

# Functional Disability in Relation to Radiological Damage and Disease Activity in Patients with Rheumatoid Arthritis in Remission

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**ABSTRACT. Objective.** To investigate the relationship between functional disability, disease activity and radiological damage in patients with rheumatoid arthritis (RA) in remission.

**Methods.** One hundred and eighty-six patients with RA in remission or with low disease activity were studied. The following variables were assessed at one time point: joint count, visual analog scale for pain, functional disability, i.e., health assessment questionnaire (HAQ) score, radiological joint damage as assessed by radiographs of hands and feet and scored according the Sharp-van der Heijde method, and presence of comorbidity. Disease activity was expressed as the disease activity score (DAS). Correlations were calculated by Spearman's rho coefficient of correlation. In addition, variables associated with the score were analyzed by logistic regression.

**Results.** The median HAQ score was 0.25 [interquartile (IQR) range 0-0.75] and the median DAS was 1.0 (IQR 0.7-1.5). Of the 186 RA patients included, 82% were in remission according to the DAS. The median joint damage as assessed by the Sharp-van der Heijde score was 21 (IQR 9-74). Functional disability was significantly correlated with pain ( $\rho$  0.48,  $p < 0.001$ ), disease activity ( $\rho$  0.42;  $p < 0.001$ ), disease duration ( $\rho$  0.39;  $p < 0.001$ ), radiographic joint damage ( $\rho$  0.37;  $p < 0.001$ ), and age ( $\rho$  0.19;  $p = 0.01$ ). In a logistic regression model functional disability was independently related to presence of pain, disease activity, radiographic joint damage and disease duration in decreasing order of strength, but not to age, sex and co-morbidity.

**Conclusion.** Patients with RA who are in remission might experience minimal functional disability and radiographic joint damage. Functional disability in RA patients in remission is most strongly related to the presence of pain and in lesser extent to disease activity, radiographic joint damage, and disease duration. (J Rheumatol 2002;29:267-70)

## Keys Indexing Terms:

RHEUMATOID ARTHRITIS                      DISABILITY                      REMISSION                      OUTCOME

Functional disability is an important end-point for patients with rheumatoid arthritis (RA) and can be assessed by the Health Assessment Questionnaire (HAQ). Functional disability in RA is influenced by disease activity<sup>1</sup>, radiological joint damage<sup>2</sup>, co-morbidity<sup>3</sup>, pain<sup>4</sup>, and psychological factors<sup>5</sup>. In general, functional disability is mainly influenced by variables of disease activity in the first years of the disease<sup>6</sup>, while in established disease, functional disability is also related to radiological joint damage<sup>7</sup>. To our knowledge, no study assessing the functional disability in RA patients in remission has been performed.

Based on these observations, we assumed that the functional disability in patients with RA in remission is strongly associated with radiographic joint damage but not with

disease activity. Our objective was to investigate the relationship between functional disability, radiographic joint damage, variables of disease activity, and co-morbidity in patients with RA in remission.

## MATERIALS AND METHODS

**Patients.** The present study is part of a larger cohort study of which the longterm followup is still under investigation, including 186 patients with RA in remission as defined by modified American College of Rheumatology (ACR) criteria for remission. The majority of patients ( $n = 135$ ) were recruited from the Jan van Breemen Instituut which is a large outpatient clinic for about 1 million inhabitants in the Amsterdam region. Around 2,400 patients diagnosed with RA are treated in this outpatient clinic. An additional 51 patients were recruited from the outer region of Amsterdam. The first selection of patients was done using a clinical database and by chart review. Subsequently, patients were selected for the study if they fulfilled the criteria of remission as defined by modified ACR criteria for clinical remission<sup>8</sup>. Accordingly, clinical remission is present when 5 out of the following 6 requirements are fulfilled: (1) duration of morning stiffness less than 15 minutes; (2) no fatigue; (3) no joint pain; (4) no joint tenderness or pain on motion; (5) no soft tissue swelling in joints or tendon sheaths; (6) erythrocyte sedimentation rate (ESR)  $< 30$  mm/h for a female or  $< 20$  mm/h for a male. The criteria were modified by omitting the requirement "no fatigue," so that a patient was considered to be in remission when 4 of the remaining 5 criteria were fulfilled. Patients had to meet the modified ACR criteria for clinical remission for at least 6 months

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prior to the time of inclusion into this study. All assessments were performed by one assessor (EM).

**Clinical assessments.** Functional capacity was assessed by a Dutch version of the HAQ<sup>9</sup>, which is scored from 0 to 3 points. Disease activity was expressed as a composite index consisting of the 44 swollen joint count, the Ritchie score, ESR, and a visual analog scale (VAS) for general health (the Disease Activity Score, DAS)<sup>10</sup>. Pain was assessed on a VAS. Comorbidity was considered to be present when a patient was medically treated for a disease. The most frequently reported co-morbidity was hypertension, diabetes mellitus, cardiovascular disease and pulmonary disease.

