

Disability Related to Function of the Upper Extremities in Early Rheumatoid Arthritis – Course and Relation to Other Disease Parameters Over 10 Years: A Cohort Study

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Abstract

Background: The objective of this study was to investigate the course of disability related to the upper extremities (UE) in early rheumatoid arthritis (RA), and to assess correlations between such disability and clinical parameters, including grip force.

Methods: In an inception cohort of patients with early RA (N=222), disability of the UE was assessed using a subscore of the Health assessment questionnaire disability index (HAQ-DI), and average grip force of the dominant hand was measured. Changes between consecutive follow-up visits in the HAQ-DI-UE subscore were assessed using the paired samples t-test, and correlations with key disease parameters using Spearman's rank test. The relation between joint involvement and HAQ-DI-UE was examined using multivariate linear regression analysis.

Results: The HAQ-DI-UE decreased significantly from inclusion to the 6-month follow-up (mean change -0.26; 95% CI -0.18 to -0.34), and increased significantly after 2 years. There were fairly strong correlations for HAQ-DI-UE with grip force (r: -0.50 to -0.62), patient's global assessment (r:0.58 to 0.64) and patient's assessment of pain (r:0.54 to 0.60) at all time points up to 5 years, but only moderate to weak correlations with swollen joints, CRP and ESR. At inclusion wrist synovitis and tender PIP joints had both an independent impact on HAQ-DI-UE, whereas tenderness of the shoulder and the wrist had a greater importance at 6 months.

Conclusions: Disability related to the upper extremities decreased significantly during the first 6 months, and increased again after 2 years. The correlations with clinical parameters underline the major impact of pain and impaired hand function in early RA.

Significance And Innovations

- Disability related to the upper extremities decreased significant during the first 6 months after diagnosis in patients with RA, and increased significantly again after 2 years.
- HAQ-DI-UE scores correlated strongly with grip force and pain and to a lesser extent with joint counts and laboratory markers of inflammation.
- The results underline the major impact of pain and impaired hand function in early RA.

Background

Rheumatoid arthritis (RA) is a chronic inflammatory disease, which is often associated with disability (1, 2). RA usually involves the distal upper extremity joints, and over 80% of the patients have dysfunction in their hands (3). Patients with RA have been shown to have reduced grip force in comparison with age- and sex matched healthy populations (4–6). Reduced hand function contributes to impairment of activities in daily life (ADL), particularly in manual performance that require some grip force (7). We have previously reported improvement in age- and sex standardized grip force in early RA, in particular during

the first year after diagnosis (6). However, grip force remained significantly reduced compared to the general population, even in patients in clinical remission (6).

In rheumatological care, patient-reported outcomes measures (PROMs) are used for the purpose of assessing severity of RA, including disability (8–11). One of the most commonly used instruments to measure disability in RA is the Health Assessment Questionnaire Disability Index (HAQ-DI) (12–16). PROMs, e.g. HAQ, and RA disease activity measures (e.g. DAS28), have been found to be moderately correlated (17). A moderate association has also been found between HAQ-DI and grip force in patients with RA (18). Therefore, it is important to study the course of disability as a separate outcome in RA (11).

HAQ-DI is a general measure of disability (13, 14), and only a subset of the questions are related to ADL that are affected by hand function. Pain and limited range of movements of joints have the greatest impact on individual sub dimensions of the HAQ-DI (19). Studies have shown that higher HAQ-DI scores at baseline are associated with long-term disability (20, 21), especially for women, older patients and those with high pain scores (21). Decreased grip force, a great number of swollen and tender joints in the upper extremities (UE) and limitations in wrist and shoulder motion were related to many of the sub dimensions and explained increased disability with higher HAQ scores (19, 22). Previous studies have addressed HAQ overall, or individual subdimensions, and not dimensions reflecting disability related to the UE.

The objective of this study was to specifically investigate the course of disability related to the UE in early RA, using a subset of the HAQ-DI (HAQ-DI-UE), and to assess relations between HAQ-DI-UE and disease parameters. Furthermore, correlations between HAQ-DI-UE and grip force were studied.

Patients And Methods

Patients. An inception cohort of patients with early RA (symptom duration \leq 12 months), recruited in 1995–2005, was investigated. The patients were diagnosed with RA by a rheumatologist and fulfilled the 1987 American College of Rheumatology (ACR) classification criteria for RA (23). The study included individuals from a defined area, the city of Malmö, Sweden (population 260 000 in 2000). Patients were recruited from the rheumatology outpatient clinic of Malmö University Hospital, which was the only hospital serving the city, and from the four rheumatologists in private practice in Malmö. All patients gave their written informed consent to participate, and the study was approved by the Regional Ethical Review Board for southern Sweden (Lund, Sweden).

Clinical assessment. Patients were managed according to usual care, with no pre-specified protocol for pharmacotherapy or rehabilitation. The patients were included before the current practice of treat-to-target (24) was implemented, and before early treatment with biological disease-modifying anti-rheumatics drugs (bDMARDs) came into widespread use.

