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Conventional radiography and correlated factors of enthesopathies of the Achilles tendon and plantar fascia in patients with axial spondyloarthritis

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Informed consent: written consent was acquired by each patient enrolled.

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Summary

Objective. This study aimed to investigate the correlated risk factors and presence of radiological enthesopathies of the Achilles tendon and plantar fascia in patients with axial spondyloarthritis (axSpA).

Methods. 242 patients (121 female and 121 male) with axSpA were included in this study. The Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), the Bath Ankylosing Spondylitis Functional Index (BASFI), the Ankylosing Spondylitis Disease Activity Score with C-reactive protein (ASDAS-CRP), the Bath Ankylosing Spondylitis Radiology Index (BASRI), the Maastricht Ankylosing Spondylitis Enthesitis Score (MASES), and CRP were evaluated in all patients. The lateral foot X-rays of the patients were assessed for enthesopathies of the Achilles tendon and plantar fascia attachments.

Results. Calcaneal spur and Achilles enthesopathies were present in 57.4% of the patients. 39.3% of patients had enthesopathies in both regions. The male and female groups differed statistically in terms of weight, height, body mass index (BMI), positive family history, and duration since diagnosis ($p < 0.05$). The presence of calcaneal spur and Achilles enthesopathies was found to be significantly correlated with age, weight, BMI, symptom duration, and the score of BASDAI, BASFI, ASDAS-CRP, BASRI, and MASES ($p < 0.05$).

Conclusions. The presence of enthesopathies appears to be associated with age, weight, BMI, symptom duration, and disease activity. Conventional radiography can be used as an auxiliary tool in the evaluation of enthesal abnormalities in patients with SpA, especially in patients with advanced age, long symptom duration, and high BMI.

Introduction

Enthesitis is a primary lesion in all spondyloarthritis (SpA) subtypes, characterized by inflammation of the tendons, ligaments, joint capsules, and fascia at the site of bone attachment (1). The demonstration of enthesitis is very important both for the diagnosis of SpA and for the assessment of disease activity. Although the incidence of peripheral enthesitis in SpA varies between 25% and 58%, the actual prevalence depends on the type of evaluation (such as clinical, imaging, or histological) (2). Normally, enthesitis is expected to manifest clinically as pain, swelling, and tenderness due to inflammation in the enthesal area. However, it mostly occurs without any obvious clinical signs of inflammation (2, 3). Therefore, it has been suggested that imaging techniques such as conventional radiography, ultrasonography (US), magnetic resonance imaging (MRI), and bone scintigraphy are superior to clinical examination in the diagnosis and follow-up of enthesitis. Enteseal inflammatory alterations can produce proliferation, erosion, and peripheral ossification of bone (2, 4). US and MRI are superior in detecting early signs of enthesopathy (3), but it is possible to show erosions, bone proliferation changes, fragmentation, and crystal deposits such as peripheral and para-articular ossification with conventional radiography in advanced stages (2, 4). Although inflammation can occur in any enthesal region, it is more common in those of the lower extremities, particularly of the foot (3, 5-7). The most common sites of enthesitis in SpA are knee, heel, and ischial tuberosity (5). Conventional radiography has long been used as an adjunct tool in the diagnosis and follow-up of axial SpA (axSpA). Even if radiography shows changes appearing long time after the onset of the inflammatory process, it remains a valuable tool for assessing structural changes associated with enthesitis. Also, only a small number of studies have examined the radiographic assessment of enthesitis since lower extremity enthesitis was generally investigated by MRI and ultrasonographic methods in previous studies (8, 9). Moreover, understanding the factors associated with enthesitis is crucial for both diagnosis and effective management in axSpA patients. Factors associated with the occurrence of enthesitis were considered to be high body mass, disease activity, and younger age (10). Therefore, this study aimed to investigate the presence of radiological enthesopathies of the Achilles tendon and plantar fascia in patients with axSpA and the correlated risk factors.

