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The relation between upper extremity joint involvement and grip force in early rheumatoid arthritis: a retrospective study

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Abstract

To investigate the relation between joint involvement in the upper extremities and grip force in patients with early rheumatoid arthritis (RA). An inception cohort of 225 patients with early RA was followed according to a structured protocol. The same rheumatologist assessed all patients for swollen joints and joint tenderness. Grip force was measured (Grippit; AB Detektor, Gothenburg, Sweden) at the same visit. Average grip force values for the dominant hand were expressed as % of expected, based on age- and sex-specific reference values from the literature. Associations between grip force and current synovitis or tenderness of individual joints, and other disease parameters measured at the same visit, were examined. Patients with current synovitis of the wrist joint or ≥ 1 metacarpophalangeal (MCP) joint of the dominant hand had a significantly lower grip force at inclusion, at 1 year and at 5 years. Proximal interphalangeal joint tenderness and MCP joint tenderness were consistently associated with reduced grip force. In multivariate analysis, extensive MCP joint synovitis was associated with lower grip force at inclusion (β −2.8% per joint; 95% CI −5.3 to −0.4), and also at the 1-year follow-up. Patient reported pain scores and erythrocyte sedimentation rates had independent negative associations with grip force at all time points. In patients with early RA, extensive synovitis of the MCP joints was associated with reduced grip force, independently of other upper extremity joint involvement. Pain and inflammation have effects on hand function beyond those mediated by local synovitis.

Keywords Early rheumatoid arthritis · Grip force · Joint tenderness · Synovitis

Abbreviations

ACR	American College of Rheumatology
ADL	Activities of daily living
CI	Confidence intervals
CRP	C-reactive protein
DAS28	Disease activity score for 28 joints
DASH	Disabilities of the Arm, Shoulder and Hand Questionnaire
DMARDs	Disease modifying anti rheumatic drugs
ESR	Erythrocyte sedimentation rate
HAQ	Health Assessment Questionnaire
HAQ-DI	Health Assessment Questionnaire Disability Index
IQR	Interquartile range
MCP	Metacarpophalangeal joints
N	Newton
PIP	Proximal interphalangeal joints
RA	Rheumatoid arthritis
VAS	Visual Analogue Scale

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Background

Rheumatoid arthritis (RA) is characterized by chronic synovitis, in which the highly cellular inflammatory pannus tissue infiltrates both the cartilage, ligaments and tendons. This leads to erosion of the cartilage, gradual bone destruction, disruption of ligaments and impaired tendon glide that contribute to stiffness, pain and finally joint deformities [1]. Deformities in early untreated RA are initially passively correctable, but may with time lead to limited motion, and finally to fixed deformities [2]. RA typically involves the joints in the distal upper extremity, and more than 80% of the patients have dysfunction in the hands [3]. Joint inflammation and joint deformity both contribute to functional limitations in RA [4]. Progressive joint damage and disability lead to difficulties in performing activities of daily living (ADL). Symptoms due to wrist and hand involvement, and related limitations in function and ADL are common in both early and late RA [5, 6].

In comparison with age- and sex matched healthy populations, patients with RA have been shown to have reduced grip force [7–13] and finger extension force [10, 13]. We have recently reported that although grip force improved over time in patients with early RA, most patients in a community-based inception cohort of patients with RA still had < 60% of the expected grip force values, based on age and sex-specific reference values, 5 years after diagnosis [12]. In the evaluation of clinical trials, grip force, swollen joint count, patient reported pain and functional status measured by the Health Assessment Questionnaire (HAQ) [14] were all found to be outcome measures with intermediate responsiveness in patients with RA [15].

Several components contribute to grip force. Different muscle groups of the distal upper extremities produce the power, for instance the forearm flexor activation and the extensor synergist. It is important that the wrist is stabilized by the extensor muscles when the hand is gripping with force [16]. Wrist deformities are known to have a significant major impact on hand function [17–19.].

Furthermore, muscle strength in the upper extremity has been proposed to correlate with grip force [20]. Already 1.5 years after disease onset, patients with RA have been shown to have significantly reduced shoulder muscle strength in comparison with age-matched healthy controls [11]. There were significant associations between grip force, the Disabilities of the Arm, Shoulder and Hand (DASH) questionnaire score and shoulder muscle strength of the dominant arm [11]. A study of patients with early RA (disease duration of ≤ 12 months) showed that the lean mass of arms and legs was significantly reduced in both women and men compared to age-matched controls [21]. In the upper extremity, shoulder, elbow and wrist were the three joints with the greatest contributions to HAQ scores in patients with RA [22]. However, there are limited data on the relation between the involvement of specific joints and objective measures of hand function. Such information could be useful for targeted rehabilitation and other interventions. The potential importance of such findings is underlined by the demonstrated success of structured rehabilitation programs in RA [23, 24]. For example, in the randomized controlled SARAH trial, a tailored hand exercise program was shown to improve hand function in patients with RA [24].

