Japan College of Rheumatology
MODERN RHEUMATOLOGY

http://informahealthcare.com/mor
ISSN 1439-7595 (print), 1439-7609 (online)

Mod Rheumatol, 2014; 24(4): 651–656

DOI: 10.3109/14397595.2013.850182

informa
healthcare

ORIGINAL ARTICLE

Correlations among enthesitis, clinical, radiographic and quality of life parameters in patients with ankylosing spondylitis

Aylin Rezvani[1], Hatice Bodur[2], Şebnem Ataman[3], Taciser Kaya[4], Derya Soy Buğdaycı[5], Saliha Eroğlu Demir[1], Hikmet Koçyiğit[6], Lale Altan[7], Hatice Uğurlu[8], Mehmet Kırnap[9], Ali Gür[10], Erkan Kozanoğlu[11], Ayşen Akıncı[12], Ibrahim Tekeoğlu[13], Günşah Şahin[14], Ajda Bal[15], Konçuy Sivrioğlu[7], Pelin Yazgan[16], Gülümser Aydın[17], Simin Hepgüler[18], Neşe Ölmez[19], Ömer Faruk Şendur[20], Mahmut Yener[21], Zühal Altay[22], Figen Ayhan[23], Oğuz Durmuş[24], Mehmet Tuncay Duruöz[25], Zafer Günendi[26], Barış Nacır[27], Öznur Öken[28], Hasan Toktaş[29], Sibel Ünsal Delialioğlu[28], Deniz Evcik[30], and Filiz Meryem Sertpoyraz[31]

[1]*Department of Physical Medicine and Rehabilitation, Bezmialem Vakif University, Faculty of Medicine, Istanbul, Turkey,* [2]*Physical Medicine and Rehabilitation Clinic, Ankara Numune Training and Research Hospital, Ankara, Turkey,* [3]*Division of Rheumatology, Department of Physical Medicine and Rehabilitation, Ankara University, Faculty of Medicine, Ankara, Turkey,* [4]*Physical Medicine and Rehabilitation Clinic, Izmir Bozyaka Training and Research Hospital, Izmir, Turkey,* [5]*Istanbul Physical Medicine and Rehabilitation Training and Research Hospital, Istanbul, Turkey,* [6]*Physical Medicine and Rehabilitation Clinic, Izmir Katip Celebi University Atatürk Training and Research Hospital, Izmir, Turkey,* [7]*Department of Physical Medicine and Rehabilitation, Uludağ University, Faculty of Medicine, Bursa, Turkey,* [8]*Department of Physical Medicine and Rehabilitation, Selcuk University, Meram Faculty of Medicine, Konya, Turkey,* [9]*Department of Physical Medicine and Rehabilitation, Erciyes University, Faculty of Medicine, Kayseri, Turkey,* [10]*Department of Physical Medicine and Rehabilitation, Gaziantep University, Faculty of Medicine, Gaziantep, Turkey,* [11]*Department of Physical Medicine and Rehabilitation, Çukurova University, Faculty of Medicine, Adana, Turkey,* [12]*Department of Physical Medicine and Rehabilitation, Hacettepe University, Faculty of Medicine, Ankara, Turkey,* [13]*Division of Rheumatology, Department of Physical Medicine and Rehabilitation, Sakarya University, Faculty of Medicine, Sakarya, Turkey,* [14]*Department of Physical Medicine and Rehabilitation, Mersin University, Faculty of Medicine, Mersin, Turkey,* [15]*Physical Medicine and Rehabilitation Clinic, Dışkapı Yıldırım Beyazıt Training and Research Hospital, Ankara, Turkey,* [16]*Department of Physical Medicine and Rehabilitation, Harran University, Faculty of Medicine, Urfa, Turkey,* [17]*Department of Physical Medicine and Rehabilitation, Kırıkkale University, Faculty of Medicine, Kırıkkale, Turkey,* [18]*Department of Physical Medicine and Rehabilitation, Ege University, Faculty of Medicine, Izmir, Turkey,* [19]*Physical Medicine and Rehabilitation Clinic, Atatürk Training and Research Hospital, Izmir, Turkey,* [20]*Department of Physical Medicine and Rehabilitation, Adnan Menderes University, Faculty of Medicine, Aydın, Turkey,* [21]*Department of Physical Medicine and Rehabilitation, Süleyman Demirel University, Faculty of Medicine, Isparta, Turkey,* [22]*Department of Physical Medicine and Rehabilitation, İnönü University, Faculty of Medicine, Malatya,Turkey,* [23]*Physical Medicine and Rehabilitation Clinic, Ankara Training and Research Hospital, Ankara, Turkey,* [24]*Physical Medicine and Rehabilitation Clinic, GATA Haydarpaşa Training and Research Hospital, İstanbul, Turkey,* [25]*Division of Rheumatology, Department of Physical Medicine and Rehabilitation, Celal Bayar University, Faculty of Medicine, Manisa, Turkey,* [26]*Department of Physical Medicine and Rehabilitation, Gazi University, Faculty of Medicine, Ankara, Turkey,* [27]*Physical Medicine and Rehabilitation Clinic, Ankara Training and Research Hospital, Ankara, Turkey,* [28]*AnkaraPhysical Medicine and Rehabilitation Training and Research Hospital, Ankara, Turkey,* [29]*Department of Physical Medicine and Rehabilitation, Kocatepe University, Faculty of Medicine, Afyon,Turkey,* [30]*Department of Therapy and Rehabilitation, Ankara University, Haymana Vocational School; Department of Physical Medicine and Rehabilitation, Ufuk University, Faculty of Medicine Ankara, Ankara, Turkey, and* [31]*Physical Medicine and Rehabilitation Clinic, Tepecik Training and Research Hospital, Izmir, Turkey*