Materials and Methods

Study design

This cross-sectional study was performed at the Department of Physical Medicine and Rehabilitation at Bezmialem Vakif University (Ethical Committee of Bezmialem Vakif University, Trial Registration: 2022/270). Written consent was acquired by each patient enrolled.

Participants and data extraction

Two hundred forty-two patients (121 female and 121 male) with axSpA were included in this study. Each patient was diagnosed with radiographic-axSpA according to the Assessment of SpondyloArthritis International Society classification criteria (11). All patients had their diagnosis at least one year prior to enrolment. Exclusion criteria were patients having previous joint surgery of the ankle or foot, local corticosteroid injection at the foot within 6 weeks before the clinical and radiographic evaluation, lower limb neuropathy, and those under 18 years of age. Data including age, sex, weight, height, body mass index (BMI), smoking, family history of SpA, duration since diagnosis, symptom duration and the HLA-B27 status was collected. A thorough clinical examination for tenderness and swelling at the Achilles tendon and plantar fascia was performed by an experienced physiatrist. The Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), the Bath Ankylosing Spondylitis Functional Index (BASFI), the Ankylosing Spondylitis Disease Activity Score with C-reactive protein (ASDAS-CRP), the Maastricht Ankylosing Spondylitis Enthesitis Score (MASES), and CRP were recorded in all patients. The lateral radiographs of the foot were assessed for the enthesopathies of Achilles tendon and plantar fascia attachments. The presence of enthesophyte (new bone formation) in each of the two enthesal regions was evaluated by a specialist

radiologist (ÜE). Each criterion was scored 1 if present and 0 if absent for each foot. The radiographic score could range from 0 to 4. By evaluating the location, shape and severity of the changes in the heel area, the radiologist decided whether the presence of heel enthesitis was caused by mechanical load and/or a degenerative process. Moreover, the Bath Ankylosing Spondylitis Radiology Index (BASRI-total) was evaluated by the same radiologist.

Statistical analysis

Numbers and percentages are used in the descriptive statistics for the qualitative variables, and mean, standard deviation, median, minimum, and maximum are used in the descriptive statistics for the quantitative variables. Pearson chi-square analysis was used to compare the groups in terms of the presence of the related variable. The Kolmogorov-Smirnov test was used to determine if the quantitative variables adhered to the normal distribution. The homogeneity of variance was investigated by Levene's test. Student's *t*-test was used to compare the mean of two independent groups, and the Mann-Whitney U test was used for the median comparison. The Spearman correlation coefficient was used to assess relationships between quantitative variables. The calculations were performed with IBM SPSS Statistics for Windows, Version 26 (IBM Corp., Armonk, NY, USA), with 0.05 as statistical significance level.

Results

The mean age of the patients was 59.15 ± 10.58 years. Of them, 50% were female and 50% male; 73.1% were non-smokers, and 26.9% were smokers. The mean BMI was 27.04 ± 4.36 . There was a positive family history of axSpA in 32.2% of the patients and 66.1% was HLA-B27 positive. While 69% of the patients had no chronic comorbidities, 19.8% had hypertension, 11.5% had diabetes mellitus, 5.9% hyperlipidemia, and 6.9% hypothyroidism. Calcaneal spurs and Achilles enthesopathies were present in 57.4% of the patients; 39.3% of them ($n=95$) had enthesopathies in both regions. None of the patients had swelling in the foot area on examination, but all patients (57.4%) with radiological Achilles enthesopathies had tenderness. The male and female groups differed statistically in terms of weight, height, BMI, positive family history, and duration of diagnosis ($p < 0.05$) (Table 1). The presence of calcaneal spur and Achilles enthesopathies was correlated with age, weight, BMI, symptom duration, and the score of BASDAI, BASFI, ASDAS-CRP, BASRI, and MASES ($p < 0.05$) (Table 2).

