis are currently available and MASES, SPARCC and LEI have been chosen because they were considered more feasible and usually employed in daily practice in the participating centers [12–20]. Furthermore, MASES and UCSF showed to be highly correlated [36].

There are many ways to classify the intensity of correlations and in this work we used the Dancey classification. The choice of other criteria could have changed the cut-offs to define weak, moderate and strong correlations, leading to a different interpretation of data [29].

Another important limitation is the utilization of the 28-joint count to evaluate peripheral arthritis. Although recent work showed that the DAS28 is not the most adequate tool to evaluate disease activity in PsA (since it can miss around 25% of active joint disease in oligoarticular patients), the 28-joint count was part of the routine care protocol in the three university hospitals at the time of data collection [37]. There is a lag of several years from study conception until data publication with continuous improvement in the SpA assessment along these years.

Another limitation is that the cross-sectional design of the study did not permit to assess the sensitive to change of the three enthesitis scores and whether they correlate to changes in other validated measures.

Conclusion

Regardless of its limitations, this study suggests that MASES performed statistically slightly better than SPARCC and LEI regarding correlation with disease activity and function in this Brazilian sample of SpA patients. However, in clinical practice it's difficult to stablish some superiority among the three scores since their performance was quite similar.

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Authors' contributions

PEP and PDS contributed to the conception and design of study. PEP, APBC, SLER, JWX, FBO, BG, CS, AAG contributed to acquisition of data. PEP, RMX, ACBM, CLK and PDS contributed to analysis and interpretations of data. PEP and PDS drafted the manuscript and all authors revised the manuscript critically for intellectual content. All authors read and approved the final manuscript.

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Availability of data and materials

The data used and analyzed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

This study was performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. All patients gave their informed consent prior to their inclusion in the study. The study obtained ethical approval from Comitê de Ética em Pesquisa da Fundação Universidade do Amazonas (number 686619), Comitê de Ética em Pesquisa do Hospital de Clínicas de Porto Alegre (number 814431) and Comitê de Ética em Pesquisa da Sociedade Evangélica Beneficiente de Curitiba (number 1013720).

Consent for publication
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Competing interests
The authors declare that they have no competing interests.

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