Association of physical activity and medication with enthesitis on ultrasound in psoriatic arthritis

Authors: Kim Wervers[1], Irene Herrings[1], Jolanda J Luime[1], Ilja Tchetverikov[2], Andreas H Gerards[3], Johanna M W Hazes[1], Marijn Vis[1]

1. Department of Rheumatology, Erasmus MC, University Medical Centre, Rotterdam, The Netherlands, 2. Department of Rheumatology, Albert Schweitzer Hospital, Dordrecht, The Netherlands, 3. Department of Rheumatology, Sint Franciscus Vlietland Group, Schiedam, The Netherlands

KEY INDEXING TERMS: Enthesitis, Psoriatic Arthritis, Healthy Volunteers, Ultrasound

K. Wervers, Department of Rheumatology, Erasmus MC, University Medical Centre, Rotterdam, The Netherlands

I. Herrings, Department of Rheumatology, Erasmus MC, University Medical Centre, Rotterdam, The Netherlands

J.J. Luime, PhD, Department of Rheumatology, Erasmus MC, University Medical Centre Rotterdam

I. Tchetverikov, MD, PhD, Department of Rheumatology, Albert Schweitzer Hospital, Dordrecht

A.H. Gerards, MD, Department of Rheumatology, Vlietland Hospital, Schiedam

J.M.W. Hazes, MD, PhD, Department of Rheumatology, Erasmus MC, University Medical Centre Rotterdam

M. Vis, MD, PhD, Department of Rheumatology, Erasmus MC, University Medical Centre Rotterdam

Corresponding author: Marijn Vis, Department of Rheumatology, Erasmus MC, University Medical Centre, PO Box 2040, 3000 CA Rotterdam, The Netherlands. E-mail: marijn.vis@erasmusmc.nl

SHORT RUNNING HEAD: Enthesitis Ultrasound in PsA

ABSTRACT

Objective: Enthesitis is a manifestation of psoriatic arthritis (PsA), but its symptoms are difficult to interpret clinically. We investigated the associations of ultrasonographic changes in entheses with clinical characteristics in PsA patients, and compared enthesis changes of PsA patients aged 35 to 60 with healthy volunteers of that age.

Methods: Consecutive PsA patients participated in this cross-sectional study, irrespective of enthesitis complaints and age. We collected data about complaints, physical activity and activity avoidance, medication and clinical enthesitis. Inflammatory and structural enthesis changes were scored with the modified MAdrid Sonographic Enthesitis Index (MASEI). Among all PsA patients, associations between ultrasound scores and clinical characteristics were investigated using linear regression. We compared ultrasound scores of healthy volunteers and PsA patients aged 35-60 years using Wilcoxon rank tests.

Results: Eighty-four PsA patients and 25 healthy volunteers participated. In PsA patients, we found a small association between higher inflammatory modified MASEI score and higher age (β:0.07, 95% CI:0-0.13) and current use of biologicals (β:1.56 95% CI 0.16-2.95). Patients reporting avoiding activities had significantly lower inflammatory modified MASEI scores (β:-1.71, 95% CI:-3.1;-0.32) than those who did not. The PsA patients aged 35-60 (n=50) had similar inflammatory scores as healthy volunteers but higher structural scores (median 6 vs. 2, p=0.01).

Conclusion: Within PsA patients, avoiding physical activity, younger age and not using biologicals was associated with less entheses inflammation. PsA patients and healthy volunteers aged 35 to 60 years displayed similar levels of inflammatory changes of the entheses, but PsA patients had more structural damage.