Abstract

Objectives. To investigate the relationship between enthesitis and disease activity, functional status, fatigue, joint mobility, radiological damage, laboratory parameter and quality of life in patients with ankylosing spondylitis (AS).

Methods. A total of 421 patients with AS (323 male and 98 female) who were included in the Turkish League Against Rheumatism Registry were enrolled in the study. The Bath AS Disease Activity Index (BASDAI), fatigue, the Bath AS Functional Index (BASFI), the Bath AS Metrology Index (BASMI), the Maastricht AS Enthesitis Score (MASES), AS quality of life (ASQoL), the Bath AS Radiology Index (BASRI) and erythrocyte sedimentation rate (ESR) were evaluated.

Keywords

Ankylosing spondylitis, Disease activity parameters, Enthesitis scores, MASES, Quality of life

History

Received 1 February 2013
Accepted 27 September 2013
Published online 31 October 2013

Correspondence to: Aylin Rezvani, MD, Physical Medicine and Rehabilitation Specialist, Department of Physical Medicine and Rehabilitation, Bezmialem Vakif University, Faculty of Medicine, Istanbul, Turkey. Vatan Caddesi, Fatih/Istanbul. Tel: + 0090 5336848. Fax: + 0090 2126217580. E-mail: aylin_rezvani@yahoo.com

Results. Enthesitis was detected in 27.3% of patients. There were positive correlations between MASES and BASDAI, BASFI and fatigue ($p < 0.05$). MASES was not correlated with BASRI, BASMI, ASQoL and ESR. The mean MASES score was 1.1 ± 2.4. The most frequent regions of enthesopathies were right iliac crest, spinous process of L5 and proximal to the insertion of left achilles tendon, respectively.
Conclusions. Enthesitis was found to be associated with higher disease activity, higher fatigue, worse functional status and lower disease duration. As enthesitis was correlated with BASDAI, we conclude that enthesitis can reflect the disease activity in patients with AS.

Introduction

Ankylosing spondylitis (AS) which is the best known and characterized of the family of spondyloarthritides, is a chronic inflammatory disease affecting the axial skeleton, the entheses and less frequently the peripheral joints [1]. Enthesitis, a universal hallmark of spondyloarthritides, is inflammation of the origin and insertion of ligaments, tendons, aponeuroses, annulus fibrosis, joint capsules and fascia [2]. Enthesitis has been considered to be the initial site of inflammation in SpA, which only later extends to juxtaposed synovial tissues [3]. Entheses are metabolically highly active [4] and extremely sensitive because of their high content of nerve terminals [5]. However entheses has been viewed as an organ with fibrocartilage as the main component which connects the entheses to immediately adjacent bone and trabecular bone [6]. Enthesitis may occur at any entheses in axial and peripheral sites of skeleton in AS but the most prominent and common enthesitis do occur in the lower limbs especially in the foot at the insertion of the Aschilles tendon and of the plantar fascia onto the calcaneus [7]. Francois et al. stated that inflammatory enthesitis is clinically detectable in only 10% of patients with early-stage AS and 50% of those with established AS [8]. The most common clinical features of enthesitis are pain as a symptom and swelling as a sign. Magnetic resonance imaging and ultrasonography are suggested as the best imaging methods in detecting early signs of enthesopathy [9]. Although in 1995 the 'ASsessment in Ankylosing Spondylitis' working group (ASAS) recommended enthesitis as a domain of clinical setting in core set, no instrument was addressed for measuring enthesitis [10].