In a structured follow-up program, all patients were examined by the same rheumatologist. Visits were scheduled at 6, 12 and 24 months as well as 5 and 10 years after inclusion. Using a standardized

protocol, individual joints were assessed as swollen/not swollen and tender/not tender, and standard 28-joint swollen joint counts (SJC) and tender joint counts (TJC) were obtained. Disability was assessed using the HAQ-DI (12). The Swedish validated translated version of the HAQ-DI (25) was used. Patient reported pain and patients' global assessment of disease activity were assessed using Visual Analogue Scales (VAS; scale 0-100). Information on treatment was obtained as previously described (6). In brief, information on current treatment with disease-modifying anti-rheumatic drugs (DMARDs) and corticosteroids was obtained through a structured interview at each visit. Data on treatment with bDMARDs during the study period was obtained through linkage to a regional biological register (26). Most patients were started on a DMARD at the time of diagnosis. The use of Methotrexate as a first choice increased gradually during the study period. A limited number of patients with severe, refractory disease were treated with bDMARDs after their introduction in 1999. Blood samples were obtained at the visit when the joint assessment was performed (within 1 hour). C-reactive protein (CRP) and the Erythrocyte Sedimentation Rate (ESR) were analyzed using standard methods at the Department of Clinical Chemistry, Malmö University Hospital.

Assessment of grip force. Grip force (Newton, N) was measured by using the electronic instrument Grippit (AB Detektor, Gothenburg, Sweden). This was performed at the same visit as the joint assessment (within 1 hour). The patient was seated comfortably in a chair without armrests, with the shoulder, arm and hand in standard positions as previously described (27). The other arm was resting on the table. Standardized instructions were given. When using this procedure, the test-retest scores for Grippit measures have been demonstrated to be high (27). The grip force was measured alternately in the dominant hand and the non-dominant hand three times, and the mean of the three measurement values from each hand was used. Average values of the ten second uninterrupted grip were obtained, as previously described (6). Average grip force values of the dominant hand at inclusion and at the 6 month, 1, 2, 5, and 10 year follow-up visits were compared to the expected, based on age- and sex-specific reference values from a convenience sample from a cross-sectional study of volunteers in the region of Oslo, Norway (28). Grip force values for each patient were expressed as % of the expected, based on the reference values.

Disability related to the upper extremities. To estimate disability based on self-reported activity limitations during the study period we used the validated Swedish version (12) of the HAQ (25). This assessment instrument included 20 questions divided into eight domains: Dressing and grooming, Arising, Eating, Walking, Hygiene, Reach, Grip, and Other usual activities, and is used in practice to calculate the HAQ disability index (HAQ-DI); range 0–3). In previous studies, subscore for lower extremities (HAQ-DI-LE), which included 10 questions that cover activities that are mainly dependent on function of the lower extremities (LE), has been calculated (29–31). To more specifically address disability of the upper extremities, we computed a subscore, HAQ-DI upper extremities (HAQ-DI-UE), which includes the remaining 10 questions on activities mainly performed using the UE (Additional File 1, Supplementary Table 1).

Statistics. Changes in HAQ-DI-UE between two consecutive follow-up visits were assessed using the paired samples t-test. Correlations between HAQ-DI-UE and key disease parameters, i.e. grip force, ESR,

CRP, visual analogue scales for patient global assessment (VAS global) and VAS pain, swollen and tender joint counts (SJC and TJC), at each visit were assessed using Spearman's rank test. Furthermore, the distributions of HAQ-DI-UE at different time points in patients with and without current synovitis, and with and without tenderness, of ≥ 1 joint in each joint group (i.e. shoulders, elbows, wrists, metacarpophalangeal (MCP) and proximal interphalangeal (PIP) joints) were compared using the Mann-Whitney test. To further assess the relation between joint involvement (as above) and HAQ-DI-UE at inclusion and 6 months of follow up were examined using linear regressions analysis. Normality of distribution for the residuals was examined using the Shapiro-Wilk test. Covariates with p-values of < 0.10 in the bivariate models were included in multivariate models. Collinearity between covariates was examined using Spearman's test. In cases of major collinearity, the covariate with the strongest association with the dependent variable was selected for the multivariate analysis.

Results

Patients. A total of 222 patients with early RA (71% women, mean age 61 years, median symptom duration 7 months) were investigated (Table 1). At inclusion, the mean DAS28 was 4.6 (SD 1.4), and the median HAQ-DI was 0.75 (IQR 0.38–1.25) (Table 1). Most patients were treated with Methotrexate (Table 1). The mean average grip force of the dominant hand increased from 40% of expected at inclusion to 66% of expected at 10 years (Table 1). Data on both HAQ-DI-UE and average grip force of the dominant hand were available for 222 patients at inclusion, 207 patients at 6 month, 209 at 1 year, 200 at 2 years, 167 at 5 years and 110 at 10 years (Table 1).