INTRODUCTION

Psoriatic arthritis (PsA) is a chronic inflammatory musculoskeletal disease that belongs to the group of spondyloarthropathies. It has a heterogeneous presentation of arthritis, psoriasis, spondylitis, dactylitis and enthesitis.(1, 2) Enthesitis is one of the distinguishing features of spondyloarthropathies and is defined as inflammation of tendon, ligament or joint capsule insertion. Enthesitis is found at clinical examination in a third of PsA patients(3), but tenderness of the enthesis does not necessarily have an inflammatory origin. A better technique is needed to distinguish PsA-related inflammatory enthesitis from other enthesiopathies, such as metabolic, degenerative and mechanical processes.(4)

With ultrasound, inflammatory and structural changes of the entheses can be assessed (5) and quantified with a composite ultrasound score, such as the MAdrid Sonographic Enthesitis Index (MASEI).(6) In a previous study we evaluated the value of use of the MASEI in an extreme comparison; we compared patients newly diagnosed with PsA, patients with established disease and young healthy volunteers.(7) We found that increased thickness of knee entheses and a subtle Power Doppler (PD) signal were present in all groups, even in young healthy volunteers. We therefore modified the MASEI score: we excluded knee enthesis thickness (i.e. quadriceps and both patellar tendon insertions) from the evaluation and graded PD severity. This modified MASEI score showed a good discrimination between entheses of patients and those of young healthy volunteers. As the number of enthesis abnormalities varied within all groups, we suspected other factors than PsA-related inflammation could cause these ultrasound abnormalities. Previous studies, for example, showed that higher age and higher body mass index (BMI) were associated with more entheseal abnormalities on ultrasound both in PsA patients and in healthy volunteers.(8, 9) Studies in healthy volunteers showed that physical activity is also associated with changes in entheses on ultrasound(10, 11), although this is not confirmed in PsA, to our knowledge. We, therefore, aimed to investigate associations between modified MASEI scores and clinical characteristics in an average PsA

population. In addition we aimed to compare the modified MASEI scores of PsA patients and healthy volunteers aged 35 to 60.

METHODS

Patients and Setting

Consecutive patients of all ages with established PsA for at least two years attending the rheumatology clinic were eligible to participate, irrespective of disease activity or complaints. Patients were recruited from three outpatient clinics in The Netherlands (the academic hospital Erasmus MC, and the general hospitals Vlietland hospital and Albert Schweitzer hospital) between May and August 2016. Healthy volunteers were invited if they were aged 35-60 years, without a history of any of the following: any rheumatic disease, Crohn's disease, uveitis, familial hypercholesterolemia or diabetes. Written informed consent was obtained from all participants according to the Declaration of Helsinki. The study was approved by the local medical research ethics committee of Erasmus MC, MC, University Medical Centre Rotterdam, The Netherlands (MEC-2012-549).

Data collection

In a structured interview, patients answered questions about their disease duration, physical activity and avoidance of activity. Regarding physical activity, patients were asked whether they exercised regularly. With respect to avoidance, patients were specifically asked whether they avoided activities due to complaints or fear of complaints in daily life during exercise, work, household activities and chores. We scored avoidance when patients reported avoiding activities because of pain or fear of pain. Fulfilment of Classification criteria for PsA (CASPAR) criteria(12) and medication use was obtained from chart review.

Data collected during physical examination were height, weight, 66 swollen joint count, 68 tender joint count, enthesitis at clinical examination (Leeds Enthesitis Index, LEI and Maastricht Ankylosing Spondylitis Enthesitis Score, MASES), and psoriasis area and severity index (PASI).