Several clinical scoring methods such as Mander's Enthesal Index (MEI) [11], Maastricht AS Enthesitis Score (MASES) [2], Stoke Enthesitis Index (SEI) [12,13], Spondyloarthritis Research Consortium of Canada [14], the Shichikawa's criteria [15] have been designed to evaluate enthesopathy. Each of these indices has advantages and limitations according to OMERACT Filter criteria [16]. As MEI is time consuming and applying it is rather hard for either physician or patient (based on the intensity of pain produced by local pressure on 66 entheseal points, and scoring severity of pain in a 0–3 point scale), MASES, a simplified MEI (based on 13 entheseal points without graduating the pain) is being used in evaluating enthesitis in daily practice and clinical trials [2]. MASES has good metrological properties and includes the main peripheral and axial entheseal sites involved in AS and seems to be a good alternative, but it is also less sensitive to distinguish AS patients with a low severity of enthesitis [11].

As enthesitis has been proposed as the primary lesion of AS, its relationship with the overall level of disease activity and function is expected.

Using MASES as a modern clinical enthesitis score with good metrological properties, the aim of this study was to investigate the correlation between the severity of enthesitis and disease activity, gender differences, functional status, spinal mobility, structural damage, laboratory parameters and quality of life in a great number of AS patients.

Methods

A total of 421 patients with AS who included in TRASD-IP (Turkiye Romatizma) Arastirma Savas Dernegi (TRASD) AS Study Group which is the first registry designed for patients with AS who were diagnosed according to the modified New York criteria [17] in Turkey were enrolled in the study [18]. The sociodemographic characteristics (age, gender and disease duration) of the patients were recorded. The patients were assessed using ASAS recommendations for core outcome domains for the assessment in AS [10]. Turkish versions of Bath AS Disease Activity Index (BASDAI) [19], Turkish version of Bath AS Functional Index (BASFI) [20], fatigue (BASDAI-question 1, Visual analogue scale (VAS) 0–10) [19], Bath AS Metrology Index (BASMI) [21] and Maastricht AS Enthesitis Score (MASES) [2] were evaluated. The MASES was developed from the MEI, which includes 13 sites and with local pressure, scores the intensity of pain in each site as 0 ('no pain') or 1 ('painful'), giving a total possible score of 0–13. The MASES score includes entheses at the 1st and 7th costochondral joints, the posterior superior iliac spines (PSIS), the anterior superior iliac spines (ASIS), the iliac crests, the insertion of the Achilles tendons and the 5th lumbar spinous process.

The Bath AS Radiology Index (BASRI) was used for evaluating the radiological damage [22]. A disease-specific measure entitled AS Quality of Life (ASQoL) were performed. ASQoL comprises 18 items and each item is scored as '1' or '0'. A score of '1' indicates poor QoL. Total scores range from 0 to 18, with a higher score indicating poor quality of life [23]. Before the study, in order to provide standardization among the centers, interactive meetings and practical applications were performed. Booklets on physical and radiographical assessment methods were provided to the centers that participated. Ethical Committee approval was obtained from the local boards and the Ministry of Health.

Statistical analysis was performed with SPSS for Windows. Descriptive data were presented as mean $\pm$ standard deviation (SD). Correlations between study parameters were evaluated by Spearman correlation test as variables did not show normal distribution. A p value less than 0.05 was considered as statistically significant. Demographic characteristics were compared using the Chi-squared test. Mann–Whitney U test was used for the comparison of male and female patients with AS.

Results

In the present study, 421 patients with AS (323 men and 98 women) were enrolled, with a male/female ratio of 3.3. The mean age and disease duration were 39.66 ± 10.81 years and 12.05 ± 0.70 years, respectively. The demographic and clinical characteristics of the patients were given in Table 1.

Enthesitis was present (enthesitis score > 0) in 27.3% (77 male, 38 female) and absent (enthesitis score 0) in 72.7% (246 male, 60 female) of patients with AS. The MASES score of female patients were significantly higher than that of male ($p < 0.05$).

Table 1. Demographic and clinical characteristics of the patients with AS.