The objective of this study was to investigate the relation between synovitis of different joints in the upper extremities and grip force in patients with early RA.

Patients and methods

Patients

An inception cohort of patients with early RA (symptom duration ≤ 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 [25]. 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 prespecified protocol for pharmacotherapy or rehabilitation. 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 years after inclusion. Using a standardized protocol, individual joints were assessed as swollen/not swollen and tender/not tender. Disability was assessed using the Health Assessment Questionnaire Disability Index (HAQ-DI) [14]. 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 [12]. Blood samples were obtained at the visit when the joint assessment was performed (within 1 h). 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 h). All Grippit procedures were performed after 9.20 a.m. to limit the impact of morning stiffness. The patient was seated comfortably in a chair without armrests, with the shoulder, arm and hand in standard positions as previously described [26]. 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 [26]. Nordenskiöld et al. reported a methodological error of 18% in patients with RA [26] and in studies of healthy children, intraclass correlation coefficients of 0.78–0.96 were found [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 [12]. Average grip force values of the dominant hand at inclusion and at the 1-year and 5-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.

Statistics

Grip force values (% of expected values of the dominant hand) in those with vs without current synovitis and with vs without current tenderness of individual joints in the dominant arm at each time point were compared using Student's *t* test.

Linear regression analysis was used to further explore the relation between upper extremity joint involvement in individual joints of the dominant arm and grip force (% of expected values of the dominant hand). The presence/absence of synovitis/tenderness in each joint or joint group [i.e. proximal interphalangeal (PIP) joints and metacarpophalangeal (MCP) joints] were included as covariates. In addition, the impact of the number of swollen/tender MCP (0–5) and PIP joints (0–5) was assessed. Furthermore, associations with VAS pain and ESR were explored in separate models. To examine potential synergistic effects, interactions between involvement (synovitis or joint tenderness, assessed separately) of different joints were tested, with grip force (% of expected values of the dominant hand) as the dependent variable. 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 (e.g. presence of MCP synovitis and number of swollen MCP joints, or wrist synovitis and wrist tenderness) the covariate with the strongest association with the dependent variable was selected for the multivariate analysis. The multivariate models were adjusted for significant interaction terms. In sensitivity analyses, the models were further adjusted for current glucocorticoid use.

To explore the impact of grip force on disability and overall disease impact, correlations between grip force (% of expected values of the dominant hand) and HAQ-DI and VAS global were investigated using Pearson's test.

Statistical analyses were performed using IBM SPSS Statistics version 22.0, Armonk, NY, USA: IBM Corp.

Results

Patients

A total of 225 patients with early RA (71% women; mean age 60 years) were investigated. The median symptom duration at inclusion was 7 months; interquartile range (IQR) 5–10. Data on average grip force of the dominant hand were available for 200 patients at inclusion, 202 patients at 1 year, and 173 patients at 5 years (Table 1).

A majority of the patients was treated with methotrexate (Table 1). A total of 17% initiated treatment with a biologic DMARD within 5 years. At baseline, the mean average grip force of the dominant hand was 105 N (mean 40% of expected). This increased over time to 139 N (mean 57% of expected) at 5 years (Table 1).

Frequency of joint involvement in early RA: overtime

Among patients with data on average grip force at inclusion 53% had synovitis of ≥ 1 PIP joint in the dominant hand, whereas synovitis of MCP, wrist, elbow and shoulder joints on the dominant side was observed in 79%, 64%, 8% and 7%, respectively (Table 2).

Whereas tenderness was more common compared to clinical synovitis in the shoulder, the reverse was the case for wrist, MCP and PIP joints (Table 2). Proportions with current joint involvement decreased somewhat over time, in particular the prevalence of PIP joint synovitis (Table 2).

There was major collinearity between the presence of synovitis and joint tenderness in the same joint/joint group at inclusion ($r=0.30$–0.56; $p<0.001$ for all correlations), at 1 year ($r=0.32$–0.59; $p<0.001$ for all correlations) and at 5 years ($r=0.23$–0.50; $p<0.01$ for all correlations).

