## ORIGINAL ARTICLE

# We should not forget the foot: relations between signs and symptoms, damage, and function in rheumatoid arthritis

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Abstract We studied rheumatoid arthritis (RA) patients with foot complaints to address the associations between clinical signs and symptoms, radiographic changes, and function in connection with disease duration. Secondly, we describe the contribution of several foot segments to the clinical presentation and function. In 30 RA patients with complaints of their feet, attributed to either signs of arthritis and/or radiographic damage, we compared radiographic, ultrasound, clinical, and functional parameters of the feet and ankle. Pain and swelling of the ankle were correlated weakly but statistically significantly with limitation and disability (0.273 to 0.293) as measured on the 5-Foot Function Index (FFI). The clinical signs of the forefoot joints did not influence any of the functional outcome measures. Radiographic scores for both forefeet (SvdH) and hindfeet (Larsen) were correlated with the total Health Assessment Questionnaire Disability Index (HAQ DI) and the 5-FFI limitation subscale. Pain and disease duration, more than radiographic damage, influence the total HAQ

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H. Baan (🖂) Department of Rheumatology, ZGT, Locatie Twenteborg Ziekenhuis, Postbus 7600, 7600 SZ Almelo, The Netherlands e-mail: h.baan@a1.nl DI significantly. With the progression of time, structural damage and function of the rheumatic foot worsen in RA patients. Pain and swelling of the ankle contribute more to disability than radiographic damage of the foot and ankle.

**Keywords** Ankle · 5-FFI · Foot · Function · HAQ · Radiographic damage · Rheumatoid arthritis

## Introduction

In rheumatic conditions, especially rheumatoid arthritis (RA), signs and symptoms of the feet are common. The majority of RA patients present with arthritis of the feet and 20% of them have radiographic damage at the time of diagnosis [1]. In RA, both forefoot and hindfoot involvement is associated with disease duration and lead to severe impairment and disability [2, 3]. After 6 years of disease duration, up to 50% of the patients have considerable radiographic damage in the ankle and the tarsus [4]. Despite the extent of the problem, the rheumatoid foot is neglected. Although in the last few years some scientific interest has arisen, there is still limited interest in the foot in RA in the clinic possibly causing under treatment [1]. In this study, we examined patients suffering from RA and common foot complaints to investigate the associations between clinical signs and symptoms, structural damage, and function in connection with disease duration. Secondly, we explored the contribution of several foot segments to the clinical presentation and function.

## Patients and methods

We performed a cross-sectional observational study. Thirty consecutive RA patients of the outpatient clinic of the

Arthritis Centre Twente were recruited. To be included, patients had signs or symptoms of arthritis and/or radiographic damage of the feet or ankles due to RA. They had to meet the 1987 ACR criteria for RA. The local ethical committee approved this study and a written informed consent was obtained from each patient.

The following demographic and clinical variables were collected: age, sex, disease duration, total number of used DMARDS, rheumatoid factor DAS 28 [5], and painful or swollen joints in the foot.

All patients underwent ultrasound investigation of the feet and ankles to measure synovitis (0 to 3), effusion (0 to 3), and power Doppler (PDUS) signals (0 to 3) according to the method described by Szkudlarek [6]. The following joints were examined: the tibiotalar joint, the subtalar joint, the talonavicular joint, and the five metatarsophalangeals (MTPs). An experienced rheumatologist, who had undertaken specific postgraduate training in ultrasonography, performed the ultrasound investigation on a Logic 9 (GE) with a 9–13 MHz linear probe. To simplify the analysis, a total PDUS score was calculated for the MTPs as well as for the hindfoot joints by adding up the PDUS of the individual joints. This was also done for total synovitis, total effusion, and total erosion score.

To assess radiological structural damage, two experienced readers (WD, HB) read the radiographs of the feet. According to the method, Sharp/van der Heijde, each side of the MTP or IP joint was scored for erosions from 0 to 5 with a maximum of 10 for both sides of the joint, and for joint space narrowing from 0 to 4 with a maximum of 4 per joint. For the total Sharp/van der Heijde score, the erosions and joint space narrowing scores were added. The maximum total score for both feet adds up to 168 [7].

In addition, we read the tibiotalar joint, the subtalar joint, and the talonavicular joint following the Larsen method, in which erosions and joint space narrowing as well as other signs of inflammation are expressed in one score with a range from 0 (normal) to 5 (total mutilation of the joint). The scoring is based on the comparison with the standard film series as described by Larsen [8].