	Patients (n:421)	Male (n:323)	Female (n:98)	*p*
Age, years	39.67 ± 10.8	39.4 ± 10.7	40.4 ± 11.1	>0.05
BMI	24.7 ± 6.1	25.09 ± 5.5	23.41 ± 7.6	>0.05
Disease duration, years	12.1 ± 8.7	12.7 ± 8.9	9.9 ± 7.5	**<0.05**
Fatigue (BASDAI1)	4.2 ± 2.9	4.1 ± 2.9	4.6 ± 2.9	>0.05
Spinal pain (BASDAI2)	5.0 ± 3.0	4.9 ± 2.9	5.3 ± 3.6	>0.05
Peripheral joint pain (BASDAI3)	2.7 ± 2.9	2.6 ± 2.9	2.9 ± 3.1	>0.05
Local tenderness (BASDAI4)	3.4 ± 3.2	3.2 ± 3.2	3.8 ± 3.3	>0.05
Severity of Morning stiffness (BASDAI5)	3.7 ± 3.2	3.6 ± 3.2	3.7 ± 3.2	>0.05
Duration of Morning stiffness (BASDAI6)	3.4 ± 3.2	3.4 ± 3.2	3.5 ± 3.2	>0.05
BASDAI Total	3.7 ± 2.4	3.6 ± 2.4	4.0 ± 2.4	>0.05
BASFI	3.3 ± 2.8	3.3 ± 2.7	3.1 ± 2.9	>0.05
BASRI	7.8 ± 3.8	8.1 ± 3.8	6.6 ± 3.4	**<0.001**
BASMI	3.7 ± 2.4	3.9 ± 2.4	2.89 ± 2.2	**<0.001**
ASQoL	4.2 ± 5.7	4.01 ± 5.6	4.6 ± 6.0	>0.05
ESR	23.7 ± 20.8	22.4 ± 20.5	27.9 ± 21.2	**<0.05**
MASES	1.1 ± 2.4	0.9 ± 2.2	1.7 ± 2.9	**<0.001**

n, Number of cases; MASES, Maastricht AS Enthesitis Score; BASDAI, Bath AS Disease Activity Index; BASFI, Bath AS Functional Index; BASRI, Bath AS Radiology Index; BASMI, Bath AS Metrology Index; ESR, Erythrocyte Sedimentation Rate; ASQoL, AS Quality of Life.

Correlations between MASES and ESR and clinical parameters were shown in Tables 2 and 3. There was a weak correlation between MASES and all BASDAI questions ($p < 0.001$, r:0.228), MASES and BASFI ($p < 0.001$, r:0.195) and also MASES and fatigue (BASDAI1) ($p < 0.001$, r:0.226). MASES was negatively correlated with disease duration and body mass index (BMI) (p:0.017, r:− 0.116 and p:0.047, r:− 0.115, respectively). MASES was not correlated with age, BASRI, BASMI, ASQoL and ESR ($p > 0.05$).

The mean MASES score was 1.1 ± 2.4. The most frequent regions of enthesopathies were right iliac crest, spinous process of L5, proximal to the insertion of left Achille tendon, left iliac crest and left first costochondral joint, respectively (Table 4).

Discussion

Although enthesitis has been recognized since 1966 as a radiological characteristic of SpA, their clinical correlation has so far been poorly described and elevated enthesitis scores were reported to be associated with worse outcomes in patients with AS [24].

There are limited number of studies using different enthesitis score in evaluating the correlation of enthesitis with disease-related variables. Some of these studies evaluated enthesitis in patients with SpA [25–28] and the other studies evaluated in patients only with AS [2,11,12,29–33].

As it is difficult to define AS disease activity because of clinical diversity, both in severity and in localization of the disease among different patients [34] there is still no 'gold standard' for assessing disease activity objectively so, BASDAI was measured as an indicator for disease activity in our study. As is known BASDAI is a self-administered questionnaire and consists of six questions on fatigue, pain of the spine and hips, pain or swelling of the peripheral joints, localized tenderness as a proxy for enthesitis, and severity and duration of morning stiffness; and the questions are answered on a 10-cm VAS, anchored with the labels 'none' and 'very severe' at either end of the first five questions, and with '0 hours' and 'two hours' at either end of the question on duration of morning stiffness [19]. Not only total BASDAI, the correlation between enthesitis and every question in BASDAI were investigated separately in our study. Although patients' reports are subjective and need a well understanding of patients to evaluate themselves on a VAS score and given answers are entirely patients own perception, MASES showed poor but significantly positive correlation both with total and all of the questions within BASDAI in our study. The relationship between MASES and disease activity has been reported by several studies and the results were consistent with ours [26,30,32,35].

Missaoui and Revel stated that fatigue represents the third most common complaint after pain and stiffness which are the major symptoms of AS [36]. Using Multidimensional Assessment of Fatigue (MAF) it is reported that more than half of the patients with AS have a severe fatigue [37–39]. We did not evaluate MAF in our study but using the first question of BASDAI we found MASES to be correlated with fatigue. The correlation of MASES with fatigue was shown by Bodur et al. study as well [18].