Table 1
Characteristics of the early RA with data on HAQ-DI-UE*

	Inclusion ¹	6 month ²	1 year ³	2 years ⁴	5 years ⁵	10 years ⁶
NS	222	207	209	200	167	110
Female sex % (n)	71 (157)	71 (147)	71 (148)	71 (142)	72 (120)	73 (80)
Age (years)	61 (14.3)	61 (14.1)	62 (14.3)	63 (14.5)	65 (13.9)	68 (13.2)
Symptom duration at inclusion (months); Median (IQR)	7 (5–10)	7 (5–10)	7 (5–10)	7 (5–10)	7 (5–10)	8 (5–10)
RF-positive % (n)	61 (135)	60 (124)	61 (127)	60 (120)	65 (108)	63 (69)
Anti-CCP positive % (n)	57 (116/202)	58 (108/187)	58 (109/189)	57 (104/182)	60 (91/153)	57 (58/101)
DAS28 (0–10)	4.6 (1.4)	3.8 (1.3)	3.7 (1.4)	3.6 (1.4)	3.6 (1.4)	3.2 (1.1)
HAQ (0–3); Median (IQR)	0.75 (0.38–1.25)	0.50 (0.13–0.88)	0.50 (0.13–1.00)	0.50 (0–1.00)	0.75 (0.13–1.12)	0.63 (0.38–1.12)
HAQ-DI-UE (0–3); Median (IQR)	0.80 (0.40–1.20)	0.60 (0–1.00)	0.40 (0–1.00)	0.40 (0–1.00)	0.60 (0.20–1.00)	0.60 (0.20–0.85)
Patient's global assessment (VAS 0–100)	43 (27)	33 (25)	30 (24)	34 (27)	35 (25)	31 (25)
Pain (VAS 0–100)	40 (27)	32 (26)	30 (24)	32 (27)	31 (24)	30 (24)
Swollen joint count (out of 28)	7.6 (4.9)	5.4 (4.8)	4.8 (4.1)	5.2 (5.0)	5.4 (5.0)	2.8 (3.7)
Tender joint count (out of 28)	6.3 (6.4)	4.0 (5.4)	3.6 (4.7)	3.4 (5.3)	3.2 (5.2)	1.7 (3.6)
Methotrexate treatment % (n)	53 (117)	57 (118)	61 (127)	60 (119)	61 (102)	61 (67)
Other DMARD % (n)	32 (70)	34 (71)	33 (69)	32 (64)	25 (42)	19 (21)

§ All patients with ≥ 1 grip force measure at inclusion, 6 month, 1, 2, 5 and 10 years

*Values are Mean (SD) unless otherwise indicated.

RA = Rheumatoid Arthritis; IQR = Interquartile range; RF = rheumatoid factor; anti-CCP = anti-cyclic citrullinated peptide; DAS28 = Disease Activity Score in 28 joints; HAQ = The Health Assessment Questionnaire; HAQ-DI-UE = the Health Assessment Questionnaire Upper Extremities; VAS = Visual analogue scale; DMARD = disease-modifying drug; CRP = C-reactive protein; ESR = erythrocyte sedimentation rate.

	Inclusion ¹	6 month ²	1 year ³	2 years ⁴	5 years ⁵	10 years ⁶
Corticosteroid treatment % (n)	39 (86)	35 (72)	31 (64)	30 (60)	29 (48)	23 (25)
CRP (mg/l; Median (IQR))	< 9 (< 9–27)	< 9 (< 9–11)	< 9 (< 9–10)	< 9 (< 9–12)	< 9 (< 9–10)	< 9 (< 9–10)
ESR (mm/h); Median (IQR)	20 (10–43)	15 (8–30)	15 (8–28)	16 (9–27)	16 (9–25)	18 (11–29)
Average grip force of the dominant hand (N)	106 (78)	126 (83)	132 (85)	139 (93)	140 (96)	148 (85)
Average grip force of the dominant hand (% of expected)	40.2 (25.9)	49.0 (27.3)	52.0 (27.5)	54.7 (28.9)	57.4 (30.8)	65.8 (26.7)
§ All patients with ≥ 1 grip force measure at inclusion, 6 month, 1, 2, 5 and 10 years						
*Values are Mean (SD) unless otherwise indicated.						
RA = Rheumatoid Arthritis; IQR = Interquartile range; RF = rheumatoid factor; anti-CCP = anti-cyclic citrullinated peptide; DAS28 = Disease Activity Score in 28 joints; HAQ = The Health Assessment Questionnaire; HAQ-DI-UE = the Health Assessment Questionnaire Upper Extremities; VAS = Visual analogue scale; DMARD = disease-modifying drug; CRP = C-reactive protein; ESR = erythrocyte sedimentation rate.						

Changes in HAQ-DI-UE in early RA - over time. In the paired analysis of patients with available data at both time points there was a significant decrease in HAQ-DI-UE from inclusion to the 6 month follow-up (median HAQ-DI-UE 0.80 (interquartile range (IQR) 0.40–1.20) vs 0.60 (IQR 0.00–1.00)) (Fig. 1). The mean change in HAQ-DI-UE between inclusion to 6 month follow up was -0.26 [95% confidence interval (CI) -0.18; -0.34]. HAQ-DI-UE levels were stable between 6 month and 2 years (Fig. 1), whereas between 2 years and 5 years, there was a significant increase (from 0.40 (IQR 0.00–1.00) to 0.60 (IQR 0.20-1.00)) (Fig. 1). The mean change in HAQ-DI-UE between 2 and 5 years was 0.10 [95% CI 0.03–0.17].

Correlations for disease parameters with HAQ-DI-UE. There were strong correlations for HAQ-DI-UE with grip force, VAS global and VAS pain at all time points (Fig. 2, Additional file 1 (Supplementary Table 2)), and moderate to weak correlations with SJC, TJC, ESR and CRP (Fig. 2, Additional file 1 (Supplementary Table 2)). HAQ-DI-UE correlated significantly with grip force at inclusion ($r = -0.62$; $p = < 0.001$) (Fig. 2A), and at all other time points (Additional file 1 (Supplementary table 2)). Similar correlations were noted for both VAS Global (Fig. 2C, Additional file 1 (Supplementary Table 2)) and VAS pain (Fig. 2D, Additional file 1 (Supplementary Table 2)).

