

Foot and Ankle Problems in Patients With Rheumatoid Arthritis in 2019: Still an Important Issue

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Objective. To study the prevalence of foot pain in patients with rheumatoid arthritis (RA) and whether including a 12-joint foot count in addition to the 28-joint count (from the Disease Activity Score 28 [DAS28]) improved detection of foot or ankle pain. In addition, the association between the self-reported foot and ankle score (SEFAS), patient-reported function, and disease-specific factors was studied.

Methods. Physician-reported data (swollen/tender 12-joint foot count, DAS28, and medication) and patient-reported data (foot/ankle pain, physical function, global health, and SEFAS) were assessed during a clinical visit. Data were analyzed with *t* test, χ^2 tests, and regression analysis.

Results. A total of 320 patients with RA were included (mean age 63 years, SD 13 years; 73% women), of whom 69% reported foot or ankle pain. Patients who reported foot or ankle pain had a lower mean age and worse disease activity, general pain, function, and global health ($P \leq 0.016$), and fewer were in remission (50% versus 75%; $P < 0.001$) compared with patients without foot pain. The 12-joint foot count identified 3.2% and 9.5% additional patients with swollen and tender joints, respectively, compared with the 28-joint count. The SEFAS was associated with walking problems ($\beta = -2.733$; 95% confidence interval [CI] = -3.963 to -1.503) and worse function ($\beta = -3.634$; 95% CI = -5.681 to -1.587) but not with joint inflammation severity.

Conclusion. The prevalence of foot or ankle pain in patients with RA is high. The 12-joint foot count had minor effects on detecting patients with foot pain. However, the SEFAS contributed additional information on foot problems that was not identified by joint examinations alone.

INTRODUCTION

Rheumatoid arthritis (RA) is a chronic, systemic inflammatory disease, and its prevalence in the Nordic adult population is approximately 0.9% (1). The feet and ankles are commonly affected by the disease, and synovitis may lead to tenderness, swelling, pain, stiffness, joint destruction, and altered foot mechanics, which increase the risk of falls and impair quality of life (2–5). New and more effective medication and the treat-to-target strategy have placed more patients in remission and decreased the number of patients in need of surgical treatment (6,7). Nevertheless, 70% to 90% of the RA population still report daily pain from the feet or ankles (8,9). As many as one-third of the patients in remission may present with foot synovitis, which increases the

risk of structural joint damage (3). These problems are sometimes underestimated and undertreated by the physician because the foot joints are not part of the composite global disease activity indice, the 28-joint evaluation (the Disease Activity Score 28 [DAS28]). The DAS28, recommended by the American College of Rheumatology and the European League Against Rheumatism (EULAR) as a measure of disease activity in patients with RA, is used daily in clinical practice to define clinical remission and guide medical treatment (10,11). In the mid-1990s, a disease activity score including an evaluation of 44 joints was modified into the DAS28, and swollen and tender joints in the feet and ankles were omitted (12). Even though the DAS28 is considered to reflect overall joint inflammation (12), some clinics still assess swollen and painful metatarsophalangeal joints and ankles (13). Foot or ankle

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SIGNIFICANCE & INNOVATIONS

- Foot and ankle pain are common complaints among patients with rheumatoid arthritis throughout the disease course, affecting their overall health. Therefore, improving detection and treatment of foot and ankle pain is important.
- Of patients who reported foot pain, 9 of 10 did not have any swollen foot joints, and 6 of 10 did not have any tender foot joints.
- Including a single question concerning foot pain as a screening tool in clinical practice or a more comprehensive patient-reported outcome measure such as the self-reported foot and ankle score can be recommended.

problems could potentially be an issue in the early stages of RA as well as later, in more advanced stages, when deformities may occur (12,13), which is why relying only on the DAS28 to identify foot pain may delay treatment and increase the risk for joint damage in the feet.