In each patient, we measured the Joint Alignment and Motion (JAM) scale of feet and ankle according to the description of Spiegel et al. [9]. It consists of a five-point scale for each joint. A score of 0 represents a normal range of motion (ROM) and alignment, a score of 1, a 0% to 5% decrease in ROM or malalignment, a score of 2, a 6% to 25% decrease in ROM or mild malalignment, a score of 3, a 26% to75% decrease in ROM or joint subluxation, and a score of 4, a 76% to 100% decrease in ROM or joint fusion or joint dislocation. The JAM score for an individual joint represents the most severe or limiting aspect of either motion or alignment.

Function was measured by the following variables: Health Assessment Questionnaire (HAQ), Arthritis Impact Measurement Scales (AIMS), and 5-Foot Function Index (5-FFI). The HAO has been developed by Fries et al. and was adapted for the Dutch population [10]. The questionnaire consists of eight categories, which represent the activities of daily living, and for each category, there are two to four questions. The responses are scored on a fourpoint scale: 0 without difficulty; 1 with some difficulty; 2 with difficulty; and 3 impossible. The questionnaire has a final column in which respondents can indicate the use of any aid or device. The use of any of these devices is scored by at least a 2. The highest score for each of the eight categories is taken as the score for that category. The final score of the questionnaire is the averaged score of all the categories and ranges between 0 and 3.

The AIMS score is a widely used instrument and has been adapted and validated for the Dutch language and culture [11]. The score consists of 77 items divided into 12 scales. These 12 scales can be combined into five components: physical health, psychological health, symptoms, social interaction, and work. The scales vary from 0 (good health) to 10 (bad health). The components for psychological health and social interaction and work were used to describe psychosocial functioning.

The 5-FFI is a self-administered index consisting of 23 items divided into three scales (Limitation, Pain, and Disability). We used the validated five-point Dutch language version [12]. The items of the FFI-5pt are identical to those of the FFI but are rated on a five-point visual rating scale ranging from "never" (0) to "always" [4] on the Limitation scale, "no pain" (0) to "intense pain" [4] on the Pain scale, and "no difficulty" (0) to "impossible" [4] on the Disability scale. To calculate the definitive scale scores, the item scores are summed, divided by the maximum possible sum of the item scores, and then multiplied by 100. The total score is the mean of the three scale scores [12].

*Statistical analysis* The association between the signs, symptoms, damage, and function parameters were calculated using Spearman's correlation. Afterwards, we performed regression analysis in order to assess the most important variables that predict the functional outcome (HAQ) in our model. For the data analysis, we used the Statistical Package for the Social Sciences (SPSS 16.0).

### Results

Thirty patients were included, of whom 25 were female. The mean age was 54 years, and median disease duration was 8 years. Twenty had a positive rheumatoid factor. The median HAQ DI was 1.18, and Larsen and Sharp/van der Heijde scores were 1.0 and 4.0, respectively.

Table 1 presents Spearman's correlation coefficients of the correlation between clinical signs and function. Clinical signs were the presence of either swelling or pain as a sign of joint inflammation. Pain and swelling of the ankle showed weak but statistically significant correlation coefficients between 0.273 and 0.293 with limitation and disability, measured on the 5-FFI, as well as with the HAQ and the mobility subscale of the AIMS. The clinical signs of the forefoot joints did not correlate with any of the functional outcome measures. Of the ultrasound (US) parameters, only PDUS of the hindfoot showed a weak but statistically significant correlation with the HAQ walking.

In Table 2, we present the Spearman's correlation coefficients between structural damage and function. Both the Larsen and the Sharp/van der Heijde showed a statistically significant correlation ( $r_s=0.263$  and 0.277, respectively) with the total HAQ DI. Further, the Larsen score correlated with the 5-FFI limitation subscale ( $r_s$ = 0.282). There was a moderate negative correlation between the JAM and 5-FFI pain ( $r_s$ =-0.325). The JAM did not correlate significantly with any of the other functional measures. Swelling of the MTPs showed a negative correlation ( $r_s = -0.516$ ) with disease duration. All measures of structural damage as well as the total HAQ DI correlated moderate with disease duration: JAM ( $r_s$ =-0.584), SvdH  $(r_s=0.660)$ , (Larsen  $r_s=0.470$ ), and HAQ DI  $(r_s=0.470)$ . None of the 5FFI subscales correlated with disease duration.