Table 1 Characteristics of patients with RA and data on average grip force of the dominant hand

	Inclusion[b]	1 year[c]	5 years[d]
N	200[a]	202[a]	173[a]
Female sex % (*n*)	70 (140)	71 (143)	71 (123)
Age (years)	59.8 (14.7)	60.9 (14.6)	64.6 (14.3)
Symptom duration at inclusion (months); median (IQR)	7 (5–10)	7 (5–10)	7 (5–10)
RF positive % (*n*)	62 (125)	63 (127)	65 (113)
Anti-CCP positive % (*n*)	56 (99)	58 (104)	59 (89)
DAS28 (0–10)	4.6 (1.4)	3.7 (1.4)	3.6 (1.4)
HAQ (0–3)	0.85 (0.63)	0.64 (0.60)	0.75 (0.66)
Patient's global assessment (VAS 0–100)	42 (26)	31 (24)	34 (24)
Pain (VAS 0–100)	41 (27)	31 (24)	30 (24)
Swollen joint count (out of 28)	7.9 (5.0)	4.8 (4.1)	5.2 (4.9)
Tender joint count (out of 28)	6.3 (6.4)	3.6 (4.8)	3.0 (5.1)
Methotrexate treatment	54% (108)	63% (128)	61% (106)
Other DMARD	31% (62)	31% (63)	24% (42)
Glucocorticosteroid treatment	40% (79)	31% (64)	30% (51)
CRP (mg/l); median (IQR)	9 (<9–23.5)	<9 (<9–10)	<9 (<9-–10)
ESR (mm/h); median (IQR)	10 (20.5–42)	15 (8–27)	16 (9.5–25)
Average grip force of the dominant hand (*N*)	105 (78)	133 (85)	139 (95)
Average grip force of the dominant hand (% of expected)	40 (26)	52 (28)	57 (30)

Values are mean (SD) unless otherwise indicated

IQR interquartile range, *VAS* Visual Analogue Scale

[a]All patients with ≥ 1 grip force measure at inclusion, 1 and 5 years

[b]Missing data for joint assessment n = 3

[c]Missing data for joint assessment n = 3

[d]Missing data for joint assessment n = 4

Table 2 Frequency of synovitis and tender joints in the dominant hand over time in early RA

	Inclusion	1 year	5 years
N	197	199	169
Shoulder synovitis	7 (13)	5 (10)	1 (2)
Elbow synovitis	8 (16)	6 (13)	4 (7)
Wrist synovitis	64 (127)	41 (82)	35 (59)
≥ 1 MCP joint synovitis	79 (156)	65 (129)	69 (116)
≥ 1 PIP joint synovitis	53 (105)	29 (58)	27 (45)
No of swollen MCP joints; median (IQR)	2 (1–3)	1 (0–2)	1 (0–3)
No of swollen PIP joints; median (IQR)	1 (0–2)	0 (0–1)	0 (0–1)
Tender shoulder joint	30 (60)	25 (50)	19 (32)
Tender elbow joint	12 (23)	4 (9)	2 (4)
Tender wrist joint	45 (88)	28 (55)	14 (23)
≥ 1 tender MCP joint	54 (106)	34 (67)	31 (52)
≥ 1 tender PIP joint	42 (82)	22 (44)	23 (39)
No of tender MCP joints; median (IQR)	1 (0–2)	0 (0–1)	0 (0–1)
No of tender PIP joints; median (IQR)	0 (0–2)	0 (0–0)	0 (0–0)

Values are % (*n*) unless otherwise indicated

There was also major collinearity between presence of synovitis in MCP joints and the number of MCP joints with synovitis ($r = 0.74$–0.86; $p < 0.001$) and the presence of PIP synovitis and the number of PIP joints with synovitis ($r = 0.92$–0.99; $p < 0.001$) at all time points, and similar findings for joint tenderness (MCP: $r = 0.93$–0.98, $p < 0.001$; PIP: $r = 0.96$–0.99; $p < 0.001$).

Associations between joint involvement and grip force: bivariate analyses

Current synovitis of the wrist joint or ≥ 1 MCP joint of the dominant hand were associated with a significantly lower grip force at inclusion (Fig. 1a) as well as at 1 year (Fig. 1b) and 5 years (Fig. 1c). There were similar trends for PIP and elbow synovitis, although these did not reach statistical significance (Fig. 1a–c). The presence of joint tenderness was consistently associated with a significantly reduced grip force, except for elbow tenderness at 5 years (Fig. 2a–c).