Relation between joint involvement and HAQ-DI-UE. Among patients with data on HAQ-DI at inclusion, 192 patients had synovitis of ≥ 1 MCP joint in the UE, whereas presence of synovitis of wrists, PIP, elbows and

shoulders was observed in 153, 139, 20 and 19 patients, respectively. Whereas tenderness at inclusion was more common compared to clinical synovitis in the shoulders (n = 77) and elbows (n = 34), respectively, the reverse was the case for MCP joints, wrists and PIP joints, where tenderness was observed in 136, 118 and 119 patients, respectively.

Proportions with current joint involvement decreased somewhat over time, in particular PIP joint synovitis and tenderness (Supplementary Tables 3 and 4). Overall, there was a greater reduction in tenderness of different joints in the UE from inclusion until 10 years of follow up, compared to the reduction in synovitis (Additional file 1 (Supplementary Tables 3 and 4)).

At inclusion, higher HAQ-DI-UE scores were found in those with current wrist synovitis MCP synovitis and shoulder synovitis, compared to those without such joint involvement (Fig. 4A). There were also significant associations between tenderness of elbows, wrists, MCP joints and PIP joints with higher HAQ-DI-UE (Fig. 3B).

Patients with wrist synovitis had significantly higher HAQ-DI-UE scores at 6 months, 1 year and 5 years, but not at 2 and 10 years (Additional file 1 (Supplementary table 3)). Tenderness was associated with higher HAQ-DI-UE, in wrists and elbows at all time points from inclusion to 10 years of follow up and in MCP and PIP joints through 5 years and in shoulders from 6 months to 10 years (Additional file 1 (Supplementary Table 4)).

Joint involvement and disability related to the upper extremities – multivariate analyses. In bivariate and multivariate linear regression models on the relation between joint involvement and HAQ-DI-UE at inclusion and after 6 months, the residuals were normally distributed (Shapiro-Wilk statistic > 0.90). Models including data at other time points did not fulfill normality of distribution for the residuals. Results of the linear regression analyses at inclusion and at 6 months are shown in Table 2. In multivariate analysis, there was a significant association between wrist synovitis and higher HAQ-DI-UE at inclusion (B = 0.37; 95% CI 0.20 to 0.54) but not at 6 months (Table 2). The presence of PIP tenderness was associated with higher HAQ-DI-UE at inclusion, independent of other joint involvement (Table 2). At the 6-month of follow-up, PIP joint synovitis (B = 0.22; 95% CI 0.07 to 0.36), tender shoulder (B = 0.28; 95% CI 0.12 to 0.44) and tender wrist (B = 0.30; 95% CI 0.12 to 0.47) were all associated with higher HAQ-DI-UE in multivariate analysis (Table 2).

Table 2.

Relation between joint involvement and HAQ-DI-UE at inclusion and 6 months

– Linear regression

Joint	Inclusion (N=222)					6 months (N=207)				
	N	Bivariate		Multivariate		N	Bivariate		Multivariate	
		B	95% CI	B	95% CI		B	95% CI	B	95% CI
Shoulder synovitis	19	0.30	-0.01 to 0.60	0.13	-0.14 to 0.40	6	0.52	0.08 to 0.97	0.20	-0.22 to 0.62
Elbow synovitis	20	-0.04	-0.34 to 0.26	*NI	*NI	7	0.19	-0.22 to 0.60	*NI	*NI
Wrist synovitis	153	0.47	0.29 to 0.65	0.37	0.20 to 0.54	99	0.26	0.11 to 0.41	0.05	-0.11 to 0.22
MCP joint synovitis	192	0.36	0.10 to 0.62	*NI	*NI	158	0.14	-0.05 to 0.33	*NI	*NI
PIP joint synovitis	139	0.17	-0.01 to 0.35	*NI	*NI	81	0.22	0.07 to 0.38	0.22	0.07 to 0.36
Tender shoulder	77	0.15	-0.03 to 0.32	*NI	*NI	54	0.37	0.21 to 0.54	0.28	0.12 to 0.44
Tender elbow	34	0.34	0.11 to 0.57	0.21	-0.01 to 0.42	26	0.39	0.17 to 0.61	0.13	-0.10 to 0.35
Tender Wrist	118	0.47	0.31 to 0.63	*NI	*NI	83	0.36	0.22 to 0.51	0.30	0.12 to 0.47
Tender MCP	136	0.42	0.25 to 0.59	*NI	*NI	89	0.19	0.04 to 0.34	*NI	*NI
Tender PIP	119	0.49	0.33 to 0.65	0.41	0.26 to 0.57	74	0.34	0.19 to 0.49	*NI	*NI
*NI: Not Included.										

Discussion

In this study of patients with early RA, the HAQ-DI-UE decreased significantly from inclusion to the 6-month follow-up. HAQ-DI-UE levels were stable between 6 months and 2 years, whereas between 2 years and 5 years, there was a significant increase. Furthermore, there were strong correlations for HAQ-DI-UE with grip force and PROMs at all time points, and moderate to weak correlations with joint counts and laboratory parameters of inflammation. The strong and consistent negative association between grip force and disability related to the UE underlines the importance of the grip in this context.

Involvement of several joint groups contributed to disability related to the upper extremities. At inclusion wrist synovitis and tender PIP joints had both an independent impact on HAQ-DI-UE, whereas tenderness of the shoulder and the wrist had a greater importance at 6 months.

Our results suggest that patients with poor PROMs in early RA are at increased risk of persistent limitations in daily life activities that are performed using the UE. Previous studies have investigated disability overall, and not the HAQ-DI-UE. Disease activity, measured as swollen and tender joint counts, as well as pain, have both been shown to be associated with the total HAQ score (32). Several other studies demonstrated similar results, with associations between high disease activity and impaired PROs like HAQ (17, 33–35).