Discussion

As extra-articular structures, entheses are a major affected site by musculoskeletal inflammation in conditions like SpA (10, 12). From a physiological perspective, synovial tissue is highly vascular and undergoes extensive hyperplasia with inflammatory immune cell infiltration and joint space effusions during inflammatory episodes. However, the attachment sites of the entheses are entirely avascular and have a sparse blood vessel density in the adjacent ligaments and tendons (10). Enthesitis typically develops without any obvious clinical indications of inflammation, although it can sometimes lead to mild swelling of the surrounding soft tissues and increased vascularity, which can only be detected by dynamic imaging. Therefore, imaging studies such as conventional radiography, US and MRI have an important place in understanding the tissue reactions linked to enthesitis that cannot be detected by physical examination (10, 12). Although pseudo erosions may develop in the context of enthesitis, its net effect is new bone formation, which is frequently defined by extreme local apposition of periosteal bone (enthesophytes) at enthesitis sites. Since enthesophyte formation in peripheral joints may be the initial indication of musculoskeletal system involvement in patients with SpA, the presence of enthesitis as an early characteristic of the disease is significant. Clinical data suggest that mechanical stress plays a major role in the development of enthesitis. Therefore, enthesitis primarily influences the lower extremities, which are subjected to greater mechanical stresses than the upper extremities (10). The most commonly involved entheses are the heel inserts of the Achilles tendon and the plantar fascia (6). Therefore, in this study, we evaluated enthesopathies of the Achilles tendon

and plantar fascia in patients with axSpA by radiography, an inexpensive and easily available method. We found that calcaneal spur and Achilles enthesopathies were present in 57.4% of the patients. Moreover, 39.3% of patients had enthesopathies in both regions. We also evaluated the factors linked to the presence of radiological enthesopathies: they appear to be associated with age, weight, BMI, symptom duration, and disease activity.

In the literature, there are several studies evaluating the radiographic presence of enthesopathies in the Achilles tendon and plantar fascia attachments in patients with SpA. Borman *et al.* found that radiological enthesopathies at the Achilles tendon and plantar fascia were detected in 50% and 56.8% of patients, respectively. They also reported pathological US abnormalities at insertions of the Achilles tendon and plantar fascia on the calcaneus in 56.8% of 44 patients, whereas pain and swelling at enthesal insertions were detected in only 37%. They also found a correlation between the scores of US and X-Ray, particularly at the Achilles and plantar fascia insertion sites (7). Hamdi *et al.* found that radiological enthesopathies at the Achilles tendon and plantar fascia were detected in 22.5% and 20.8% of patients, respectively. They also found that the radiographic score correlated with enthesal pain, disease activity, and functional status, whereas there was a good correlation between the clinical and sonographic scores (9). Rezvani *et al.* found that enthesitis was detected in 27.3% of patients and the most common sites of enthesopathies were the right iliac crest, the spinous process of L5, and the proximal region of the insertion of the left Achilles tendon, respectively. They also found that enthesitis was linked to higher disease activity, higher fatigue, worse functional status, and lower disease duration. They proposed that enthesitis could reflect disease activity in patients with ankylosing spondylitis (3). Siddiq *et al.* found that the presence of radiological Achilles tendon and plantar fascia enthesitis was 45% (n=9) for both in the juvenile group, while it was 49% (n=25) and 45% (n=23), respectively, in the adult group. They suggested that the definition and classification of enthesitis is important in the early diagnosis of this rheumatological condition (13). Matallah *et al.* observed that radiological plantar fascia involvement was present in 37% of the patients while ultrasonographic plantar fascia involvement was present in 71% of them. They also found that the presence of radiological enthesopathy was related to plantar fascia pain palpation, MASES and the Spondyloarthritis Research Consortium of Canada score. They observed that the presence of enthesopathy was the radiographic finding most associated with clinical enthesitic involvement. They proposed that the plantar fascia in axSpA is usually asymptomatic and linked to disease activity and functional impairment (14). In this study, the frequency of both Achilles enthesopathies and plantar calcaneal enthesopathy (calcaneal spur) was present in 57.4% of the patients. Moreover, 39.3% of patients had enthesopathies in both regions. We think that this result may be due to exposure to excessive mechanical stress because of the advanced age, high weight, and BMI of the patients included in the study.