Ultrasound examination was performed directly after clinical examination by a sonographist trained in enthesis sonography (IH), who was blinded for clinical information. Patients were instructed not to communicate any clinical information to the sonographist by the researchers who conducted the interview and physical examination (MM, KW). The six MASEI entheses and the lateral epicondyle were bilaterally examined using an Esaote MyLab60 with linear probes LA435 (6-18 MHz; Doppler frequency of 8.3 MHz, pulse repetition frequency of 750 Hz and a wall filter of 3) and LA532 (4-13 MHz; 6,3 MHz, 750 Hz and a wall filter of 4). The former was used for entheses of the upper limbs and the latter for the entheses of lower limbs. In each site, we scored calcifications, erosions, structural changes, thickness, Power Doppler (PD) signal and bursitis. Only presence of PD signal within 2 mm of the cortex was scored. Patients were positioned according to the MASEI, but with the knee flexed at approximately 30° (rather than 70°) and resting on a pillow to ensure relaxing of the quadriceps muscle. The lateral epicondyle was examined in 90° flexion and a cut off of 4.2 mm was used in this enthesis.(13) If a PD signal was present, images of the severest PD signal were saved and scored by KW and IH, who had an interrater agreement of 93% (intraclass correlation coefficient). Besides the original MASEI score, we calculated the modified MASEI by excluding the knee entheses thickness (i.e. quadriceps and proximal and distal patellar tendon insertion) and grading of PD signal. All abnormalities were recorded during ultrasound evaluation, and PD signal was graded by a second scorer (KW) on the static images. PD signal intensity was scored: 0: absent, 1: 1 spot, 1.5: 2 spots, 2: confluent signal, 3: confluent severe signal (Supplemental Figure 1). Absolute agreement was 93% and weighted Cohen's kappa using linear weights was 0.92. We distinguished an inflammatory component (sum of points for increased thickness, bursitis and PD signal) and structural component (sum of points for structure, calcifications/enthesophytes and erosions).

Statistical analysis

Within the total PsA population, the association between clinical characteristics, and 1) inflammatory modified MASEI and 2) structural modified MASEI were investigated using multiple linear regression analyses. Using a forward selection ($p<0.30$), the following independent variables were tested: age, BMI, disease duration (square-transformed), current use of disease modifying antirheumatic drugs (DMARDs), current use of nonsteroidal anti-inflammatory drugs (NSAIDs), current use of biologicals, avoidance of activities, exercise and enthesitis at clinical examination. This was done for both inflammatory modified MASEI and structural modified MASEI as dependent variable. The latter was transformed ($(y+1)^2$) because of its skewed distribution. Modified MASEI scores of a subgroup of patients between the age of 35 and 60 and of the healthy volunteers of the same age-range were compared using the Wilcoxon rank-sum test.

RESULTS

In total, 84 consecutive patients with established PsA participated; mean age was 55 years (standard deviation, SD 11, age range 26 to 76), 45 (54%) were male and mean BMI was 27 (SD 5). Median disease duration was 8 years. Disease activity was mild in our usual care consecutive cohort: median swollen joint count was 0 (interquartile range, IQR 0-2) and median tender joint count 3 (IQR 0-7). Median LEI score was 0.5 (IQR 0-2). Forty patients (48%) reported to exercise regularly and avoiding activities was reported by 17 (43%) of those patients with regular exercise. Among patients not exercising regularly, avoidance of any physical activity was reported by 28 (64%, table 1).

Association between ultrasound scores and clinical characteristics

Within patients, a small association was found between a higher inflammatory modified MASEI score and 1) higher age (β 0.07, 95% CI 0-0.13) and 2) current use of biologicals (β 1.56 95% CI 0.16-2.95). Patients that reported to avoid activities had significantly lower inflammatory modified MASEI scores (β -1.71, 95% CI -3.1;-0.32, table 2). Higher age was also associated with a higher score on structural modified MASEI (β 0.03, 95% CI 0.01-0.05, p=0.001, table 3). Current use of NSAIDs or DMARDs,

regularly exercising, gender and enthesitis at clinical examination were not associated with any of the modified MASEI scores.

Enthesis ultrasound scores

Total ultrasound scores of patients aged 35-60 years were compared with those of 25 healthy volunteers in the same age range. Healthy volunteers had a mean age of 47 (SD 6) years, 12 were male (48%) and average BMI was 25 (SD 4, Supplemental Table 1). The original median (IQR) MASEI scores of 50 PsA patients aged 35-60 years (14 (9-21)) were comparable to those of the 25 healthy volunteers (13 (9-18), Table 4). The prevalence of each abnormality in the total PsA group, in the subgroup aged 35 to 60, and in the healthy volunteer group is shown in Table 5. After excluding knee enthesis thickness and grading PD score, the resulting modified MASEI scores were 11 (IQR 6.5-15) in patients and 7.5 (IQR 5-9, p=0.01) in healthy volunteers. The inflammatory contribution (i.e. thickness, bursitis and PD signal) to this modified MASEI was similar in patients (5 (IQR 2-7)) and healthy volunteers (3.5 (IQR 2-5.5)). The structural contribution (i.e. calcification, erosion and structural changes) was significantly higher in patients (6 (IQR 3-10)) than in healthy volunteers (2 (IQR 1-6, p=0.01)). Presence of PD signal was similar in patients and healthy volunteers.