MASES was correlated with the second question of BASDAI as pain of the spine and hips in our trial. Sivas et al. found MEI and MASES evaluated by both doctor and patients to be correlated with VAS-spinal pain [30]. Such a correlation was found in other studies too. In contrast Kaya et al. and Turan et al. [26,31] could not find a relationship between severity of enthesitis and pain in their trial.

In our study a correlation was found between MASES and the third question of BASDAI as pain or swelling of the peripheral joints. Heuft-Dorenbosch et al. stated that the presence of peripheral arthritis indicated high disease activity which might result with high BASDAI score [39]. In contrast Sivas et al. found no correlation between enthesitis score and VAS-peripheral joints in

Table 2. Correlations between MASES and some laboratory and clinical parameters.

	Age	Disease duration	BMI	BASFI	BASRI	BASMI	ASQoL	ESR
MASES								
r	− 0.052	− 0.116	− 0.115	0.195	− 0.027	− 0.040	0.086	0.081
p	0.284	**0.017**	**0.047**	**0.000**	0.575	0.415	0.077	0.095

r, Correlation coefficient; MASES, Maastricht AS Enthesitis Score; BMI, Body–Mass Index; BASFI, The Bath AS Functional Index; BASRI, The Bath AS Radiology Index; BASMI, Bath AS Metrology Index; ASQoL, AS Quality of Life; ESR, Erythrocyte Sedimentation Rate.

Table 3. Correlations between MASES and BASDAI questions.

	BASDAI Total	BASDAI1	BASDAI2	BASDAI3	BASDAI4	BASDAI5	BASDAI6
MASES							
r	0.228	0.226	0.278	0.235	0.214	0.214	0.140
p	**0.000**	**0.000**	**0.000**	**0.000**	**0.000**	**0.000**	**0.004**

r, Correlation coefficient; MASES, Maastricht AS Enthesitis Score; BASDAI, The Bath AS Disease Activity Index.

their study [30]. The explanation of the contradiction might be due to that of MASES enthesitis score detects the objective presence or absence of local pressure at time of examination and BASDAI scores define the subjective pain during the last one week without any examination.

MASES was also correlated with localized tenderness as a proxy for enthesitis (the fourth question of BASDAI questionnaire). Kaya et al. found no relationship between SEI and the average of the BASDAI components excluding the question concerning enthesitis [31]. They stated that the relationship between BASDAI and SEI could be probably due to the question related to enthesopathy which BASDAI covers. Spoorenberg stated that as the most peripheral entheses are located near the joints, the unawareness of patients about swollen joints could make the number of tender and swollen joints different when evaluated by the patients or by the physicians [40].

In our study MASES was correlated with the severity and duration of morning stiffness which reflects the inflammation and the severity of inflammation, respectively, in AS patients. Pain and morning stiffness were evaluated on VAS apart from BASDAI questionnaire in Kaya et al. study [31]. While finding a correlation between SEI and BASDAI which consists of pain and morning stiffness, they found no apparent relationship between SEI, pain and morning stiffness.

There was not any correlation between enthesitis and inflammatory parameters such as ESR in our trial. A positive correlation was not observed in previous studies either [2,11,12,26,30–32]. Although acute phase reactants such as CRP and ESR are considered more objectively in assessing disease activity, elevation of these markers are frequently absent in AS [34], so the sensitivity of these markers are poor and their value in determining whether the disease is active or not is rather limited [40].

It is well known that characteristic features of AS which are formation of syndesmophytes and the progressive ossification of extraspinal joint capsules and ligaments, may subsequently lead to complete loss of spinal movements, and functional disability [41]. Reduction in functional capacity and restriction in daily activities are prominent complaints which reflects the disease acitivity from the perspective of the patient with AS [30]. There is a controversial result in correlation between the enthesitis score and BASFI in literature. When some of these trials are in line with our study [30,32,33] the others are not [26,29,31].

It is considered that patients with high disease activity and worse functional status had significantly poorer QoL scores. Bodur et al. in their study with a large number of patients with AS, found MASES to be one of the most significantly correlated variables with ASQoL and SF-36 following BASDAI, BASFI, fatigue and pain [42]. Turan et al. reported that the quality of life of patients with AS were mostly related with enthesis involvement in their study [35]. We did not use SF 36 in our trial. Although in line with Bodur et al.'s study, MASES was correlated with BASDAI, BASFI, fatigue and pain in our study, we could not find any correlation between MASES and ASQoL.

The correlation between MASES and disease duration is controversial in the previous studies. MASES was negatively correlated with disease duration in our study. Laatiris et al. [32] did not find any correlation between enthesitis and disease duration while Bejia et al. [33] and Turan et al. [26] found significant correlation between MASES and disease duration. The obtained results from those studies show that the enthesitis could occur in every stage of the disease.