Siddiq *et al.* proposed that persistent enthesitis is one of the most common clinical manifestations of SpA and is usually linked to high erythrocyte sedimentation rate (ESR) and HLA-B27 positivity (13). However, HLA-B27 is detected in only 30-70% of cases of the peripheral form of SpA (15). Sudoł-Szopińska *et al.* prospectively assessed the Achilles tendon, plantar aponeurosis and flexor digiti brevis tendon entheses by the US in patients with clinically suspected enthesitis. HLA-B27 positivity was detected in 10 (33.3%) of 30 patients admitted with the preliminary diagnosis of Achilles tendon enthesitis, and in 10 (26.3%) of 38 patients admitted with the preliminary diagnosis of plantar aponeurosis or flexor digiti enthesitis. They found no relationship between the intensity of inflammatory lesions detected by US and HLA-B27 positivity (15). In our study, no relationship was found between the presence of enthesopathies and HLA-B27 positivity.

Balin *et al.* evaluated five enthesal regions of the lower extremities (such as the upper pole and lower pole of the patella, tibial tuberosity, Achilles tendon and plantar aponeurosis) of 35 SpA patients with US. They found that there was no significant correlation between the US score of enthesitis and acute phase reactants, such as CRP and ESR (5), an association not found in our study. Although acute phase reactants such as CRP and ESR seem to be more objective parameters in the evaluation of disease activity, the decrease in functional capacity and limitation in daily activities due to progressive

ossification of spinal and extraspinal structures are prominent in SpA. While some earlier research showed no correlation between enthesitis and disease duration, others found it. This suggests that enthesitis can occur at any stage of the disease (3). Since enthesitis may be the only symptom of early SpA, especially in patients without HLA-B27, other signs of the disease and more specific markers on imaging should be sought for early diagnosis (14). Therefore, it should also be kept in mind that there may be a delayed diagnosis due to the insidious nature of the disease. Besides, some entheses areas (such as iliac crests, symphysis pubis, ischial tuberosity, vertebrae, and greater trochanter) are not always clinically reachable due to their deep anatomical locations, and imaging techniques are needed to detect them. Although only the foot radiography was evaluated in terms of the entheses area in this study, enthesopathies was detected in different regions in some of the patients as well (Figure 1-3). Even if it is not within the scope of the study, radiographic examination of the areas where tenderness is detected at physical examination may be beneficial in terms of investigating the prevalence of enthesopathies areas and the diagnosis of the disease.

The study has some limitations such as small sample size, the lack of healthy control subjects, the evaluation of the images by only one radiologist, the absence of assessment of erosive changes, the lack of radiographic evaluation of entheses sites other than the foot, and the absence of ultrasonographic examination. According to the results of the study, enthesopathies in the foot region are quite common in patients with axSpA and should be considered in the diagnosis of the disease.

Conclusions

Enthesitis, a separate disease process that can manifest without the presence of arthritis, is thought to be the main pathogenic mechanism underlying SpA. Even in patients without clinical enthesitis, peripheral enthesitis at imaging has been proposed as a potential indicator of the severity of SpA. The demonstration of enthesitis in daily practice is difficult for several reasons, such as the frequent lack of obvious clinical inflammatory signs and of raised inflammatory markers, and the limitations of current imaging techniques in providing proof of inflammation in these regions. Enteseal areas may not be fully assessed on standard clinical examinations, and it is unclear whether lack of tenderness excludes enthesitis. Since the entheses are directly connected to the joints, the source of arthralgia can be considered synovitis, even if it is due to enthesitis. This may lead to underestimation of the presence of enthesitis (10, 12, 16). According to the results of our study, the presence of enthesopathies appears to be associated with age, weight, BMI, symptom duration, and disease activity. Considering that it is both an inexpensive and easily available method, conventional radiography can be used as an auxiliary tool in the evaluation of enteseal abnormalities in patients with SpA, especially in those with advanced age, long symptom duration, high BMI, and detection of tenderness on physical examination. Even though radiography is conditionally recommended in the clinical practice guideline for screening and evaluation of enthesitis in patients with SpA (16), more research is required to define its place in detecting enthesopathies in SpA.