One of these compared two large inception cohorts of patients with early RA, the Early Rheumatoid Arthritis Study (ERAS, inclusion period 1986–1997), and the Norfolk Arthritis Register (NOAR, 1990–1994), both from the United Kingdom (33). Both these studies analyzed trajectories, i.e. patterns of progression of disability (33). The overall pattern for HAQ-DI was similar to our observations on HAQ-DI-UE. They also reported an association with DAS28 (33) but did not investigate the importance of the subcomponents (swollen, tender, ESR, VAS pain and VAS Global), in contrast with our study.

In a study based on the Canadian Early Arthritis Cohort (CATCH), the HAQ-DI and DAS28 decreased significantly over time from baseline to 24 months (34), but no further follow-up was reported. The Swedish TIRA study (Early Interventions in Rheumatoid Arthritis) group reported that disability decreased significantly during the first year after inclusion in their inception cohort (1). This was followed by gradually worsening of disability up to the 8-year follow-up (1). In that study, grip force and pain intensity were major contributors to disability measured using HAQ-DI (1), similar to our findings on HAQ-DI-UE. Taken together, these studies suggest that although disability may decrease in early RA, subsequent worsening of disability is common, in particular in those with active disease and severe pain (1, 33, 34).

In a study of early RA, performed by the Swedish BARFOT (Better Anti-Rheumatic Pharmacotherapy) group, outcomes including the disease activity score, VAS pain, Patient Global Assessment (PatGA) and HAQ were followed during five years (35). Interestingly, patterns were similar in patients diagnosed 1992–

1999 and 2000–2006, with no difference in VAS pain or HAQ-DI between the groups, despite the fact that the latter group was more actively treated (35). The authors suggest that other mechanisms than inflammation might be of importance for persistent disability and pain (35). This is in accordance with the results of the present study, with limited correlation between HAQ-DI-UE and markers of inflammation, in particular with long term follow-up.

A major impact of reduced grip force on disability has been demonstrated in several previous studies (1, 3, 18, 19, 32), including a survey of the cohort investigated in the present study (6). This suggests that hand training should be beneficial in early RA. Indeed, structured rehabilitation, including tailored exercise program for the distal UE have been shown to improve the grip strength and reduce the impact of the disease on the individual (36–38). Furthermore, multiprofessional interventions may prevent progressive disability in RA (1, 36, 37, 39).

Our results also showed a varying contribution of joint involvement to disability related to the UE. Like in the present cohort, a Japanese study of 3457 patients with established RA that analyzed the importance of change in joint involvement over time found that involvement of wrist and shoulder joints contributed significantly to worse HAQ scores in patients with RA, whereas for the small joints in the hand (MCP and PIP), the effect was modest (22). In our study, there was a greater importance for PIP joint involvement, which may characterize early RA. Furthermore, several studies found no (19, 40, 41), or limited (22), impact of involvement of the small joints in the hands on HAQ-DI. This, contrasts with our result that PIP joint tenderness was independently associated with HAQ-DI-UE at baseline. Impairment of small joints could influence particular subdimensions of the HAQ score (22), which might explain our finding.

A German study of RA patients describes that wrist involvement is strongly associated with disability, assessed by HAQ-DI (42). In a large cohort of 4 530 patients with established RA, the most frequently affected joint was shown to be the wrist (45.5%). Together with shoulders and elbows, wrist joints accounted for the greatest contributions to disease activity, HAQ-DI and long term functional prognosis (41). Several other studies demonstrated a major impact of wrist involvement on grip force in RA (19, 22, 43–45).

A limitation of the study is that the HAQ-DI-UE subscore of the HAQ-DI has not been studied before, and is not a validated outcome measure. A corresponding subscore for the lower extremities (LE), (HAQ-DI-LE) which has been used in previous studies (29–31), included 10 questions that cover activities that are mainly dependent on function of the LE. Due to the heterogeneity of RA and the differential impact on various joints in individual patients, there is a rationale for constructing separate questionnaires, sorting the 20 sub dimensions in two groups, one for the LE and one for the UE. Further studies should evaluate the utility of this approach.

Another limitation in the present study is related to the loss of patients that for various reasons have not been assessed at all follow-up visits. This may lead to underestimation of long term disability in RA. However, changes over time were assessed using paired analyses of patients with data at two

consecutive visits. Furthermore, due to the limited sample size, some factors that contribute to higher HAQ-DI-UE may not be identified in this study.

Strengths of this study include the structured longitudinal follow-up of an inception cohort from a defined catchment area. Therefore, selection bias is not a major issue in this study, and the results could be generalized to patients with RA seen in clinical practice. On the other hand, they may not apply to other ethnic or geographic settings, or patients managed using completely different strategies for pharmacologic treatment and rehabilitation. The protocol includes detailed documented joint assessments performed by the same rheumatologist at all follow-up visits, and structured assessment of PRO's including the widely used HAQ-DI (46–49) at all visits.

Conclusion

In conclusion, in this study of patients with early RA, disability related to the upper extremities decreased significant from inclusion to the 6 month follow-up, and increased significantly again after 2 years. HAQ-DI-UE scores correlated strongly with grip force and patient reported outcomes at all time points and to a lesser extent with joint counts and laboratory markers of inflammation. The results underline the major impact of pain and reduced grip strength in early RA.