In addition, the DAS28 or the 12-joint count do not assess other issues commonly found in people with RA (14), nor do they capture physical functioning and disability due to foot pain. For this reason, a supplementary patient-reported outcome measure (PROM) of foot and ankle problems is needed. The self-reported foot and ankle score (SEFAS) is a commonly used questionnaire for people with RA and foot problems (15). The SEFAS measures the constructs of pain and functional status. By including the SEFAS to reflect the patients' view as a supplement to the rheumatologists' joint assessment, the consequences of living with foot pain can be better understood and treated.

This study aimed to assess the prevalence of foot and ankle pain in patients with RA attending a specialist clinic and whether inclusion of the swollen and tender 12-joint foot count in addition to the 28-joint count in the DAS28 improved detection of foot or ankle pain. Furthermore, the association between SEFAS, patient-reported function, and disease-specific factors was studied.

PATIENTS AND METHODS

Recruitment. Participants were consecutively recruited from the Danish Hospital for Rheumatic Diseases from September 2019 to December 2019. Adults (≥ 18 years) with a diagnosis of RA (16) attending rheumatology care at the hospital who were capable of reading and understanding Danish were included.

Data collection. All participants were asked an initial question "Do you experience any pain in your feet or ankles at this clinical visit?" Patients who reported foot or ankle pain were asked to complete the SEFAS questionnaire and were asked the following two additional questions: "Did your foot or ankle problems start before or after you were diagnosed with RA?" and "Is it a unilateral

or bilateral problem?" In addition, ordinary clinical parameters registered in the Danish nationwide database of patients with inflammatory arthritis (DANBIO) from the same visit were extracted (17).

Clinical data. The patients' clinical data were used to describe differences between patients with versus without foot or ankle pain. Some parameters were physician recorded, including diagnosis, age, disease duration, sex, medication, C-reactive protein (CRP), swollen and tender joints (28-joint count), swollen and tender metatarsophalangeal and ankle joint (pressure point between the extensor hallucis longus tendon and the extensor digitorum longus tendon) count (12-joint foot count), and physician-rated global health. Some parameters were patient-reported, including global health, pain intensity, fatigue (all rated on a visual analog scale ranging from 0 to 100 [best to worst]), and function (Health Assessment Questionnaire [HAQ]).

Medication was divided into conventional synthetic disease-modifying antirheumatic drug (csDMARD) and biological disease-modifying antirheumatic drug (bDMARD) groups. If a patient received both a csDMARD and a bDMARD, they were included in the bDMARD group.

The composite score DAS28 ranges from 0.96 to 9.4 (best to worst) and consists of the number of swollen and tender joints (the 28-joint count), CRP, and the patient-reported global health scale (18). Remission was defined as a DAS28 CRP of less than 2.6 and no swollen joints according to the 28-joint evaluation (19). The 28-joint evaluation includes joints in the hands (10 per hand), wrist, elbow, shoulder, and hips. The 12-joint foot count includes the ankle joint and the five metatarsophalangeal joints of both feet (20).

The HAQ measures function and consists of 20 questions, with a summary score ranging from 0 to 3 (best to worst) (21). The following two additional questions on physical function, recorded in the DANBIO, were also included: 1) Can you walk 3 km (if you want to)? and 2) Can you participate in sport and leisure activities (if you want to)? Both are scored on a Likert scale ranging from 0 to 3 (0 = yes, without any problems; 3 = no, I cannot).

Self-reported foot or ankle problems. The SEFAS for patients with RA was originally developed for surgical interventions in the foot and ankle (15). The questionnaire assesses foot problems over the last 4 weeks, contains 12 items with five response options, and takes less than 5 minutes to complete. The questionnaire covers pain, functional limitations, and other symptoms. Each of the 12 multiple-choice questions is scored from 0 to 4, where a sum of 0 points represents the most severe disability and a score of 48 points represents normal function. The SEFAS scoring was handled according to the manual (15). The SEFAS is available in several languages and has been translated into Danish (22), and we adapted the Danish version to our group of patients (nonsurgical). To confirm methodological quality (23), we confirmed that the face and content validity, construct

validity (>78% of predefined hypothesis confirmed), internal consistency (Cronbach's $\alpha = 0.89$), floor and ceiling effects (0.4% and 0.9%), and test-retest (intraclass correlation coefficient = 0.97) of the SEFAS met the requirements (Supplementary Tables 1–2, and Supplementary Figure 1).