DISCUSSION

We found that in a PsA population not selected based on complaints of the entheses, higher age and the current use of biologicals were associated with higher inflammatory scores, while patients reporting avoidance of activity had lower inflammatory scores. More structural changes in PsA was associated with higher age only. No effects of BMI, current NSAIDs use, regular exercise, gender and clinical symptoms of enthesitis on ultrasound were seen, possibly because we did not have the power to detect a small effect. Inflammatory changes of the entheses occurred as often as in healthy volunteers of the same age. The PsA patients did however have twice as many structural changes of the entheses.

The finding that regular exercise was not related to ultrasound changes but avoidance of activity was related seems contradictory. This may relate to the way we recorded avoidance, namely in more domains than only sport activities and patients could both report avoiding activity and exercising regularly. In the statistical analysis ultrasound changes were stronger associated with avoidance than with physical activity. Physical activity is probably both influencing and influenced by pathology of tendons and entheses, which makes the interpretation of sonographic abnormalities difficult. Some patients avoiding physical activity might have suffered from enthesitis and consequently altered their behaviour. The relation between physical activity and sonographic enthesis changes has not been shown in PsA before, although some work has been done in athletes. Changes of tendons and entheses on ultrasound have been observed in the patellar tendon of athletes immediately after their high-level badminton matches(10), and after they ran a marathon(11). Their respective strain on the tendon might be different, but in both, some reaction after physical exercise was seen on ultrasound. This could be a physiological response or an early sign of a pathological reaction: other studies have shown that abnormalities on ultrasound could precede clinical manifestations of overuse injuries in healthy athletes.(14, 15) In contrast, a study assessing the MASEI scores of 30 athletes (who were running or playing soccer for at least 6 hours per week) and 29 non-athletes (who were playing a sport less than 1 hour per week) were not able to show a difference.(16) These data suggest that in a healthy situation tendons and entheses have adapted to the regular level of physical activity but do respond to a change in physical activity. We found a similar relation in PsA patients, though we did not directly study the modifying effect of PsA by comparing the relation with that in healthy volunteers. Longitudinal studies are needed to investigate whether the response of entheses to physical activity is altered in PsA.

Comparable inflammatory scores of healthy volunteers and PsA patients suggest that ultrasound evaluation of the enthesis is of limited value in screening for inflammation. This was also concluded by Groves et al., who compared MRI and ultrasound evaluation of the elbow in patients with PsA and rheumatoid arthritis who reported elbow pain.(17) In a third of cases, inflammation could be seen on

MRI but not on ultrasound. The larger extent in which structural changes were present in PsA patients in our study suggests that patients have been subject to more chronic inflammation of the entheses than healthy volunteers of similar age.

The higher occurrence of inflammatory changes of the entheses in patients using biological DMARDs was an interesting but unexpected finding as biological DMARDs are recommended in the treatment of enthesitis in PsA. One explanation is that patients on biological DMARDs are a selected population with more severe inflammation. Michelsen et al. investigated Achilles enthesitis in PsA patients and found use of biologicals was associated with more structural damage, but not with inflammatory activity.(18) This contradicts our study, as we found an association with inflammatory activity and not with structural damage. A second possible explanation is that tendons and entheses recover at a slow rate and not all patients may have used biological DMARDs for a long enough period. A study in ankylosing spondylitis showed that inflammatory ultrasound lesions did not change after six months of tumor necrosis factor blocking therapy(19). In a similar study, Ayden et al. however did find a decrease in ultrasound lesions after two months of therapy and so did Naredo et al. after six months of follow up.(20, 21) Similarly, a study using magnetic resonance imaging in axial spondyloarthritis found a decrease in enthesitis after two years of treatment with etanercept.(22) A third explanation is that the effect of biological DMARDs on enthesitis is heterogeneous and depends on the type of treatment (i.e. TNF inhibitors, anti-IL17 or anti-IL12/IL23).