List Of Abbreviations

ACR American College of Rheumatology

ADL activities in daily living

anti-CCP anti-citrullinated protein antibodies

bDMARDs biological disease-modifying anti-rheumatics drugs

CATCH the Canadian Early Arthritis Cohort

CI confidence interval

CRP C-reactive protein

DAS28 disease activity score for 28 joints

DMARDs disease-modifying anti-rheumatic drugs

ERAS the Early Rheumatoid Arthritis Study

ESR erythrocytes sedimentation

HAQ the health assessment questionnaire

HAQ-DI the health assessment questionnaire disability index

HAQ-DI-UE the health assessment questionnaire disability index upper extremities

IQR interquartile range

LE the lower extremities

MCP joint metacarpophalangeal joint

N newton

NOAR the Norfolk Arthritis Register

PatGA Patient Global Assessment

PIP joint proximal interphalangeal joint

PROMs patient-reported outcomes measures

RA rheumatoid arthritis

RF rheumatoid factor

SJC swollen joint counts

TJC tender joint counts

UE the upper extremities

VAS Visual Analogue Scales

Declarations

Ethics approval and consent to participate:

All procedures performed in studies involving human participants were in accordance with the ethical standards of the regional research committee (Regional Ethical Review Board for southern Sweden, Lund, Sweden—LU 410-94, January 30, 1995 and LU 311-02, June 10, 2002) and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. All patients gave their written informed consent to participate, and the study was approved by the Regional Ethical Review Board for southern Sweden (Lund, Sweden).

Consent for publication:

Not applicable

Availability of data and materials:

The datasets generated and/or analysed during the current study are not publicly available due to Swedish legislation (the General Data Protection Regulation), but a limited and fully anonymised dataset containing the individual patient data that support the main analyses is available from the corresponding author on reasonable request.

Competing interests:

The authors declare no conflicts of interest.

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Authors' contributions:

All authors contributed to the study conception and design. MR and IW contributed to the data collection. Statistical analyses were performed by MR and CT. IW, SH and LJ contributed to the interpretation and analysis of the results. The first draft of the manuscript was written by MR and CT. All authors read or participated in revising the manuscript critically for important intellectual content, and all authors approved the final version to be submitted for publication. Dr. Turesson 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.

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Conflicts of interest:

None

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Figures

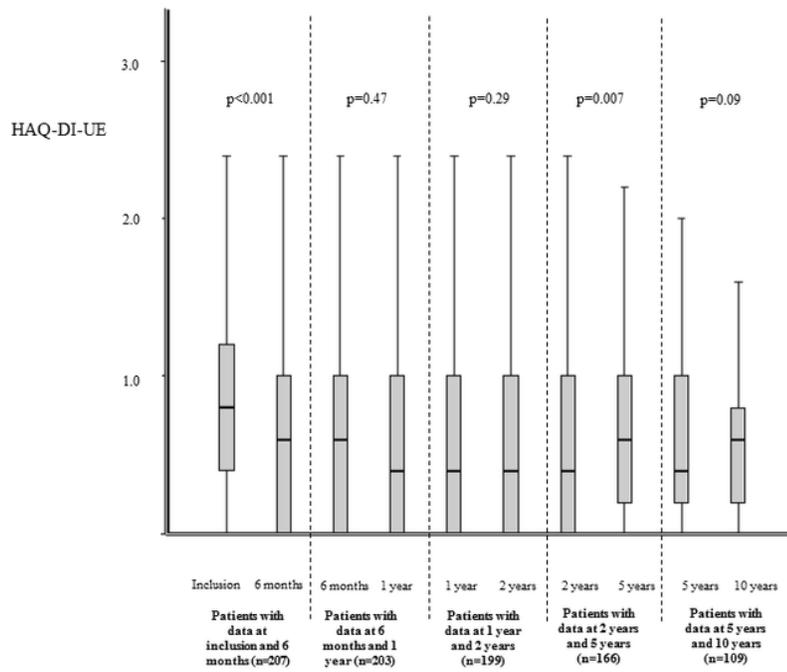


Figure 1

Changes in HAQ-DI-UE between visits; patients with data at both time points. Paired t-tests. Boxes indicates medians and quartiles, whiskers indicate 95 % highest and lowest within non-outlier range