**Radiological assessment.** Joint damage of hands and feet was assessed according to the Sharp-method modified by van der Heijde<sup>11</sup>, for which the score range is 0 to 448. All radiographs were scored by 2 experienced observers. Average scores of both observers were calculated.

**Statistical analysis.** Spearman's rho coefficient of correlation was computed between variables. To identify independent variables, univariate analysis was performed first. Variables were dichotomized on the median value, and 2 × 2 tables were made in order to calculate odds ratios (OR) and confidence intervals (CI). A value of 0.5 was used to dichotomize the HAQ. This value was chosen on the basis of earlier reports suggesting that a HAQ score ≤ 0.5 indicates hardly any difficulties in daily activities and a HAQ score > 0.5 indicates minor to major problems in performing activities of daily life<sup>8</sup>.

Variables associated with the HAQ score ( $p < 0.1$ ) were then entered in a stepwise backward logistic regression model. Number of swollen joints, tender joints, Ritchie score, VAS for general health and ESR were not included in the logistic regression model because these variables are also incorporated in the DAS. The DAS, Sharp-van der Heijde score, age, sex, disease duration, the presence of comorbidity, and the VAS for pain were entered in the regression analysis. P values less than 0.05 were considered statistically significant.

## RESULTS

Demographic and clinical characteristics are presented in Table 1. The study group consisted of patients with long-standing, established RA, in need of treatment with DMARD in a large majority of patients at the time of inclu-

Table 1. Demographic and clinical characteristics of patients with RA in remission (n = 186).

Age, yrs	59 (50–69)
Female, No. (%)	121 (65)
Disease duration, yrs	7 (4–13)
Ever RF positive (%)	128 (69)
Joint erosions (%)	171 (92)
Nodules (%)	24 (13)
Currently receiving DMARD (%)	130 (70)
Swollen joints, max 66	0 (0–0)
Tender joints, max 68	0 (0–1)
ESR, mm/h	9 (5–15)
VAS pain	15 (6–21)
DAS	1.0 (0.7–1.5)
HAQ-score	0.25 (0–0.75)
SHS radiographic score	21 (9–74)
Mean (SD)	52 (72)
Co-morbidity (%)	65 (35)

Values are expressed as number (%), or as medians with interquartile range (IQR), unless otherwise mentioned. RF: rheumatoid factor; SHS: Sharp-van der Heijde score; ESR: erythrocyte sedimentation rate; VAS: visual analog scale; HAQ: health assessment questionnaire; DMARD: disease modifying antirheumatic drug.

sion into the study. Forty-seven percent of the patients had been treated with one or two DMARD; 47% with 3 to 5 DMARD; and 7% without any DMARD. The majority of patients had been treated with sulfasalazine, methotrexate, or intramuscular gold. The disease activity was low, as shown by all variables of disease activity. Remission as defined by a DAS < 1.6<sup>12</sup> was present in 82% of the patients. The majority of patients (61%) had a HAQ score ≤ 0.5, suggesting the absence of functional disability in a large number of patients with RA in remission (Figure 1). The majority of patients had erosions on radiographs, although the severity of joint damage as assessed by the Sharp-van der Heijde score was very low in the majority of patients.

The HAQ score was significantly correlated with the VAS for pain ( $\rho = 0.48$ ;  $p < 0.001$ ), the DAS ( $\rho = 0.42$ ;  $p < 0.001$ ), disease duration ( $\rho = 0.39$ ;  $p < 0.001$ ), the Sharp-van der Heijde score ( $\rho = 0.37$ ;  $p < 0.001$ ), and with age ( $\rho = 0.19$ ;  $p = 0.01$ ), but not with co-morbidity ( $\rho = 0.13$ ,  $p = 0.12$ ). When considering patients with disease duration < 7 years (median value of the complete group), a significant correlation was found between HAQ and DAS ( $\rho = 0.41$ ;  $p < 0.001$ ), but only a trend to a significant correlation between HAQ and Sharp-van der Heijde score was found ( $\rho = 0.2$ ;  $p = 0.053$ ). When considering patients with > 7 years, a significant correlation of the HAQ with both the DAS and the Sharp-van der Heijde score was found ( $\rho = 0.42$  and  $0.37$  respectively; for both:  $p < 0.001$ ).