Ethics. The study was conducted in accordance with the Declaration of Helsinki. All patients were informed orally and in writing, and informed written consent was obtained. The Ethical Committee for Health Research of the Region of Southern Denmark approved the study (20192000-98). The project was presented to the patient user council at the Danish Hospital for Rheumatic Diseases, which recommended the project and pointed out feet in RA as an important research area.

Statistics. All data were tested for normality using a Shapiro-Wilk test, and *t*-tests or χ^2 tests were used to compare patients with foot or ankle pain with those without foot or ankle pain. The relationship between the 28-joint count and the 12-joint count was investigated with a contingency table. A linear regression analysis was used to study factors associated with self-reported foot problems (with SEFAS as the dependent variable) and patient-reported function and disease-specific factors. Two models were used. The first model was a crude analysis with one independent variable at a time, controlled for age and sex. The second model contained all variables, including age and sex. Statistical analysis was performed in SPSS version 26 (<https://www.ibm.com/products/spss-statistics>).

RESULTS

Patients. In the present study, 333 patients responded to the survey. Three patients did not have an RA diagnosis and were excluded, and one patient was later found to have been included twice, which is why the second clinical visit was excluded from the analysis. A further eight patients were excluded because they did not have data registered in DANBIO corresponding to the clinical visit. One patient had moved from the area at the time of data extraction and had to be excluded. The 320 patients had a mean age of 63.7 (SD 12.9) years and a median disease age of 11.5 years (ranging from 1 month to 55 years), and 72.8% of those included in the analysis were women.

Prevalence of foot or ankle pain. In the present study, 69% (220/320) of the patients reported present foot or ankle pain. Among them, 71% had bilateral foot or ankle pain. A total of 70% of the patients with foot or ankle pain did not experience pain prior to being diagnosed with RA. Data comparing patients with and without foot or ankle pain are presented in Table 1. No difference was found in disease duration or CRP between the two groups. Patients who reported foot or ankle pain were younger and had worse reports in all other studied variables, indicating

Table 1. Descriptive data

Characteristics	Foot Pain (n = 220)	No Foot Pain (n = 100)	P Value
Sex, male, n (%)	47 (21)	40 (40)	<0.001
csDMARD, n (%)	126 (57.2)	66 (66)	<0.001
bDMARD, n (%)	94 (42.8)	38 (38)	<0.001
Remission, n (%)	107 (48.9)	75 (75)	<0.001
Age, yr	62.5 (12.9)	66.3 (12.4)	0.016
Disease duration, yr	13.4 (10.5)	12.1 (8.9)	0.222
CRP	6.3 (10.8)	5.2 (8.6)	0.502
HAQ ^a	0.9 (0.7)	0.4 (0.5)	<0.001
Global health ^b	42.0 (28.2)	22.0 (24.2)	<0.001
Pain ^b	36.4 (25.6)	21.1 (24.4)	<0.001
Fatigue ^b	47.5 (28.9)	26.6 (26.2)	<0.001
Physician-reported global health ^b	12.9 (15.3)	8.1 (10.0)	<0.001
DAS28 ^c	2.7 (1.2)	2.0 (0.9)	<0.001
Swollen 28-joint count	0.8 (2.4)	0.2 (1.1)	0.015
Tender 28-joint count	2.5 (4.3)	0.9 (2.6)	<0.001
Swollen 12-joint count	0.2 (1.1)	0.0 (0.0)	0.004
Tender 12-joint count	1.7 (1.7)	0.2 (1.4)	<0.001
3-km walk	1.2 (1.1)	0.6 (1.0)	<0.001
Sport and leisure	1.4 (1.1)	0.9 (1.0)	0.001
SEFAS ^d	26.9 (9.3)	-	-

CRP, C-reactive protein; DAS28, Disease Activity Score 28; HAQ, Health Assessment Questionnaire; SEFAS, self-reported foot and ankle score.

Values are given in mean (SD) unless otherwise indicated.

^a Scored from 0 to 3 (best to worst).