A limitation of our study is its cross-sectional design, which makes the interpretation of the association between clinical symptoms and ultrasound scores difficult. The relation between physical activity and enthesitis might be subject to information bias and the exact impact of physical activity on entheses is better investigated in an experimental setting. For example, the reporting of physical activity and avoiding of physical activity might be influenced by a history of enthesitis and different adaptive behaviour and coping strategies. Second, physical activity and in particular long-term effects of physical activity are difficult to measure and the measurement of self-reported physical activity

could be biased. Third, this study has an exploratory nature, in which multiple factors of influence were tested. The models were fitted to this established usual care population with relatively low disease activity and use of NSAIDs and biologicals by the majority. For these reasons, future studies – preferably longitudinal studies – are needed to confirm these results.

In conclusion, in this cross-sectional study, avoiding physical activity, younger age and not using biological DMARDs were associated with less inflammation of the entheses. PsA patients and healthy volunteers aged 35 to 60 years display similar levels of inflammatory changes of the entheses, but PsA patients had more structural damage. The only way to understand these associations is to investigate changes of entheses on ultrasound in prospective longitudinal studies.

ACKNOWLEDGEMENTS

We gratefully thank all rheumatologists, patients and healthy volunteers that participated in this study and Marlies Moed for her help in data collection.

REFERENCES

1. Gladman DD, Antoni C, Mease P, Clegg DO, Nash P. Psoriatic arthritis: Epidemiology, clinical features, course, and outcome. Ann Rheum Dis 2005;64 Suppl 2:ii14-7.
2. Mease PJ. Psoriatic arthritis: Update on pathophysiology, assessment and management. Ann Rheum Dis 2011;70 Suppl 1:i77-84.
3. Polachek A, Li S, Chandran V, Gladman DD. Clinical enthesitis in a prospective longitudinal psoriatic arthritis cohort: Incidence, prevalence, characteristics, and outcome. Arthritis Care Res (Hoboken) 2017;69:1685-91.
4. Mandl P, Niedermayer DS, Balint PV. Ultrasound for enthesitis: Handle with care! Ann Rheum Dis 2012;71:477-9.
5. Terslev L, Naredo E, Iagnocco A, Balint PV, Wakefield RJ, Aegerter P, et al. Defining enthesitis in spondyloarthritis by ultrasound: Results of a delphi process and of a reliability reading exercise. Arthritis Care Res (Hoboken) 2014;66:741-8.
6. de Miguel E, Cobo T, Munoz-Fernandez S, Naredo E, Uson J, Acebes JC, et al. Validity of enthesis ultrasound assessment in spondyloarthropathy. Ann Rheum Dis 2009;68:169-74.
7. Wervers K, Vis M, Rasappu N, van der Ven M, Tchetverikov I, Kok MR, et al. Modification of a sonographic enthesitis score to differentiate between psoriatic arthritis and young healthy volunteers. Scand J Rheumatol 2018:1-4.
8. Eder L, Jayakar J, Thavaneswaran A, Haddad A, Chandran V, Salonen D, et al. Is the madrid sonographic enthesitis index useful for differentiating psoriatic arthritis from psoriasis alone and healthy controls? J Rheumatol 2014;41:466-72.
9. Abate M, Di Carlo L, Salini V, Schiavone C. Metabolic syndrome associated to non-inflammatory achilles enthesopathy. Clin Rheumatol 2014;33:1517-22.