In a logistic regression model, functional disability was independently significantly related in decreasing order of strength with the VAS for pain, the DAS, Sharp-van der Heijde score and disease duration, but not with age, sex and

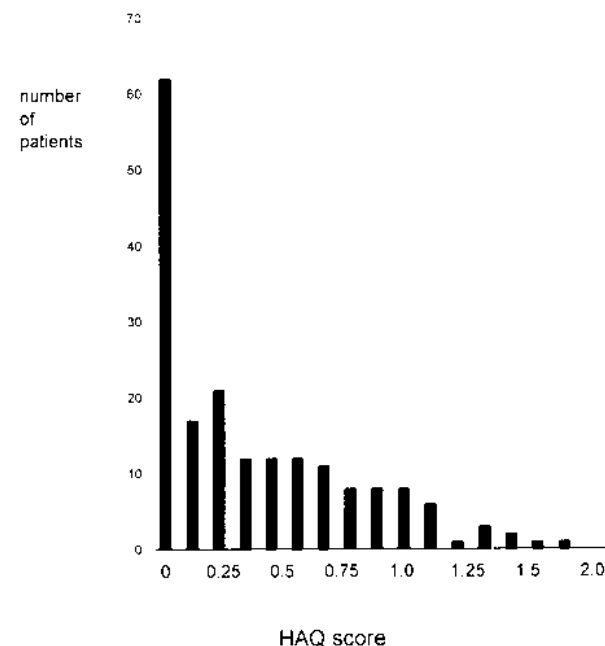


Figure 1. Distribution of HAQ scores of 186 patients with RA in remission. HAQ: Health Assessment Questionnaire.

Table 2. Results of logistic regression analysis of variables associated with the absence or presence of functional disability as measured by the Health Assessment Questionnaire.

	Regression Coefficient b	Standard Error se (b)	OR with 95% CI		p value
VAS pain	1.612	0.394	5.01	2.31–10.85	0.0000
DAS	1.289	0.447	3.63	1.51–8.71	0.0039
SHS	1.090	0.379	2.96	1.41–6.23	0.0042
Disease duration	1.061	0.373	2.88	1.39–6.00	0.0044
Constant	–3.145	0.493			

VAS pain: visual analog scale for pain; DAS: disease activity score; SHS: Sharp-van der Heijde score; OR: odds ratio; CI: confidence interval.

comorbidity (Table 2). The logistic regression model performed could correctly classify 78% of the patients. In view of the possibly more pronounced effect of joint damage on functional disability in established RA (> 7 years), logistic regression analysis was performed with the groups of patients with early RA (< 7 years) and in those with established RA (> 7 years). In patients with early RA no significant model was found. However, in patients with established RA the presence of functional capacity (HAQ > 0.5) was significantly associated with joint damage (OR with 95% CI 3.7; 1.4–9.9) and VAS pain (OR with 95% CI 3.6; 1.2–9.8).

## DISCUSSION

In patients with RA and inactive disease, functional disability was low and most strongly associated with pain, and to a lesser extent with joint damage, disease duration and, interestingly, disease activity.

The large group of patients studied was unique, consisting of patients with longstanding RA, and a high proportion of patients with rheumatoid factors and joint damage, but with a low or absent disease activity for a period of at least 6 months before inclusion in the study.

In contrast to our hypothesis, the functional disability in our patients with inactive or low disease was not primarily associated with joint damage, but with pain as experienced by the patients. Most interestingly, the functional disability was also influenced by joint damage, disease duration and disease activity, although the degree of joint damage and disease activity was low. The findings of this study are in concordance with others performed in patients with active RA<sup>6</sup>.

The implication of these findings is that, as in active RA, the goal of treatment in patients with low or inactive RA should be aimed to both retard radiographic progression and also to suppress disease activity as low as possible, in order to maintain functional capacity.

The fact that relatively few patients had a significant amount of joint damage and a minority of patients had a

HAQ score above 0.5 may have influenced the weak association of joint damage with functional disability. There might be a threshold for joint damage to have an influence on functional disability. This association might be more pronounced in a patient population with more patients with considerable joint damage.

One may argue that the presence of some patients with a low disease activity, as defined by the presence of tender or swollen joints, might explain the association of disease activity with functional disability. However, the correlation coefficients between functional capacity and the DAS, the joint damage score, VAS pain, and VAS general wellbeing were similar when considering only the patients without tender or swollen joints (data not shown). This suggests that factors other than objective joint swelling or joint pain may influence disease activity and thereby be correlated to functional disability.

Other factors that could explain the variation in HAQ scores could be psychological factors such as depression<sup>4</sup> and comorbidity<sup>3</sup>. Co-morbidity was introduced in the model but not significantly associated with functional disability. In the present study, comorbidity might range from a condition such as hypertension, which is non-disabling, to severe cardiovascular disease. In the Wolfe study, co-morbidity was assessed as a symptom count of 57 symptoms relevant to rheumatic diseases<sup>3</sup>. Differences in the definition of co-morbidity could obscure a possible association between co-morbidity and functional capacity in the present study. Psychological factors were not assessed in our study, so we can not determine whether they may influence functional disability in patients in remission.

In conclusion, patients with RA who are in remission experience minimal functional disability and radiographic joint damage. Disease activity and radiographic damage are both still related to functional disability.

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