MASES was not correlated with BASMI in our study. Our data coincide with the findings of the studies using MEI [37] and ET [12,31] in which no correlations were found between enthesitis score and spinal measurements. Interestingly when Sivas et al. found a correlation between MEI and BASMI, no correlation was found between MASES and BASMI in their study [30]. Akkoc et al. assessed the validity of the BASDAI in Turkish patients comparing with BASMI, BASFI, BAS-G and physicians' assessment of disease activity. They found BASDAI to be correlated with all of these parameters except the BASMI. They stated that it might be due to the fact that disease activity and range of motion are different constructs which necessitate a separate evaluation [19].

MASES was not correlated with BASRI also in our study. A more likely explanation for this result may be that the BASRI which measures the radiographic deterioration that is commonly associated with restricted spinal mobility, progresses over months and years and the rate of these detoriarations could differ from patient to patient. BASMI and BASRI which measure these detoriarations are objective parameters that may change over time but MASES is a subjective parameter which reflects the pain at the time of physical examination.

The mean MASES score was 1.1 ± 2.4 and the most frequent regions of enthesopathies were right iliac crest, spinous process of L5, proximal to the insertion of left achilles tendon, left iliac crest and left first costochondral joint, respectively. Laatiris et al. found costochondral joints, calcaneal insertions and Achilles tendons as the most frequent regions of enthesopathies in their study [32] with the similar results done by Turan et al. [26]. As these enthesitis regions are located closely to their adjacent joints, the tenderness might be perceived incorrectly by the patients. Kaya et al. reported the most frequent regions of enthesopaties to be the spinous process of L5 and S1, sternocostal joints, iliac crests, spinous processes of C1/C2, C7/T1, major trochanters, sternoclavicular joints, respectively, when assessing enthesitis with the SEI [31]. Most of the evaluated regions in SEI such as spinous processes of C1/C2, C7/T1 and T12/L1, major trochanters, pelvic adductor orijin, ischial tuberosities, sternocostal joints, sternoclavicular

Table 4. The frequency of enthesopathy according to MASES.

	n	%
Right 1st costochondral joint	40	9.5
Left 1st costochondral joint	45	10.7
Right 7th costochondral joint	32	7.6
Left 7th costochondral joint	34	8.1
Right PSIS	33	7.8
Right ASIS	33	7.8
Left PSIS	28	6.7
Left ASIS	38	9
Right iliac crest	51	12.1
Spinous process of L5	46	10.9
Left iliac crest	45	10.7
Proximal to the insertion of right achilles tendon	43	10.2
Proximal to the insertion of left achilles tendon	46	10.9

n, Number of cases; MASES, Maastricht AS Enthesitis Score; PSIS, The posterior superior iliac spines; ASIS, The anterior superior iliac spines.

joints and plantar fasica are not included in MASES. The evaluation of these regions is also different from those of MASES index. The results of tenderness are scored between 0 and 3 with 0: no pain and 3: severe pain in a likert scale with the highest possible SEI score of 66 while the evaluation of pain is dichotomous scoring in MASES with the highest possible score of 13. So, different clinical enthesitis scales with different methods of evaluation pain may directly affect the region of enthesitis.

Enthesitis was found to be associated with higher disease activity and higher fatigue, worse functional status, lower disease duration and lower BMI. As the severity of enthesitis was correlated with total BASDAI as well as every question in BASDAI questionnaire in our large number of patients, we conclude that enthesitis can reflect the disease activity in patients with AS.

Acknowledgments

The authors express their gratitude to all members of the TRASD-IP AS Study group for their cooperation and to Pfizer Company for the registry sponsorship.

Conflict of interest

None.