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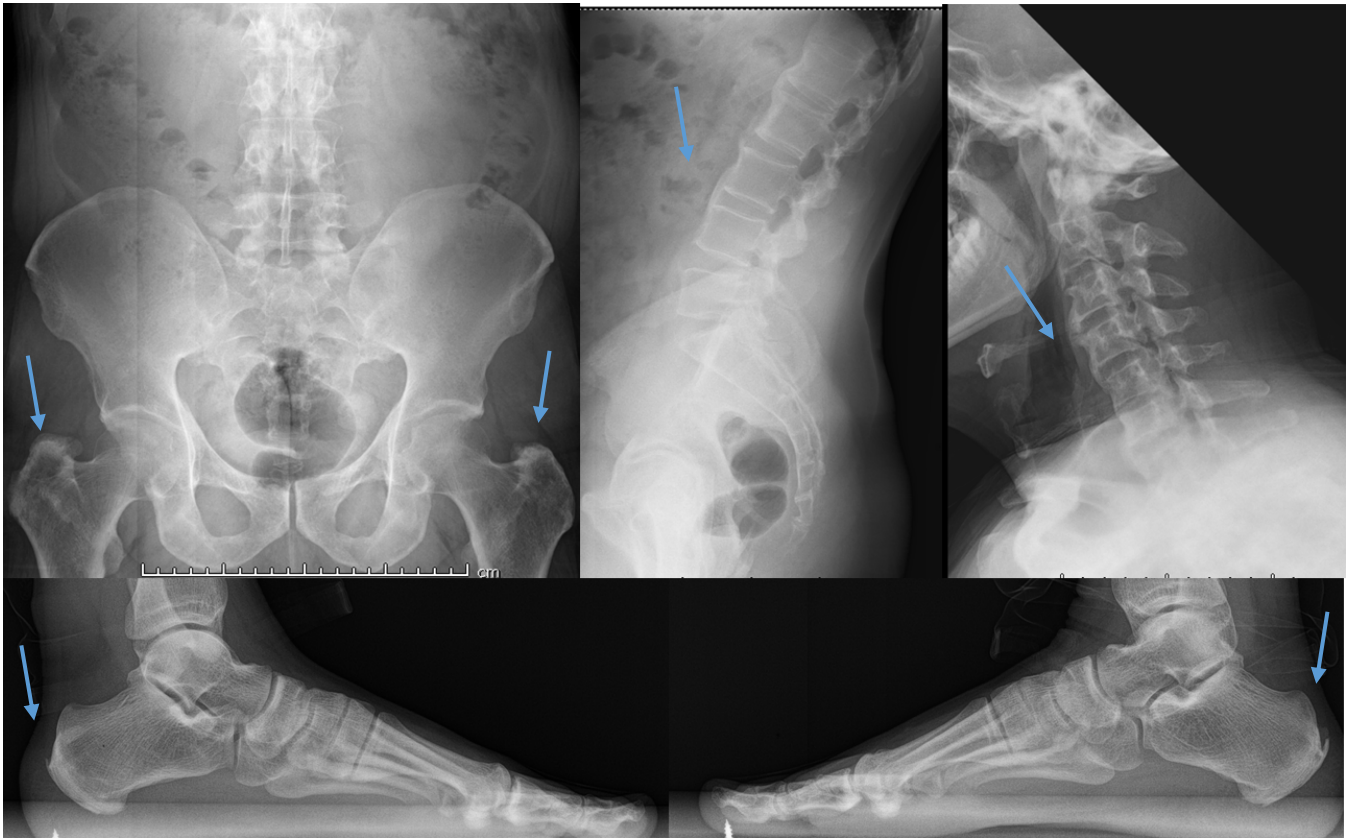


Figure 1. Radiological images of different enthesitis sites of a 46-year-old male patient with delayed diagnosis of axial spondyloarthritis.