In linear regression models, there were also negative associations for the number of swollen MCP joints, the number of swollen PIP joints, the number of tender MCP joints, the number of tender PIP joints, VAS pain and ESR with grip force at inclusion (Table 3). Similar associations

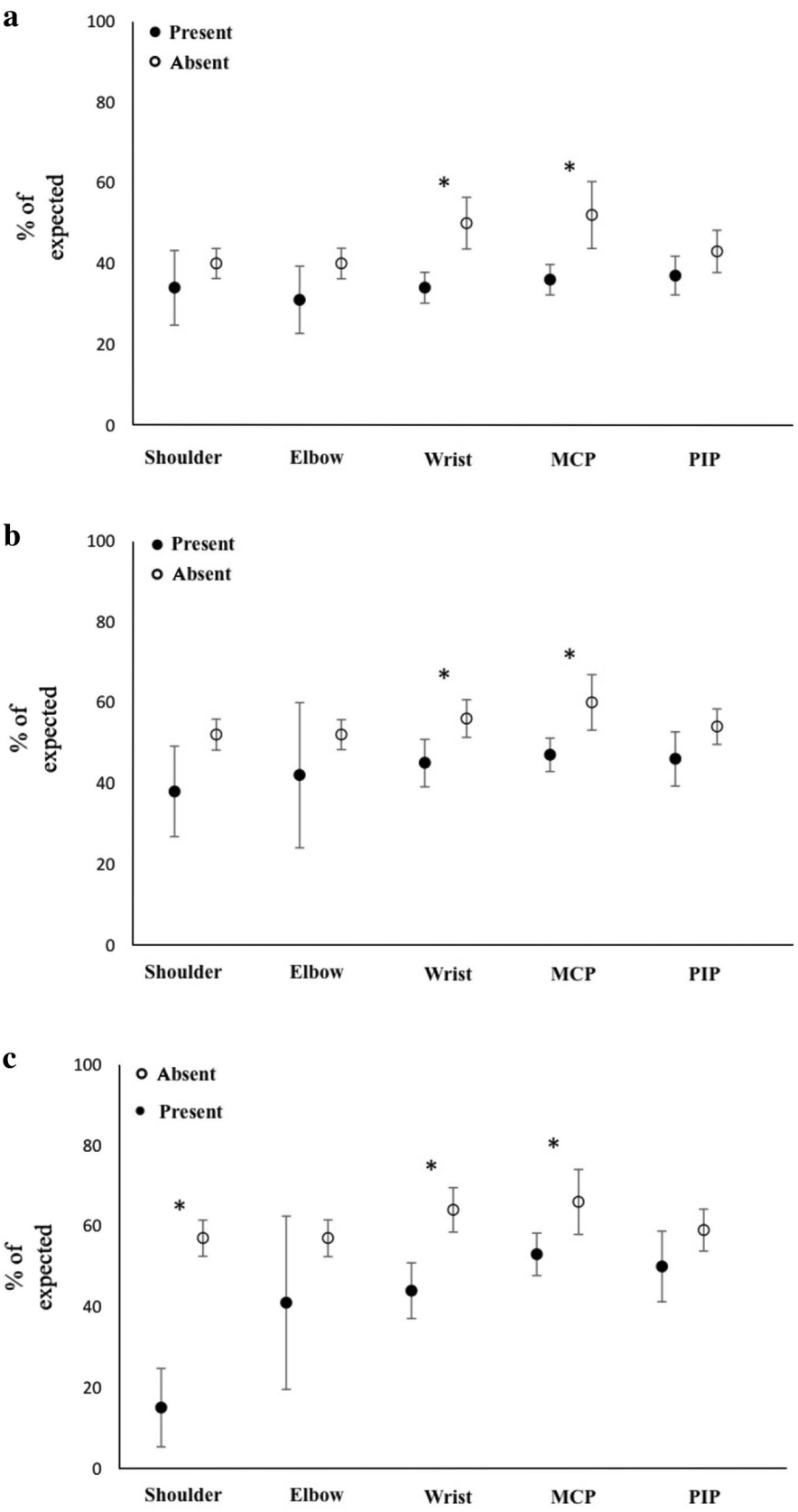

Fig. 1 Grip force in patients with early RA—by current synovitis. Average grip force (% of expected, dominant hand) in patients with early RA, by current synovitis of individual joints/joint groups at the dominant side. Mean values with 95% confidence intervals. *p* values represent comparisons of patients with vs without synovitis for each joint/joint group. *Significant differences ($p < 0.05$). **a** Inclusion. Shoulder: $p = 0.41$; elbow: $p = 0.06$; wrist: $p < 0.001$*; metacarpophalangeal (MCP) joint (≥ 1): $p = 0.001$*; proximal interphalangeal (PIP) joint (≥ 1): $p = 0.13$. **b** 1-Year follow-up. Shoulder: $p = 0.10$; elbow: $p = 0.18$; wrist: $p = 0.006$*; MCP joint (≥ 1): $p = 0.001$*; PIP joint (≥ 1): $p = 0.07$. **c** 5-Year follow-up. Shoulder: $p = 0.049$*; elbow: $p = 0.15$; wrist: $p = 0.001$*; MCP joint (≥ 1): $p = 0.01$*; PIP joint (≥ 1): $p = 0.10$