References

1. Grant JT, Husby G. The epidemiology of ankylosing spondylitis. Semin Arthritis Rheum. 1993;22(5):319–34.
2. Heuft-Dorenbosch L, Spoorenberg A, van Tubergen A, Landewé R, van der Tempel H, Mielants H, et al. Assessment of enthesitis in ankylosing spondylitis. Ann Rheum Dis. 2003;62(2):127–32.
3. McGonagle D, Gibbon W, Emery P. Classification of inflammatory arthritis by enthesitis. Lancet. 1998;352(9134):1137–40.
4. Drouart M, Saas P, Billot M, Cedoz JP, Tiberghien P, Wendling D, Toussirot E. High serum vascular endothelial growth factor correlates with disease activity of spondylarthropathies. Clin Exp Immunol. 2003;132(1):158–62.
5. Benjamin M, Redman S, Milz S, Büttner A, Amin A, Moriggl B, et al. Adipose tissue at entheses: the rheumatological implications of its distribution. A potential site of pain and stress dissipation? Ann Rheum Dis. 2004;63(12):1549–55.
6. Benjamin M, Moriggl B, Brenner E, Emery P, McGonagle D, Redman S. The "enthesis organ" concept: why enthesopathies may not present as focal insertional disorders. Arthritis Rheum. 2004;50(10):3306–13.
7. McGonagle D, Benjamin M. Enthesopathies. In: Hochberg MC, Silman AJ, Smolen JS, Weinblatt ME, Weisman MH, editors. Rheumatology. Spain: Elsevier, 2008. p. 1197–1204.
8. Francois RJ, Braun J, Khan MA. Entheses and enthesitis: a histopathologic review and relevance to spondyloarthritides. Curr Opin Rheumatol. 2001;13(4):255–64.
9. De Miguel E, Cobo T, Munoz Fernandez S. Validity of enthesis ultrasound assessment in spondyloarthropathy. Ann Rheum Dis. 2009;68(2):169–74.
10. van der Heijde D, Calin A, Dougados M, Khan MA, van der Linden S, Bellamy N. Selection of instruments in the core set for DC-ART, SMARD, physical therapy, and clinical record keeping in ankylosing spondylitis. Progress report of the ASAS Working Group. Assessments in ankylosing spondylitis. J Rheumatol. 1999;26(4):951–4.
11. Mander M, Simpson JM, McLellan A, Walker D, Goodacre JA, Dick WC. Studies with an enthesis index as a method of clinical assessment in ankylosing spondylitis. Ann Rheum Dis. 1987; 46(3):197–202.
12. Dawes PT, Sheeran TP, Beswick EJ, Hothersall TE. Enthesopathy index in ankylosing spondylitis. Ann Rheum Dis. 1987;46(9):717.
13. Averns HL, Oxtoby J, Taylor HG, Jones PW, Dziedzic K, Dawes PT. Radiological outcome in ankylosing spondylitis: use of the stoke ankylosing spondylitis spine score (SASSS). Br J Rheumatol. 1996; 35(4):373–6.
14. Maksymowych WP, Mallon C, Morrow S, Shojania K, Olszynski WP, Wong RL, et al. Development and validation of the Spondyloarthritis Research Consortium of Canada (SPARCC) Enthesitis Index. Ann Rheum Dis. 2009;68(6):948–53.
15. Schikawa K, Takenaka Y, Yukioka M, Ikawa T. Polyenthesitis. Rheum Dis Clin North Am. 1992;18(1):203–13.
16. van der Heijde D, van der Linden S, Bellamy N, Calin A, Dougados M, Khan MA. Which domains should be included in a core set for endpoints in ankylosing spondylitis? Introduction to theAnkylosing spondylitis module of OMERACT IV. J Rheumatol. 1999;26:945–7.
17. van der Linden S, Valkenburg HA, Cats A. Evaluation of diagnostic criteria for ankylosing spondylitis. A proposal for modification of the New York criteria. Arthritis Rheum. 1984;27:361–8.
18. Bodur H, Ataman S, Bugdaycı DS, Rezvani A, Nas K, Uzunca K, et al. Description of the registry of patients with ankylosing spondylitis in Turkey: TRASD-IP. Rheumatol Int. 2012;32(1):169–76.
19. Akkoc Y, Karatepe AG, Akar S, Kirazli Y, Akkoc N. A Turkish version of the Bath Ankylosing Spondylitis Disease Activity Index: reliability and validity. Rheumatol Int. 2005;25:280–4.
20. Karatepe AG, Akkoc Y, Akar S, Kirazli Y, Akkoc N. The Turkish versions of the Bath Ankylosing Spondylitis and Dougados Functional Indices: reliability and validity. Rheumatol Int. 2005;25:612–8.
21. Jenkinson TR, Mallorie PA, Whitelock HC, Kennedy LG, Garrett SL, Calin A. Defining spinal mobility in ankylosing spondylitis (AS): the Bath AS Metrology Index. J Rheumatol. 1994;21(9): 1694–8.
22. MacKay K, Mack C, Brophy S, Calin A. The Bath Ankylosing Spondylitis Radiology Index (BASRI): a new, validated approach to disease assessment. Arthritis Rheum. 1998;41(12):2263–70.
23. Duruöz T, Doward L, Cerrahoğlu L, Turan Y. Translation and validation of the Turkish version of the ankylosing spondylitis quality of life (ASQoL) Questionnaire. Ann Rheum Dis. 2008;67(Suppl II):623.
24. Vastesaeger N, van der Heijde D, Inman RD, Wang Y, Deodhar A, Hsu B, et al. Predicting the outcome of ankylosing spondylitis therapy. Ann Rheum Dis. 2011;70(6):973–81.
25. D'Agostino MA, Said-Nahal R, Hacquard-Bouder C, Brasseur JL, Dougados M, Breban M. Assessment of peripheral enthesitis in the spondylarthropathies by ultrasonography combined with power doppler: a cross-sectional study. Arthritis Rheum. 2003;48(2): 523–33.
26. Turan Y, Duruoz MT, Cerrahoglu L. Relationship between enthesitis, clinical parameters and quality of life in spondyloarthritis. Joint Bone Spine. 2009;76(6):642–7.
27. Lehtinen A, Taavitsainen M, Leirisalo Repo M. Sonographic analysis of enthesopathy in the lower extremities of patients with spondylarthropathy. Clin Exp Rheumatol. 1994;12(12):143–8.
28. Boyer GS, Lanier AP, Templin DW, Bulkow l. Spondylarthropathy and rheumatoid arthritis in Alaskin Yupik Eskimos. J Rheumatol. 1990;17(4):489–96.
29. Alcalde M, Acebes JC, Cruz M, González-Hombrado L, Herrero-Beaumont G, Sánchez-Pernaute O. A sonographic enthesiticindex of lower limbs is a valuable tool in the assessment of ankylosing spondylitis. Ann Rheum Dis. 2007;66(8):1015–9.
30. Sivas F, Mermerci Başkan B, Erkol Inal E, Akbulut Aktekin L, Barça N, Ozoran K, Bodur H. The relationship between enthesitis indices and disease activity parameters in patients with ankylosing spondylitis. Clin Rheumatol. 2009;28(3):259–64.
31. Kaya T, Bal S, Günaydın R. Relationship between the severity of enthesitis and clinical and laboratory parameters in patients with ankylosing spondylitis. Rheumatol Int. 2007;27(4):323–7.
32. Laatiris A, Amine B, Ibn Yacoub Y, Hajjaj-Hassouni N. Enthesitis and its relationships with disease parameters in Moroccan patients with ankylosing spondylitis. Rheumatol Int. 2012;32(3):723–7.
33. Bejia I, Ben Hammouda S, Said M, Ben Salem K, Touzi M, Bergaoui N. Measuring enthesitis in ankylosing spondylitis. Joint Bone Spine. 2006;73(2):216–8.
34. Spoorenberg A, van Tubergen A, Landewé R, Dougados M, van der Linden S, Mielants H, et al. Measuring disease activity in ankylosing spondylitis: patient and physician have different perspectives. Rheumatology. 2005;44(6):789–95.
35. Turan Y, Duruöz MT, Cerrahoglu L. Quality of life in patients with ankylosing spondylitis: a pilot study. Rheumatol Int. 2007;27(10):895–9.
36. Missaoui B, Revel M. Fatigue in ankylosing spondylitis. Ann Readapt Med Phys. 2006;49(6):389–91.
37. Gunaydin R, Goksel Karatepe A, Cesmeli N, Kaya T. Fatigue in patients with ankylosing spondylitis: relationship with disease-specific