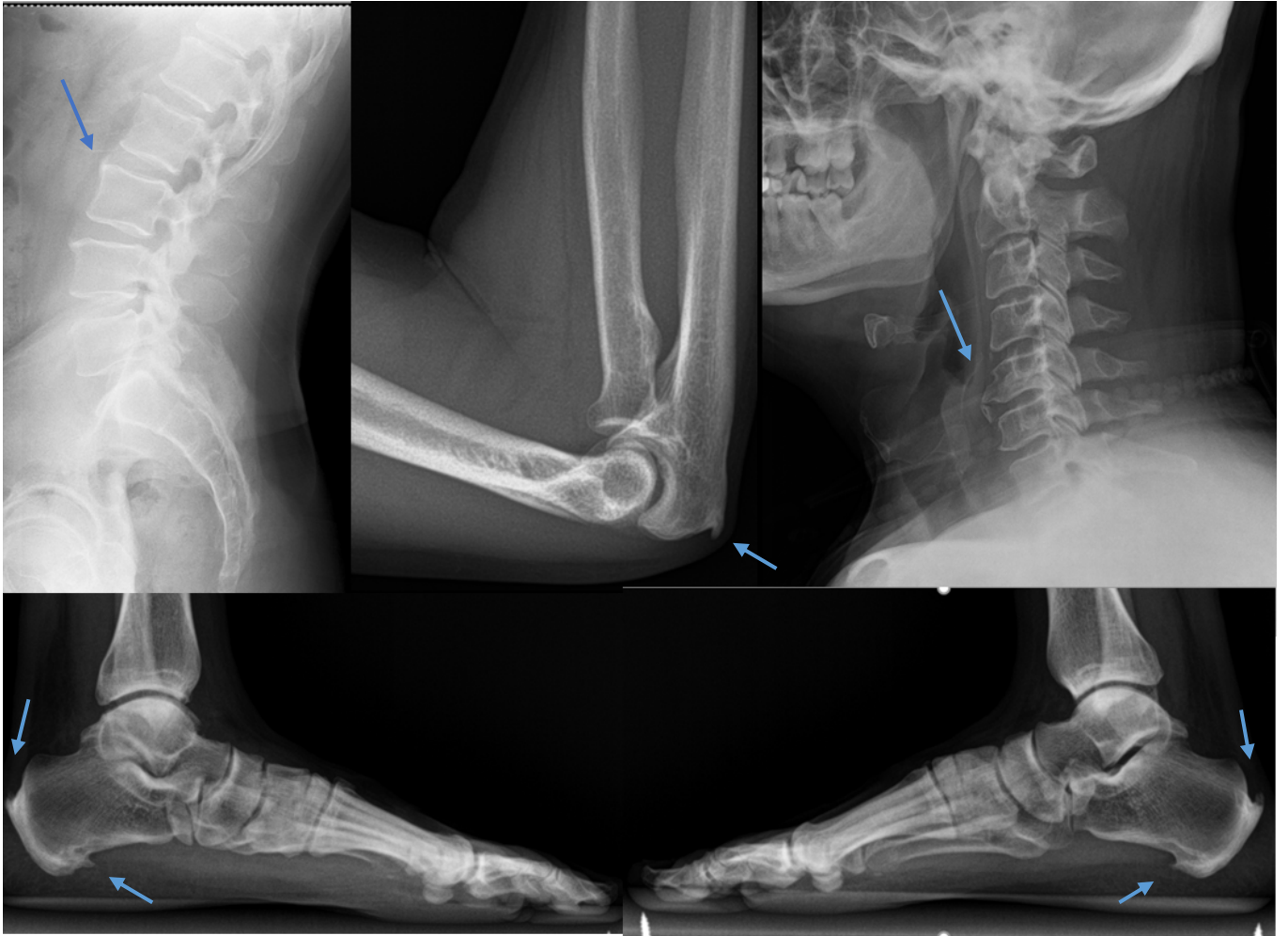


Figure 2. Radiographic images of different enthesis sites of a 50-year-old male patient with delayed diagnosis of axial spondyloarthritis.