#### Regression model

We searched for the variables explaining the variance in the total HAQ DI. The following variables were entered: disease duration, 5-FFI total pain score, swelling ankle, US synovitis total score, and the SvdH score. These variables were entered on basis of their correlation coefficient (>0.3) or they were judged as important

predictors of the HAQ in earlier studies [13]. Using the enter method, a significant model emerged (F=21.316, p<0.001). Sixty-four percent of the variance in HAQ DI score is explained by the following variables: disease duration, 5-FFI pain subscale, and swelling of the ankle. The regression coefficients with the 95% CI are presented in Table 3.

### Discussion

In this study, we explored associations between clinical signs and symptoms, structural damage, and function in connection with disease duration and the contribution of the individual foot segments.

Our data suggest that impaired foot function is associated more with signs and symptoms of the ankle than with forefoot complaints. Function of the foot is only weakly associated with overall radiological damage but again with a larger impact of the hindfoot. Finally, disease duration influences damage and function as well.

When regarding clinical signs in relation to function, we found that the results of our observational cross-sectional study are partially in line with earlier studies. In our study, pain and swelling of the ankle correlated weakly but statistically significantly with function, whereas forefoot symptoms did not. These findings confirm earlier studies suggesting that subjective pain of the forefoot does not correlate with function [14] and that patients considered their ankle complaints more impactful than forefoot complaints [1]. The ultimate function of the feet, walking, is severely and more impaired by rear foot disease than by forefoot involvement [15].

Regarding the relation between radiological damage and function, we found that both the Larsen and the Sharp/van der Heijde score correlated weakly with the HAQ DI but fell out of the regression model. The Larsen score correlated with the 5-FFI-limitation subscale, this is in line with preceding studies, which showed that general joint damage is correlated with loss of function [4, 13, 16]. Furthermore, there was a weak correlation between the

Table 1 Spearman's correlations coefficients (p value) between clinical signs/symptoms and function

	Pain ankle	Swelling ankle	Pain MTPs/toes	Swelling MTPs	US PD MTPs	US PD hind foot
5-FFI limitation	0.273 (0.034)	0.290 (0.025)	-0.200 (0.126)	-0.166 (0.206)	-0.045 (0.734)	0.127 (0.334)
5-FFI pain	0.095 (0.470)	0.010 (0.940)	-0.049 (0.710)	-0.027 (0.836)	0.176 (0.178)	0.025 (0.851)
5-FFI disability	0.293 (0.023)	0.278 (0.032)	-0.248 (0.056)	-0.168 (0.200)	0.019 (0.885)	0.023 (0.860)
HAQ walking	0.098 (0.455)	0.104 (0.428)	-0.234 (0.071)	-0.189 (0.147)	0.167 (0.203)	0.374 (0.003)
Total HAQ	0.053 (0.689)	0.353 (0.006)	-0.133 (0.309)	-0.073 (0.579)	0.169 (0.196)	0.112 (0.396)
AIMS mobility level	0.257 (0.047)	0.286 (0.027)	-0.02 (0.882)	-0.029 (0.824)	0.005 (0.967)	0.142 (0.280)

5-FFI Five Foot Function Index, HAQ Health Assessment Questionnaire, AIMS Arthritis Impact Measurement Scales, US PD ultrasound power Doppler, MTPs metatarsophalangeals

	SvdH	Larsen	JAM feet	US er HF	US er FF
5-FFI limitation	0.190 (0.154)	0.282 (0.032)	0.163 (0.212)	0.135 (0.303)	0.263 (0.046)
5-FFI pain	-0.054 (0.689)	0.051 (0.702)	-0.325 (0.011)	-0.149 (0.255)	-0.164 (0.210)
5-FFI disability	0.002 (0.991)	0.195 (0.142)	-0.080 (0.541)	0.106 (0.422)	-0.033 (0.801)
HAQ walking	0.001 (0.993)	0.242 (0.067)	0.047 (0.724)	0.137 (0.295)	0.177 (0.175)
Total HAQ	0.277 (0.035)	0.263 (0.046)	0.194 (0.138)	0.073 (0.582)	0.165 (0.208)
AIMS mobility level	0.134 (0.314)	0.162 (0.226)	-0.06 (0.648)	0.072 (0.587)	0.173 (0.187)