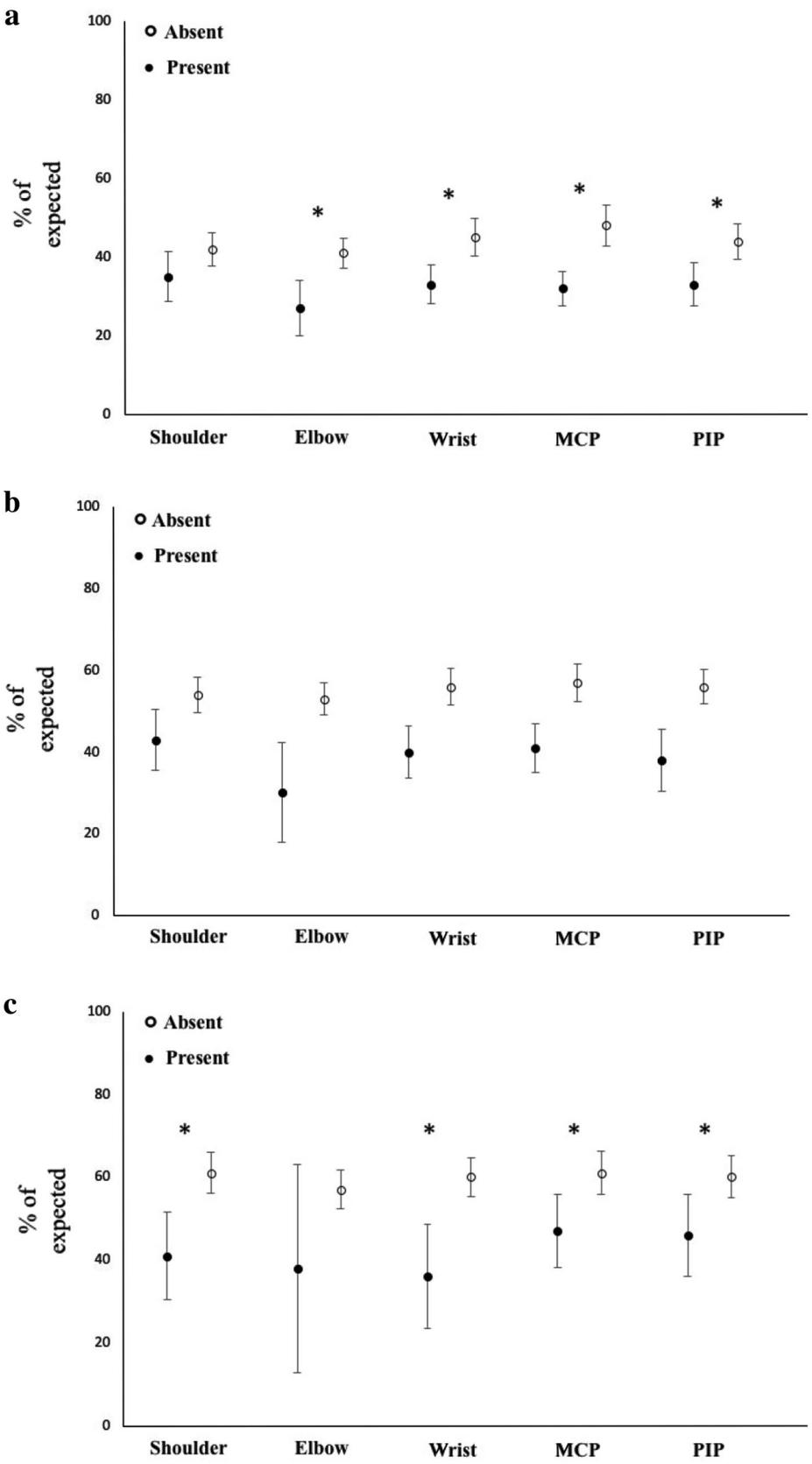

Fig. 2 Grip force in patients with early RA—by current joint tenderness. Average grip force (% of expected, dominant hand) in patients with early RA, by the tenderness of individual joints/joint groups at the dominant side. Mean values with 95% confidence intervals. *p* values represent comparisons of patients with vs without tenderness for each joint/joint group. *Significant differences ($p < 0.05$). **a** Inclusion. Shoulder: $p = 0.06$; elbow: $p = 0.008$*; wrist: $p = 0.002$*; metacarpophalangeal (MCP) joint (≥ 1): $p < 0.001$*; proximal interphalangeal (PIP) joint (≥ 1): $p = 0.003$*. **b** 1-Year follow-up. Shoulder: $p = 0.01$*; elbow: $p = 0.01$*; wrist: $p < 0.001$*; MCP joint (≥ 1): $p < 0.001$*; PIP joint (≥ 1): $p < 0.001$*. **c** 5-year follow-up. Shoulder: $p = 0.001$*; elbow: $p = 0.21$; wrist: $p < 0.001$*; MCP joint (≥ 1): $p = 0.007$*; PIP joint (≥ 1): $p = 0.02$*

Table 3 Factors associated with average grip force (dominant hand; % of expected value)—bivariate linear regression

	Inclusion			1 year			5 years		
	Unstandardized β	95% CI	p	Unstandardized β	95% CI	p	Unstandardized β	95% CI	p
VAS pain (per SD)	−10.1	−13.4 to −6.8	<0.001	−10.7	−14.2 to −7.2	<0.001	−10.5	−14.8 to −6.1	<0.001
ESR (per SD)	−6.9	−10.4 to −3.5	<0.001	−9.2	−13.1 to −5.2	<0.001	−7.5	−11.9 to −3.2	0.001
Shoulder synovitis present	−6.1	−20.5 to 8.4	0.41	−14.3	−31.6 to 3.0	0.10	−42.7	−85 to −0.4	0.048
Elbow synovitis present	−9.5	−22.6 to 3.6	0.15	−10.6	−25.9 to 4.7	0.18	−16.9	−40 to 6.2	0.15