^b Global health, pain, and fatigue visual analog scale is measured from 0 mm to 100 mm (best to worst).

^c The 28-joint disease activity score scored from 0.96 to 9.4 (best to worst).

^d Scored from 0 to 48 (worst to best).

worse overall health compared with patients who did not report foot or ankle pain. A smaller proportion of patients with foot or ankle pain were in remission (48% versus 75%; $P < 0.001$), and a larger proportion received bDMARD or csDMARD treatment compared with those without foot or ankle pain ($P < 0.001$), indicating a higher disease activity (Table 1).

Physician-reported swollen and tender foot joints. In the group reporting foot and ankle pain (n = 220), the 12-joint foot count identified seven additional patients (3.2 %) with one or more swollen joints and 21 patients (9.5 %) with one or more tender joints who were not captured with the 28-joint count (Tables 2 and 3). Consequently, the combination of the 28-joint count and the 12-foot joint count did not record any swollen or tender joints for 78.2% and 41.8% of the patients reporting foot pain, respectively (Tables 2 and 3).

In the group of patients who reported no foot or ankle pain (n = 100), the physician-reported 12-joint foot count did not

Table 2. Distribution of swollen joints in patients reporting foot pain (n = 220) identified by the 28-joint count and 12-joint count

	0 Swollen Foot Joints	≥1 Swollen Foot Joints
0 swollen 28 joints, n (%)	172 (78.2)	7 (3.2)
≥1 swollen 28 joints, n (%)	31 (14.1)	10 (4.5)

Table 3. Distribution of tender joints in patients reporting foot pain (n = 220) identified by the 28-joint count and 12-joint count

	0 tender foot joints	≥ 1 tender foot joints
0 tender 28 joints, n (%)	92 (41.8)	21 (9.5)
≥1 tender 28 joints, n (%)	43 (19.5)	64 (29.1)

register any swollen joints, and tender joints were registered for three patients (3%).

Foot and ankle-specific PROM. The average SEFAS summary score for the group with foot or ankle pain was 26.95 (SD 9.3). The multivariate model explained 77% of the variation ($R^2 = 0.767$), and variables concerning physical function were associated with the SEFAS, as follows: a worse HAQ (estimated $\beta = -3.634$; 95% confidence interval [CI] = -5.681 to -1.587), problems with walking 3 km (estimated $\beta = -2.733$; 95% CI = -3.963 to -1.503), and problems with participating in sport and recreational activities (estimated β -est = -1.290 ; 95% CI = -2.438 to -0.142) indicated a worse (lower) SEFAS (Table 4). There was a negative borderline association with a higher number of physician-reported tender 12-joint foot counts (estimated $\beta = -0.345$; 95% CI = -0.707 to 0.017) and a worse SEFAS, whereas swollen 12-joint foot count, disease activity (DAS28), and disease duration were not associated with the SEFAS (Table 4).

DISCUSSION

A large proportion of patients with RA experience foot or ankle pain throughout the disease course, affecting their overall health. Therefore, monitoring the feet remains highly relevant. Omission of the feet from the disease activity score has received criticism; it limits the clinicians’ focus on the feet (3,13). The

present study found that the 12-joint foot count identified 9.5% of patients with tender joints and 3.2% with swollen joints, which was not captured with the 28-joint count alone. However, 92.3% and 61.4% of the patients reporting foot pain did not have any swollen or tender joints in the examined foot joints, respectively. Furthermore, no swollen foot joints were observed among the patients without foot pain, and only three patients from this group had tender joints. The high prevalence of pain reported may have been due to hindfoot, midfoot, or other soft tissue diseases that were not measured in the current study. Therefore, joint examination should not stand alone. Asking the patients about pain in their feet or ankles or including a PROM will provide additional information on foot problems not identified by joint examinations. The SEFAS used in this study indicates a somewhat high level of foot problems, and the score was associated with other physical functioning measures.