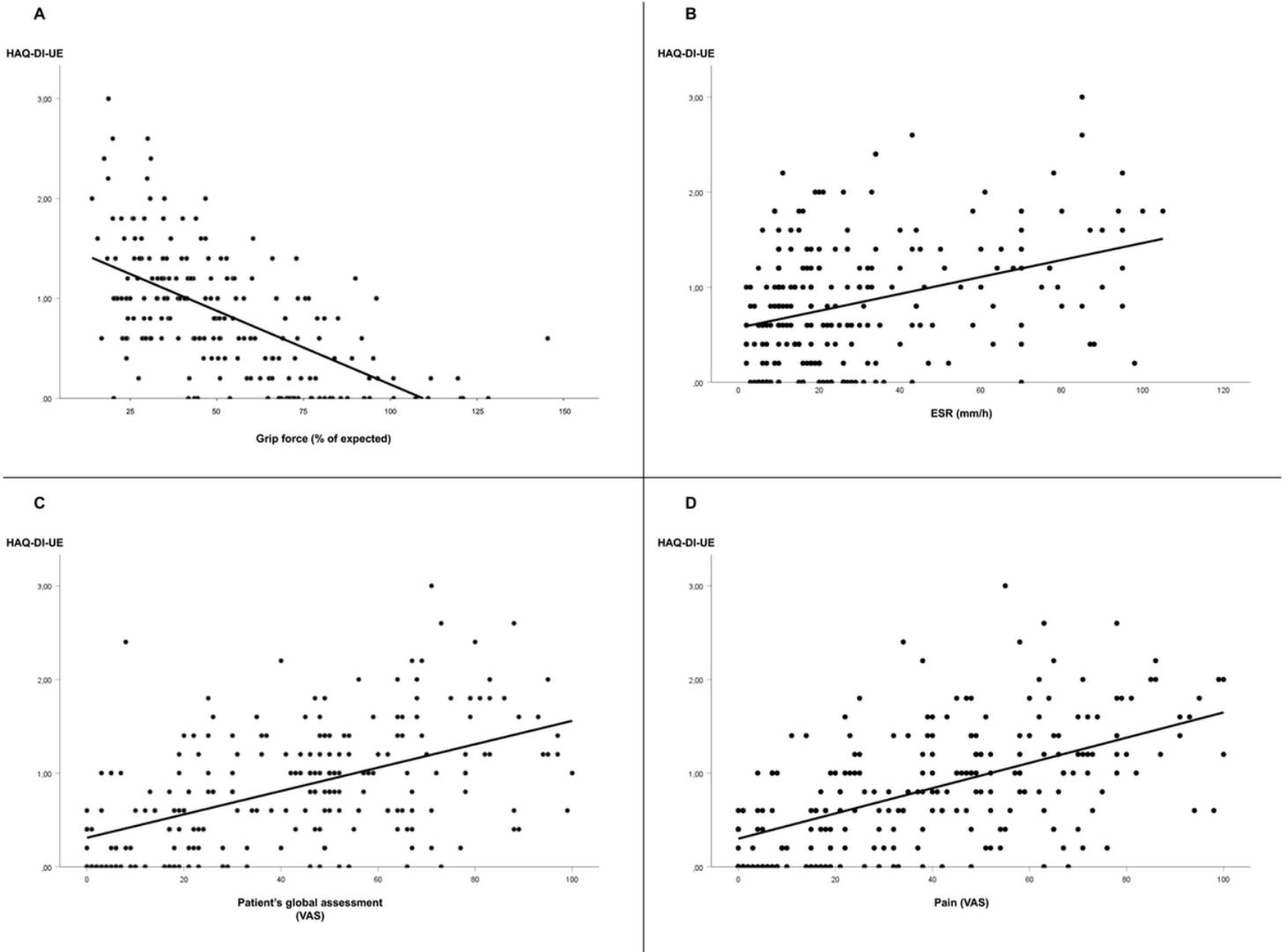


Figure 2

Correlations for disease parameters with HAQ-DI-UE at inclusion. Spearman's test. A Grip force $r = -0.62$; $p < 0.001$. B ESR $r = 0.33$; $p < 0.001$. C VAS Global $r = 0.53$; $p < 0.001$. D VAS pain $r = 0.58$; $p < 0.001$. E Swollen joint count (0-28); $r = 0.39$; $p < 0.001$. F Tender joint count $r = 0.50$; $p < 0.001$.