variables, depression, and sleep disturbance. Clin Rheumatol. 2009; 28(9):1045–51.
38. Ibn Yacoub Y, Amine B, Laatiris A, Abouqal R, Hajjaj-Hassouni N. Assessment of fatigue in Moroccan patients with ankylosing spondylitis. Clin Rheumatol. 2010;29(11):1295–9.
39. Heuft-Dorenbosch L, van Tubergen A, Spoorenberg A, Landewé R, Dougados M, Mielants H, et al. The influence of peripheral arthritis on disease activity in ankylosing spondylitis patients as measured with the Bath Ankylosing Spondylitis Disease Activity Index. Arthritis Rheum. 2004;51(2):154–9.
40. Spoorenberg A, van der Heijde D, de Klerk E, Dougados M, de Vlam K, Mielants H, et al. Relative value of erythrocyte sedimentation rate and C-reactive protein in assessment of disease activity in ankylosing spondylitis. J Rheumatol. 1999;26(4):980–4.
41. Bostan EE, Borman, P, Bodur H, Barça N. Functional disability and quality of life in patients with ankylosing pondylitis. Rheumatol Int. 2003;23(3):121–6.
42. Bodur H, Ataman S, Rezvani A, Buğdaycı DS, Cevik R, Birtane M, et al. Quality of life and related variables in patients with ankylosing spondylitis. Qual Life Res. 2011; 20(4):543–9.