One of the study’s aims was to investigate the prevalence of foot or ankle pain among patients with RA. Seven of 10 patients reported that they currently had pain in their feet, most often bilateral. The prevalence found in the present study is in the lower range compared with previous studies investigating the prevalence of current foot and ankle problems among patients with RA. An interval within 68% to 94% was reported from studies performed from 1956 to 2017 (8,9,24–29). This could indicate that the current management of the disease has slightly reduced the prevalence of foot or ankle pain in patients with RA compared with the previous investigations on foot and ankle problems. However, this finding must be interpreted with caution; the prevalence is still high. It is also important to note that some previous studies investigated the prevalence of foot problems (8,24–29), whereas the present study investigated the prevalence of foot and ankle pain. The higher prevalence reported in previous studies could be due to “foot problems” covering numerous types of problems (eg,

Table 4. Linear regression analysis with SEFAS (0–48; worst to best) as the dependent variable

	Model 1				Model 2		
	R Value	β -est	95% CI	P Value	β -est	95% CI	P Value
Sex (male =1, female= 0)	-	-	-	-	-0.950	-3.224 to 1.325	0.411
Age, yr	-	-	-	-	0.031	-0.045 to 0.107	0.442
Disease duration, yr	0.22	0.000003	-0.01 to 0.01	1	0.0002	-0.008 to 0.008	0.943
HAQa	0.68	-9.052	-10.431 to -7.673	<0.001	-3.634	-5.681 to -1.587	0.002
Physician-reported global healthb	0.46	-0.276	-0.356 to -0.195	<0.001	-0.066	-0.164 to 0.031	0.18
DAS28c	0.54	-3.958	-4.842 to -3.074	<0.001	-0.515	-1.733 to 0.702	0.405
Swollen 12-joint count	0.29	-1.543	-2.642 to -0.445	0.006	0.685	-0.335 to 1.675	0.174
Tender 12-joint count	0.40	-1.037	-1.413 to -0.661	<0.001	-0.345	-0.707 to 0.017	0.061
3-km walk	0.67	-5.691	-6.612 to -4.771	<0.001	-2.733	-3.963 to -1.503	<0.001
Sport and recreational activities	0.60	-4.855	-5.794 to -3.916	<0.001	-1.290	-2.438 to -0.142	0.028

β -est, estimated β ; CI, confidence interval; HAQ, Health Assessment Questionnaire; DAS28, Disease Activity Score 28; SEFAS, self-reported foot and ankle score.

Model 1 = one independent variable at a time controlled for age and sex. Model 2 = all variables included; age and sex are entered into the same model.

^a Scored from 0 to 3 (best to worst).

^b Global health, pain, and fatigue visual analog scale is measured from 0 mm to 100 mm (best to worst).

^c The 28-joint disease activity score scored from 0.96 to 9.4 (best to worst).

cosmetics, deformities, and issues with finding footwear; some of these can be pain-free problems). In contrast, foot and ankle pain is related to the sensation of pain in the feet or ankles. The present study results also found that patients reporting current foot and ankle pain had worse records in all studied variables except disease duration and CRP, indicating worse overall health compared with the patients without foot and ankle pain. Therefore, attention should be paid to patients' feet, whether they are in remission or not.

In the present study, 70% of the patients with foot or ankle pain did not have pain in the region before being diagnosed with RA, indicating that the joint complaint is disease related. Disease duration in RA has previously been considered an important factor for persistent foot or ankle pain (30). A longer disease duration may have impacted residual pain in the absence of disease activity. Patients with longer disease duration often have more pain and less disease activity than those in earlier disease stages (30). No difference in disease duration was observed between the patients with foot pain and those without foot pain. This finding highlights the importance of including the feet in the clinical assessment from the start and throughout the course of the disease.

The DAS28 score is often criticized for not including the feet and ankles to determine disease activity (3,8,31). The present study found that the 12-joint foot count would slightly improve pain detection in the feet and ankles. Adding the 12-joint foot count alone will not be sufficient, as some patients may still risk having their foot problems overlooked by health care professionals. A probable explanation for the joint assessments' limited detection ability could be that foot and ankle pain in patients with RA does not necessarily originate from the examined joints; it could be present in other structures, (eg, tendons and muscles) (27,32). The assessment of foot problems and foot biomechanics is a key issue in unmet needs that requires research by the EULAR research roadmap (33). Previous studies have also suggested a need for a tool to monitor the feet in patients with RA (8,34,35).