 Table 2
 Spearman's correlations coefficients (p value) between radiographic damage/limitation and function

5-FFI Five Foot Function Index, HAQ Health Assessment Questionnaire, AIMS Arthritis Impact Measurement Scales, SvdH Sharp/van der Heijde, JAM Joint Alignment Motion Scale, US er HF Ultrasound Erosion Score Hindfeet, US er FF ultrasound erosion score forefeet

Larsen score (ankle, talonavicular, and subtalar joint) and the 5-FFI-limitation subscale, which may reflect the seriousness of destruction of the hindfoot and ankle.

With disease duration, function (HAQ) also worsened. The triangle of increasing radiological damage, worsening function with longer disease duration has been described by many others, varying from stable progression rate [17] to a steeper worsening, but earlier plateau [18]. Belt et al. concluded that after 20 years of follow-up, the subtalar joint and ankle were affected in 24 of the 103 patients but leading to severe impairment [19]. The JAM, presented as a measure of joint deformity, also correlates with disease duration in our rather established RA cohort. In an early RA population, one might imagine that the JAM predominantly reflects disease activity and would not show a relationship with disease duration. Swelling of the MTPs correlated negatively with disease duration. This might reflect the treatment effect and among others is shown in the study of Welsing et al. [20].

In the regression analysis, we found that disease duration, pain, and swelling of the ankle were the only significant predictors of the HAQ DI. This is in line with other studies, which report pain as one of the most important predictors of the HAQ DI followed by disease activity and radiographic damage [21, 22]. Most large cohort studies report a significant predictive value for radiographic damage on the HAQ DI. The lack of significance in our cohort might possibly be explained by the fact that we only used the Sharp/van der Heijde and Larsen scores of the foot and ankle, scores of the hands and large joints were not included. In most studies, the Sharp/ van der Heijde score is not specified. Hulsmans et al. demonstrated that approximately half of the Sharp/van der Heijde score could be attributed to the damage of the feet. Extrapolating this to our current data, one might assume that the correlations regarding radiographic damage would have been larger [17]. Moreover, the total number of patients in this study was only small.

Although lately more interest in the foot in RA arises, we still think that the subject is somewhat neglected. It is illustrative that in the DAS 28, the most widely used instrument to measure disease activity in RA, the feet are not included, sometimes leading to an invalid definition of remission in individuals [23]. This may not only lead to insensitive scoring on population level (in the case of research) but also to the neglect of foot inflammation or damage, especially where we sense a tendency towards more strategy (DAS 28) driven care [24–26]. Within the rheumatic foot, most attention is focussed on the joints of the forefoot. However, our study supports the idea that involvement of the hindfoot and ankle may contribute to impairment and disability in the same way as the forefoot as has been suggested earlier [1, 15].

A limitation of this study is the small number of patients studied, which limits the ability to find strong correlations, but despite the small number and weak correlations, we found some significant correlations indicating the existence of true relationships. Another drawback is that the cross-

Table 3 Regression analysiswith HAQ DI as the dependentvariable

		95% CI of the regression coefficient			
Model	Regression coefficients	Lower bound	Upper bound	p value	
(Constant)		-0.401	0.310	0.798	
Disease duration	0.478	0.001	0.003	0.000	
FFI 5 total pain score	0.545	0.012	0.023	0.000	
Swelling ankle	0.281	0.140	0.521	0.001	
US synovitis total score	0.118	-0.013	0.071	0.176	
SvdH total score	0.068	-0.005	0.011	0.428	

Standardized coefficients (b) and their CI, adjusted  $R^2$  0.64

*FFI* Foot Function Index, *US* ultrasound, *SvdH* Sharp/van der Heijde, *CI* confidence interval

sectional design obstructs conclusions regarding time relations. However, cross-sectional studies, including patients with a broad range of disease durations, seem to provide fairly reliable estimates of the course of health outcomes [27]. Future research should focus longitudinally on the relation between clinical signs and structural damage of the foot and especially the ankle.

In conclusion, we suggest that in RA patients, pain and swelling of the ankle contribute more to disability than forefoot signs. In daily clinical practice and clinical research, rheumatologists should pay attention to the ankle and hindfoot as well as they contribute to disability.

#### Disclosures None

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