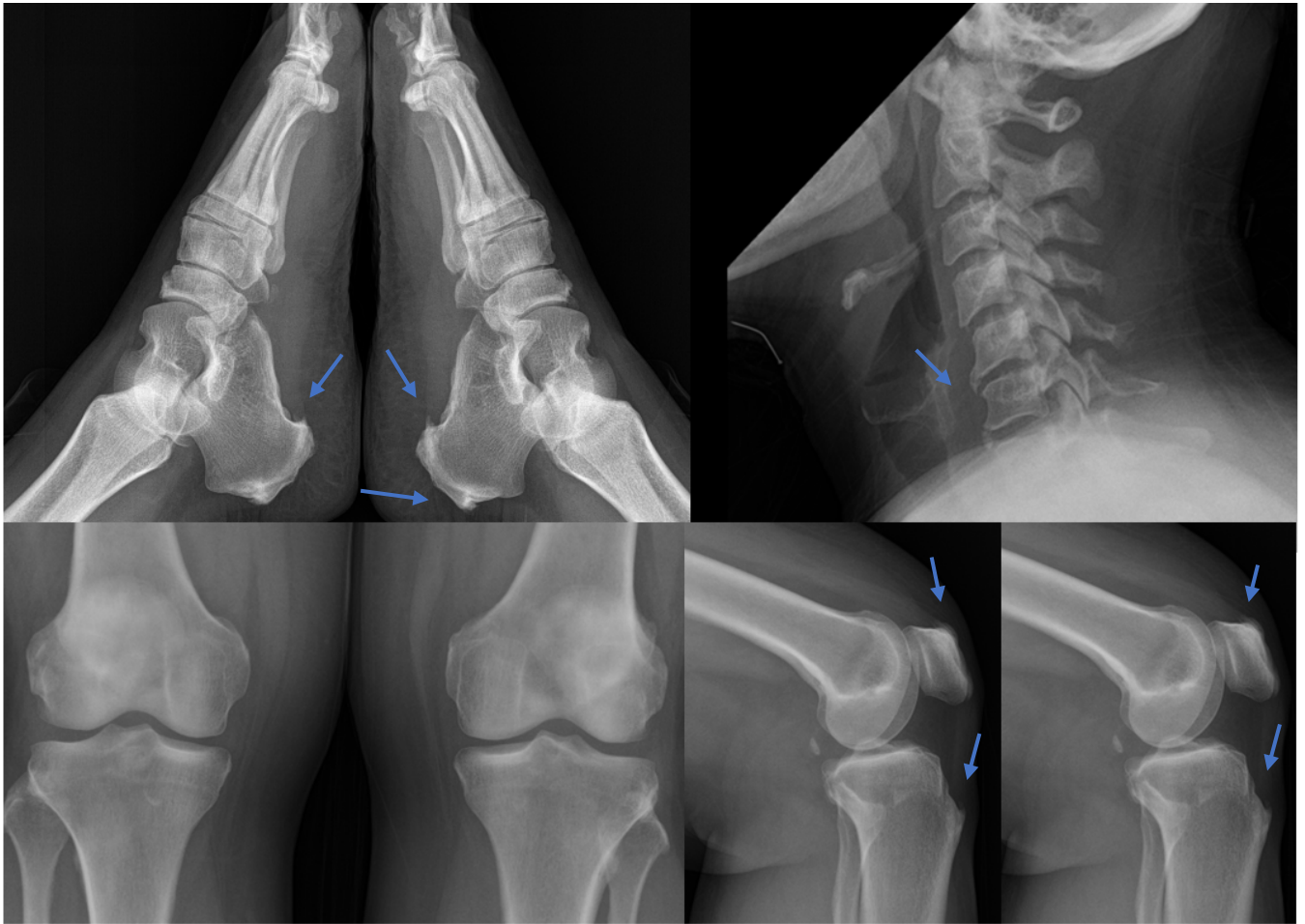


Figure 3. Radiological images of different enthesitis sites of a 40-year-old female patient with axial spondyloarthritis.

Table 1. Demographic and clinical characteristics of the patients.

Variables	Patients (n=242)	Female (n=121)	Male (n=121)	p value
Age (year)	46.12±11.98	46.55±11.56	45.68±12.41	0.570
Weight (kg)	79.60±12.91	75.12±13.04	84.07±11.15	<0.001
Height (cm)	167.64±8.92	161.05±5.84	174.24±6.17	<0.001
Body mass index (BMI)	28.39±4.54	29.06±5.38	27.71±3.41	0.021
Smoking				
No	73.1 (177)	76.9 (93)	69.4 (84)	0.192
Yes	26.9 (65)	%23.1 (28)	30.6 (37)	
Family history				
No	67.8 (164)	57 (69)	78.5 (95)	<0.001
Yes	32.2 (78)	43 (52)	21.5 (26)	
Symptom duration (years)	16.04±10.81	17.0±10.29	15.08±11.26	0.068
Time since diagnosis (years)	2.69±3.47	2.19±2.56	3.20±4.14	<0.001
HLA-B27				
(+)	66.1 (180)	62 (75)	70.2 (85)	0.242
(-)	33.9 (82)	38 (46)	29.8 (36)	
CRP (mg/L)	2.69±3.47	2.27±2.46	2.18±2.91	0.223
BASDAI	3.21±0.77	3.29±0.71	3.13±0.83	0.163
BASFI	2.91±0.83	2.96±0.81	2.85±0.85	0.171
ASDAS-CRP	2.13±1.04	2.23±1.02	2.02±1.06	0.131
BASRI	4.85±2.25	4.55±0.91	5.15±2.51	0.116
MASES	4.26±0.99	4.33±0.95	4.19±1.03	0.208