10. Boesen AP, Boesen MI, Koenig MJ, Bliddal H, Torp-Pedersen S, Langberg H. Evidence of accumulated stress in achilles and anterior knee tendons in elite badminton players. Knee Surg Sports Traumatol Arthrosc 2011;19:30-7.
11. Proft F, Grunke M, Reindl C, Mueller F, Kriegmair M, Leipe J, et al. The influence of long distance running on sonographic joint and tendon pathology: Results from a prospective study with marathon runners. BMC Musculoskelet Disord 2016;17:272.
12. Taylor W, Gladman D, Helliwell P, Marchesoni A, Mease P, Mielants H, et al. Classification criteria for psoriatic arthritis: Development of new criteria from a large international study. Arthritis Rheum 2006;54:2665-73.
13. Lee MH, Cha JG, Jin W, Kim BS, Park JS, Lee HK, et al. Utility of sonographic measurement of the common tensor tendon in patients with lateral epicondylitis. AJR Am J Roentgenol 2011;196:1363-7.
14. Comin J, Cook JL, Malliaras P, McCormack M, Calleja M, Clarke A, et al. The prevalence and clinical significance of sonographic tendon abnormalities in asymptomatic ballet dancers: A 24-month longitudinal study. Br J Sports Med 2013;47:89-92.
15. Hirschmuller A, Frey V, Konstantinidis L, Baur H, Dickhuth HH, Sudkamp NP, et al. Prognostic value of achilles tendon doppler sonography in asymptomatic runners. Med Sci Sports Exerc 2012;44:199-205.
16. Lanfranchi MA, Leluc O, Tavano A, Wormser C, Morange S, Chagnaud C, et al. Are ultrasound findings similar in patients with axial spondyloarthritis and in athlete entheses? J Rheumatol 2017;44:609-12.
17. Groves C, Chandramohan M, Chew NS, Aslam T, Helliwell PS. Clinical examination, ultrasound and mri imaging of the painful elbow in psoriatic arthritis and rheumatoid arthritis: Which is better, ultrasound or mr, for imaging enthesitis? Rheumatol Ther 2017;4:71-84.
18. Michelsen B, Diamantopoulos AP, Soldal DM, Hammer HB, Kavanaugh A, Haugeberg G. Achilles enthesitis defined by ultrasound is not associated with clinical enthesitis in patients with psoriatic arthritis. RMD Open 2017;3:e000486.
19. Wink F, Bruyn GA, Maas F, Griep EN, van der Veer E, Bootsma H, et al. Ultrasound evaluation of the entheses in daily clinical practice during tumor necrosis factor-alpha blocking therapy in patients with ankylosing spondylitis. J Rheumatol 2017;44:587-93.
20. Naredo E, Batlle-Gualda E, Garcia-Vivar ML, Garcia-Aparicio AM, Fernandez-Sueiro JL, Fernandez-Prada M, et al. Power doppler ultrasonography assessment of entheses in spondyloarthropathies: Response to therapy of entheseal abnormalities. J Rheumatol 2010;37:2110-7.
21. Aydin SZ, Karadag O, Filippucci E, Atagunduz P, Akdogan A, Kalyoncu U, et al. Monitoring achilles enthesitis in ankylosing spondylitis during tnf-alpha antagonist therapy: An ultrasound study. Rheumatology (Oxford) 2010;49:578-82.
22. Althoff CE, Sieper J, Song IH, Weiss A, Diekhoff T, Haibel H, et al. Comparison of clinical examination versus whole-body magnetic resonance imaging of enthesitis in patients with early axial spondyloarthritis during 3 years of continuous etanercept treatment. J Rheumatol 2016;43:618-24.

	PsA patients (n=84)
Age	55 ± 11
Male	45 (54)
BMI	27 ± 5
Disease duration, years	8 (5-12)
Fulfilling CASPAR criteria	81 (96)
Swollen joint count (66)	0 (0-2)
Tender joint count (68)	3 (0-7)
LEI	0.5 (0-2)
MASES	1 (0-2)
PASI[a]	0.6 (0-2.8)
Regularly exercising	40 (48)
Avoidance	45 (55)
Current medication use	
NSAID	31 (37)
DMARD	64 (76)
Prednisone	1 (1)
biological DMARD	40 (48)