Wrist synovitis present	−16.0	−23.2 to −8.9	<0.001	−10.8	−18.5 to −3.1	0.006	−19.5	−28.8 to −10.3	<0.001
MCP synovitis present	−15.4	−24.0 to −6.8	0.001	−13.5	−21.3 to −5.7	0.001	−12.8	−22.6 to −3	0.011
PIP synovitis present	−5.6	−12.8 to 1.5	0.12	−6.4	−14.7 to 1.9	0.13	−8.8	−19.2 to 1.6	0.098
No of swollen MCP joints (0–5; per joint)	−5.9	−8.4 to −3.5	<0.001	−6.4	−9.3 to −3.5	<0.001	−5.4	−8.5 to −2.2	0.001
No of swollen PIP joints (0–5; per joint)	−3.2	−5.7 to −0.7	0.013	−3.9	−7.4 to −0.4	0.03	−4.9	−9.1 to −0.7	0.022
Tender shoulder joint present	−7.3	−15.1 to 0.4	0.06	−11.1	−19.8 to −0.02	0.012	−19.7	−31.2 to −8.3	0.001
Tender elbow joint present	−14.8	−25.8 to −3.9	0.008	−22.8	−40.8 to −4.8	0.014	−19.3	−49.6 to 11	0.21
Tender wrist joint present	−11.3	−18.3 to −4.2	0.002	−15.9	−24.2 to −7.6	<0.001	−23.9	−36.9 to −10.9	<0.001
Tender MCP joint present	−16.1	−22.9 to −9.2	<0.001	−16.4	−24.2 to −8.6	<0.001	−13.6	−23.4 to −3.7	0.007
Tender PIP joint present	−10.8	−17.9 to −3.7	0.003	−17.6	−26.5 to −8.8	<0.001	−13.5	−24,3 to −2.7	0.015
No of tender MCP joints (0–5; per joint)	−5.6	−7.6 to −3.5	<0.001	−5.8	−8.8 to −2.7	<0.001	−5.5	−8.9 to −2.1	0.002
No of tender PIP joints (0–5; per joint)	−4.1	−6.4 to −1.9	<0.001	−6.7	−10 to −3.3	<0.001	−6.1	−9.9 to −2.3	0.002

were observed at the follow-up visits after 1 and 5 years (Table 3). The presence of synovitis of the glenohumeral joint was associated with a significantly lower grip force at 5 years.