An additional improvement to the clinical assessment of joint examination could be to include patient-reported measures regarding the feet at outpatient consultations. As a start, a simple yes/no question might facilitate a discussion concerning foot problems between patient and physician. If added information is needed, the SEFAS or a similar self-reported measure of foot problems can be used, such as the recently introduced Rheumatoid Foot Disease Activity Index-5 (34).

The SEFAS was developed to evaluate pain, functional limitations, and other symptoms. The present study results show that the SEFAS is associated with daily activities in patients with RA who have foot and ankle pain, indicating that the SEFAS may be a useful tool to evaluate foot and ankle problems in patients with RA. The mean summary score in the present study was worse than the normative values found in a population-based sample (36). The summary score from the present study was similar to that of patients admitted to surgery for hallux valgus deformity (37)

and forefoot disorders (38) but better than presurgical scores in patients with ankle or hindfoot disorders (38). Results based on the SEFAS in the present study indicate that patients with RA and foot or ankle pain experience functional limitations comparable with those of some individuals planned for foot surgery. However, the SEFAS' discriminative validity needs to be further studied.

The consecutive enrollment of patients in this study might challenge the external validity. Because the patients were recruited during the fall, the seasonal impact on flares was not accounted for. Earlier studies suggest a seasonal variation in disease activity, with higher disease activity scores during winter and spring but lower in the fall (39,40). If the data had been collected 2 to 3 months later, the prevalence of foot and ankle pain might have been higher. Another limitation relates to only asking about current level foot/ankle pain rather than the past week. We only asked about current pain to make a direct comparison to the clinical assessment. This decision may have affected the number of included subjects, and we might have included more patients with foot pain if we had asked about pain during longer time frame (eg, past week). The SEFAS was, in the present study, used in an RA population attending regular clinical visits, which is slightly different from the surgical focus where the SEFAS was initially developed and tested for methodological quality. The studied methodological properties based on this population were good. However, the questionnaire needs to be further validated in this nonsurgical population. Body mass index (BMI) was not recorded in the present study. Therefore, it has not been possible to include BMI in the regression models. Also, the 12-joint count is limited by lack of details; it is possible that adding the hindfoot and soft tissues (eg, ankle tendons) to the examination would improve monitoring of the feet. Future studies need to examine this. Finally, medical imaging (eg, X-ray, magnetic resonance imaging, and ultrasound) was not included in the present study. Medical imaging could have been used to examine whether there were structural changes in the feet and ankles (34,41).

A strength of the study is, firstly, that patients were recruited from a hospital specialized in the target-to-treat approach and who routinely perform the 12-joint foot count, thus strengthening the validity and reliability of the test. Secondly, the patients' disease duration was widely represented, ranging from newly diagnosed patients to patients with more than 15 years of disease duration. Therefore, we consider the included patients as representative for a specialist clinic.

The present study found that 7 of every 10 patients with RA reported foot and ankle pain and that foot and ankle pain was common throughout the disease course. These results indicate that many patients in remission experience foot and ankle pain in RA. Therefore, monitoring the feet in patients with RA is still essential. However, the presence of pain does not necessarily mean poor inflammatory control, as residual pain often persists because of joint damage and may also be part of a more widespread pain problem (42). Including the assessment of swollen and tender

ankle and metatarsophalangeal joints does not identify all patients with foot pain. Therefore, the 12-joint foot count of the foot and ankle should not be the only assessment of the feet. Including a single question concerning the presence of foot pain or a PROM, such as the SEFAS or similar, will contribute with additional information on foot problems not identified by joint examinations and may facilitate a patient–physician discussion.

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AUTHOR CONTRIBUTIONS

All authors were involved in drafting the article or revising it for intellectual content, and all authors approved the final version to be published. Dr. Simonsen had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study conception and design. Simonsen, Hørslev-Petersen, Bremander.

Acquisition of data. Simonsen, Hørslev-Petersen, Bremander.

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