Achilles enthesopathies				
No	42.6 (103)	44.6 (54)	40.5 (49)	0.516
Yes	57.4 (139)	55.4 (67)	59.5 (72)	
Calcaneal spur				
No	42.6 (103)	40.5 (49)	44.6 (54)	0.516
Yes	57.4 (139)	59.5 (72)	55.4 (67)	

All values are expressed as mean±standard deviation or number and percentage. CRP, C-reactive protein; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional Index; ASDAS-CRP, Ankylosing Spondylitis Disease Activity Score with CRP; BASRI, Bath Ankylosing Spondylitis Radiology Index; MASES, Maastricht Ankylosing Spondylitis Enthesitis Score.

Table 2. Correlation between enthesitis score (the presence of calcaneal spur and/or Achilles enthesopathies) and other parameters.

Variables	Enthesitis score (Achilles enthesopathies+calcaneal spur)	
	r value	p value
Age (year)	0.537	<0.001
Weight (kg)	0.391	<0.001
Body mass index (BMI)	0.396	<0.001
Symptom duration (year)	0.483	<0.001
BASDAI	0.530	<0.001
BASFI	0.531	<0.001
ASDAS-CRP	0.232	<0.001
BASRI	0.435	<0.001
MASES	0.637	<0.001

r, Spearman Correlation Coefficient. BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional Index; ASDAS-CRP, Bath Ankylosing Spondylitis Radiology Index; MASES, Maastricht Ankylosing Spondylitis Enthesitis Score.