At inclusion, there was a significant interaction between the presence of wrist synovitis and elbow synovitis in the dominant hand in their impact on grip force ($p = 0.02$). At 1 year, there was significant interaction between elbow synovitis and synovitis in ≥ 1 MCP joint and the number of MCP joints with synovitis ($p = 0.02$ and $p = 0.04$). Furthermore, there were significant interactions between the presence of tenderness in ≥ 1 PIP joint and in ≥ 1 MCP joint at inclusion ($p = 0.01$) and at 5 years ($p = 0.03$). In all these cases, individuals with the involvement of several joints had lower grip force than expected, based on the contribution of each joint, except for at 5 years, where the presence of both PIP and MCP tenderness was associated with higher grip force.

Table 4 Factors associated with average grip force (dominant hand; % of expected value)—multivariate linear regression

	Unstandardized β	95% CI	p
Inclusion—multivariate linear regression[a]			
VAS pain (per SD)	−5.8	−9.3 to −2.3	0.001
ESR (per SD)	−3.6	−6.9 to −0.3	0.03
Wrist synovitis present	−7.2	−14.3 to 0.0	0.05
No of swollen MCP joints (0–5; per joint)	−2.8	−5.3 to −0.4	0.02
Tender shoulder joint present	−1.2	−8.1 to 5.7	0.73
Tender elbow joint present	−5.9	−16.5 to 4.8	0.28
No of tender PIP joints (0–5; per joint)	−0.7	−2.6 to 0.4	0.68
1 year—multivariate linear regression[b]			
VAS pain (per SD)	−5.7	−9.8 to −1.7	0.006
ESR (per SD)	−5.1	−9.1 to −1.2	0.01
No of swollen MCP joints (0–5; per joint)	−3.3	−6.3 to −0.3	0.03
Tender shoulder joint present	−3.6	−11.9 to 4.6	0.38
Tender elbow joint present	−14.5	−33.7 to 4.6	0.14
Tender wrist joint present	−3.7	−12.6 to 5.1	0.41
No of tender PIP joints (0–5; per joint)	−1.9	−5.4 to 1.6	0.29
5 years—multivariate linear regression[c]			
VAS pain (per SD)	−6.2	−10.9 to −1.5	0.01
ESR (per SD)	−4.8	−9.4 to −0.2	0.04
Shoulder synovitis present	−35.0	−73.9 to 3.8	0.08
No of swollen MCP joints (0–5; per joint)	−2.2	−5.6 to 1.2	0.20
Tender wrist joint present	−6.7	−22.3 to 8.9	0.40
No of tender PIP joints (0–5; per joint)	−6.4	−12.1 to −0.8	0.03

[a]Adjusted for all variables in the table and for the interaction terms for (1) wrist synovitis and elbow synovitis and (2) presence of tender MCP joints and presence of tender PIP joints

[b]Adjusted for all variables in the table and for the interaction terms for elbow synovitis and MCP joint synovitis

[c]Adjusted for all variables in the table and for the interaction terms for the presence of tender MCP joints and presence of tender PIP joints

Associations between joint involvement and grip force: multivariate analyses

In multivariate analysis, extensive MCP joint synovitis was associated with lower grip force at inclusion and at the 1-year follow-up, but not at 5 years (Table 4). There was also a borderline negative association between wrist synovitis and grip force at inclusion (Table 4). At the 5-year follow-up visit, there was a significant association between the number of tender PIP joints and reduced grip force (Table 4). VAS pain and ESR were negatively associated with grip force in multivariate models at all time points. The proportions of the variance in grip force explained by the variables in these models were 26% at inclusion, 25% at 1 year and 22% at 5 years.

Results were similar in sensitivity analyses further adjusted for current glucocorticoid use (Supplementary Table 1).

Correlations with disability and global disease assessment

Grip force (% of expected values) correlated significantly with HAQ-DI at inclusion as well as at 1 year and 5 years ($p = 0.001$ at all time points) (Supplementary Figure 1). Similar correlations were noted for VAS global ($p = 0.001$ at all time points) (Supplementary Figure 2).