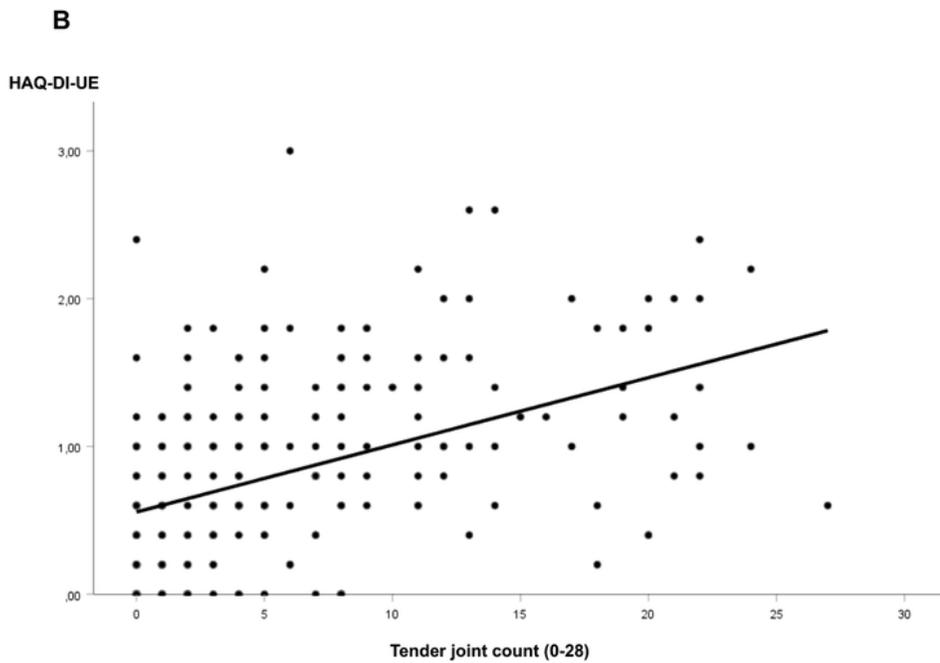
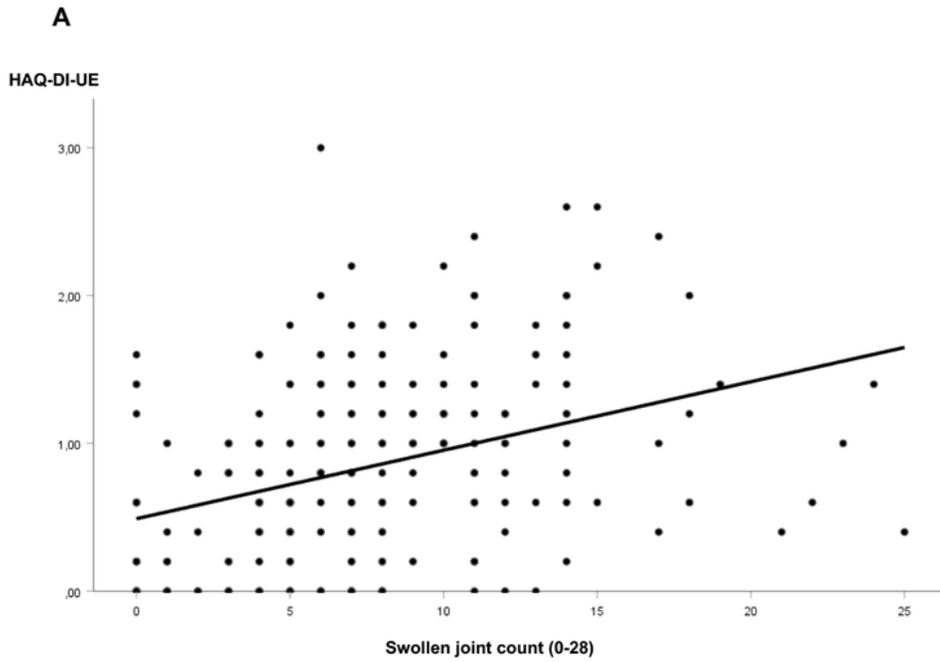
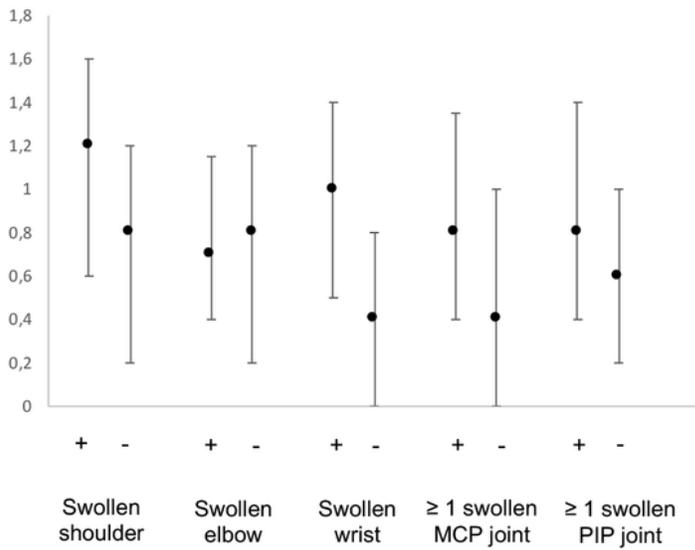


Figure 3

Correlations for disease parameters with HAQ-DI-UE at 10 years. Spearman's test. A Grip force $r = -0.45$. B ESR $r = 0.09$ $p < 0.001$. C VAS Global $r = 0.44$; $p < 0.35$. D VAS pain $r = 0.36$; $p < 0.001$. E Swollen joint count (0-28) $r = 0$; $p = 0.99$. F Tender joint count $r = 0.26$; $p = 0.006$.

A

HAQ-DI-UE



B

HAQ-DI-UE

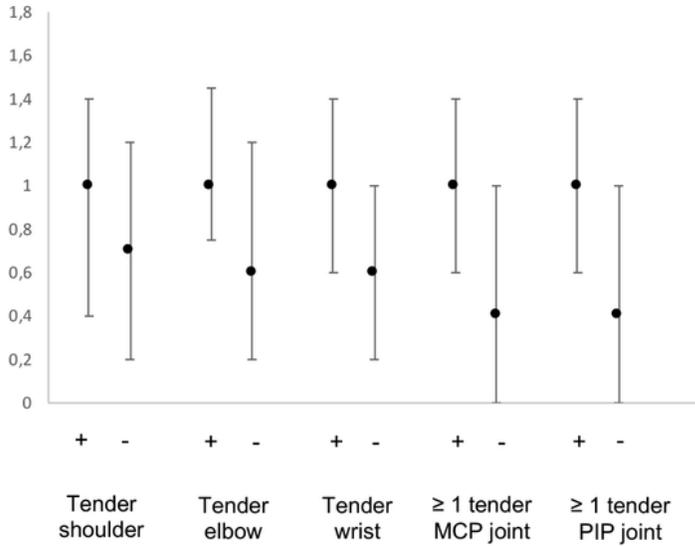


Figure 4

HAQ-DI-UE at inclusion, by presence of joint involvement in the UE. A Swollen joints – present (+) vs absent (-). Circles indicate medians, whiskers indicate interquartile ranges. Shoulder p=0.034; Elbow p=0.99; Wrist p<0.001; MCP p=0.006; PIP p=0.08. B Tender joints – present (+) vs absent (-). Circles indicate medians, whiskers indicate interquartile ranges. Shoulder p=0.08; Elbow p=0.002; Wrist p<0.001; MCP p<0.001; PIP p<0.001.

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