Table 1. Demographic and Clinical Characteristics of Patients. Data presented as mean ± standard deviation, n (%) or median (interquartile range). PsA: psoriatic arthritis; BMI: body mass index; CASPAR: Classification criteria for psoriatic arthritis; LEI: Leeds enthesitis index; MASES: Maastricht ankylosing spondylitis enthesitis score; PASI: psoriasis area and severity index; NSAID: non-steroidal anti-inflammatory drug; DMARD: disease modifying anti-rheumatic drug. [a]excluding 1 patient without a history of psoriasis

	β	(95% CI)	P
age	0.07	(0;0.13)	0.050
BMI	0.13	(-0.01;0.27)	0.063
(duration)2	0.04	(-0.73;0.82)	0.909
DMARD no vs. yes	1.23	(-0.4;2.87)	0.137
biological no vs. yes	1.56	(0.16;2.95)	0.029
avoidance no vs. yes	-1.71	(-3.1;-0.32)	0.017

Table 2. Association between ultrasound scores (inflammatory modified MASEI) and clinical characteristics Linear regression of 84 PsA patients. BMI: body mass index; DMARD: disease modifying antirheumatic drug

	β	(95% CI)	P
age	0.03	(0.01;0.05)	0.001
BMI	0.04	(0;0.08)	0.054
$(duration)^2$	0.11	(-0.1;0.32)	0.302

Table 3. Association between ultrasound scores (structural modified MASEI) and clinical characteristics Linear regression of 84 PsA patients. Transformation of structural modified MASEI: $(y+1)^2$. BMI: body mass index

	Total PsA patients (n=84)	PsA patients aged 35-60 years (n=50)	Healthy volunteers aged 35-60 years (n=25)	p-value PsA vs. HV aged 35-60 years
MASEI	15.5 (11-22)	14 (9-21)	13 (9-18)	0.39
Modified MASEI	12 (7.3-17)	11 (6.5-15)	7.5 (5-9)[a]	0.005
Inflammatory modified MASEI	5 (2.8-7.5)	5 (2-7)	3.5 (2-5.5)	0.16
Structural modified MASEI	7 (3-10)	6 (3-10)	3 (1-6)	0.005
PD				
PD in any enthesis	74 (88)	44 (88)	22 (88)	1.00
PD in two or more enthesis	47 (56)	27 (54)	17 (68)	0.25
Confluent PD in any enthesis	35 (42)	20 (40)	9 (36)	0.74
Severe PD in any enthesis	7 (8)	4 (8)	0 (0)	0.29
average PD score[b]	1.5 (1.3-1.8)	1.5 (1.3-1.7)	1.5 (1.3-1.5)	0.44

Table 4. Comparison of enthesitis ultrasound scores between patients with psoriatic arthritis and healthy volunteers. Data presented as median (interquartile range) or n (%). MASEI: Madrid sonographic enthesitis index; modified MASEI: MASEI with lateral epicondyle, excluding knee enthesis thickness and grading of Power Doppler, PD: Power Doppler. [b]in 74 and 44 patients and 22 healthy volunteers where PD was present

	Structure			Thickness			Erosion			Calcification*			PD signal			Bursitis		
	A	B	C	A	B	C	A	B	C	A	B	C	A	B	C	A	B	C
Lateral epicondyle tendon	1	1		53	50	30	4	3		49	41	16	26	30	18			
Triceps tendon	1	2		13	11		2	3		24	23	2	1	2	2			
Quadriceps tendon				70	64	60				65	66	48	34	32	42			
Proximal patella tendon	1	1		74	72	68	1	1		8	7	2	11	10	12			
Distal patella tendon				96	98		1	1		10	8	14	53	30	36			
Achilles tendon	1	1		10	12	2	2	3		52	55	42	5	4	4			
Plantar fascia				33	23	12				1								

Table 5 MASEI score per component per enthesis location. A = total PsA group, B = PsA of 35 to 60 years of age, C = healthy volunteers of 35 to 60 years of age. Data shown as number of abnormalities (%) per group. *Calcification is expressed as the number of tendons with a score >0