Discussion

In this study of patients with early RA, MCP joint synovitis had a significant impact on grip force measured at the same outpatient visit, whereas the relative contribution of PIP synovitis to impaired grip force appeared to be less pronounced in early disease. However, at 5 years, PIP tenderness was associated with reduced grip force. The interactions for elbow synovitis with synovitis in the hand, and between

PIP and MCP tenderness, in analyses of grip force suggest that multiple joint involvements contribute to worse hand function. In addition, both VAS pain and ESR levels were independently associated with reduced grip force, suggesting that pain and inflammation have effects on hand function beyond that mediated by local synovitis.

Joint involvement of the tested extremity, ESR and VAS pain explained 22–26% of the variation in grip force at the different time points, suggesting that other factors, such as motivation and general muscle strength, have a major impact in this context.

The correlation for grip force with disability and global disease activity [i.e. HAQ-DI and patients' global assessment (VAS)] at inclusion as well as 1 and 5 years confirms the major impact of impaired hand function in patients with RA.

The differential impact of the involvement of specific joints and joint groups on grip force likely reflects mechanical factors, and also the propensity for development of chronic arthritis in each location [29]. Expression of key developmental genes tightly controls morphogenesis of the limbs, and such gene expression is distinctly different in the four posterior digits (II–V) of the hands and feet, which are more prone to be involved in RA, compared to the anterior digit (I) [29]. The importance of such factors, and of involvement of individual finger joints, for grip force and hand disability, should be further studied.

Synovitis and tenderness of the wrist also had some impact on grip force. It is well known that wrist involvement is common in early RA [30–37] and that arthritis of the distal radio-ulnar joint is a particularly frequent cause of disability [35, 38, 39]. For example, with the impaired extension of the wrist, grip strength is decreased significantly [40]. This is likely due to reduced force of the extrinsic finger flexors when the wrist is not slightly extended [41]. In the present study, the number of involved finger joints correlated negatively with grip force, in particular the extent of MCP joint synovitis. This is compatible with data indicating that the four distal fingers of the hand all contribute significantly to grip force [40]. Joint deformities of the fingers are common in RA [6, 32, 42, 43] and swan neck deformity, in particular, is associated with low grip strength [44].

Motivation probably has a major impact on grip force. At the evaluation of grip force some people exert less than a maximal voluntary contraction with their hands. This may be intentional or unintentional. Individuals with symptoms from their upper extremity and related pain, fear of pain or fear for residual symptoms can unintentionally make a limited effort [45, 46]. Intentional low effort can be due to secondary gain benefits, e.g. money or attention [47, 48]. Such factors are difficult to quantify and were not assessed in the present study.

Additional limitations include the lack of a control group of individuals without RA evaluated at our unit. Instead, we used age and sex-specific reference values from the literature, based on a study from Norway [28] a country with major similarities in the ethnic background and lifestyle factors to Sweden. As we used % of expected values of grip force for each individual, we estimated the effect of other variables on age- and sex-standardized grip force.

Although the grip force measurements were partially performed by different observers, a standardized procedure was used by occupational therapists at our unit during the entire study period [26].

With the inclusion period of 1995–2005 and the follow-up of 5 years, the most recent data in this study are from 2010. Therefore, biologic/targeted therapy was not used as widely as today, and current treatment algorithms, including the treat to target strategy [49] were not implemented. These are important limitations of the study.

Strengths of this study include the standardized joint assessment performed by the same physician in all cases, using a structured protocol. In addition, we used standardized and established methods for assessment of grip force, performed in accordance with the recommendations from the American Society of Hand Therapists [50]. Calculation of the average of three assessments has been shown to give the highest reliability and validity in hand strength evaluation [50].

Furthermore, due to the structured longitudinal follow-up of an inception cohort from a defined catchment area, selection bias is not a major issue in this study, and the results could be generalized to patients with RA seen in clinical practice.

Conclusions

In conclusion, in patients with early RA, extensive synovitis of MCP joints was associated with reduced grip force, independently of other upper extremity joint involvement. Pain and inflammation (measured by ESR) appeared to have effects on hand function that were independent of local synovitis and joint tenderness. Throughout the observation period, reduced grip force was associated with more extensive disability and worse scores for patient global assessment of disease activity. The results underline the major importance of impaired hand function in patients with early RA.

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Author contributions All authors contributed to the study conception and design. Data collection was performed by MR and IW. Statistical analyses were performed by MR and CT. 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 commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no competing interests.

Ethical approval 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.

Ethical statement 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.

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