The Relation Between Disease Activity, Patient-Reported Outcomes, and Grip Force Over Time in Early Rheumatoid Arthritis

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Objective. The objective of this study is to identify early predictors of future reduced grip force in patients with rheumatoid arthritis (RA) and to identify early predictors of grip force over time.

Methods. In a structured follow-up of an inception cohort of patients with early RA, average grip force values of the dominant hand were evaluated and compared with the expected based on age- and sex-specific reference values. Potential predictors of reduced grip force (less than 50% of expected) at 5 years were examined using logistic regression. Differences in percentage of expected grip force values over the study period and differences in change over time, by baseline disease parameters, were estimated using mixed linear-effects models.

Results. Among 200 patients with early RA, 44% had reduced grip force 5 years after diagnosis. Baseline characteristics that predicted reduced grip force at 5 years included high scores for the Health Assessment Questionnaire Disability Index (odds ratio 1.54 per SD; 95% confidence interval 1.13-2.11), high scores for pain and patient global assessment, and low grip force. C-reactive protein levels, the erythrocyte sedimentation rate, the 28-joint Disease Activity Score (DAS28), rheumatoid factor, anti–cyclic citrullinated peptide antibodies, joint counts, and synovitis of individual joints in the dominant upper extremity did not predict reduced grip force. Patients with baseline synovitis of the wrist or metacarpophalangeal joints or patients with a high DAS28 had lower estimated grip force at inclusion but also greater improvement of grip force over time.

Conclusion. Patient-reported outcomes predicted reduced grip strength 5 years after diagnosis. This underlines the prognostic importance of disability in early RA. Joint counts and synovitis in individual joints may change rapidly in early RA and appear to be less predictive of long-term hand function.

INTRODUCTION

Rheumatoid arthritis (RA) is characterized by polyarthritis and commonly affects the small distal joints of the hands and feet (1). Joint destruction begins early in some cases and then often progresses rapidly, in particular in the hands (2,3). Early prediction of a severe disease phenotype remains a challenge (4). Most studies of prognostic markers have examined their relation to joint destruction. Conventional radiographic investigation of the hands and feet is, since many years, the most widely used method to estimate joint damage over time in such patients (5–7). Baseline and persistent synovitis (8) and also inflammation measured using the multi-biomarker disease activity score (9) have been shown to predict progression of structural damage in RA. Rheumatoid factor (RF) and/or anti–cyclic citrullinated peptide (CCP) seropositivity, as well as an increased erythrocyte sedimentation rate (ESR) or increased C-reactive protein (CRP) levels, predicted rapid radiographic progression over 3 years (2) and 5 years (10). Initial joint damage progression during the first year of disease is a major predictor of later progressive joint damage (11).

Assessment of objective measures of function is important in the evaluation of patients with RA (12,13). Grip force measurement is regarded as a relevant parameter of hand function in patients with RA (1,6,13,14).

Patients with early RA have substantially reduced grip force compared with expected values, based on the general population (15). Grip force has a major impact on disability, in particular, in female patients with RA (16). Lower grip force in the dominant
Patients and Methods

Patients. An inception cohort of patients with early RA (symptom duration: 12 months or fewer), recruited in 1995-2005, was investigated. The patients were diagnosed with RA by a rheumatologist and fulfilled the 1987 American College of Rheumatology classification criteria for RA (31). The study included individuals from a defined area: the city of Malmö, Sweden (population of 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 at 5 years after inclusion. By using a standardized protocol, individual joints were assessed as swollen or not swollen and tender or not tender, and standard 28-joint swollen joint counts (SJCs) and tender joint counts (TJCs) were obtained. Disability was assessed using the Health Assessment Questionnaire Disability Index (HAQ-DI) (32). The Swedish validated translated version of the HAQ-DI (33) was used. Patient-reported pain and patient global assessment of disease activity were assessed using visual analogue scales (VAS) (scale: 0-100). Information on treatment was obtained as previously described (15). Blood samples were obtained at the visit when the joint assessment was performed (within 1 hour). CRP levels and the ESR were analyzed using standard methods at the Department of Clinical Chemistry, Malmö University Hospital.

Assessment of grip force. Grip force (measured in newtons) was measured by using the electronic instrument Grippit (AB Detektor). 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 (34). 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 (34). The grip force was measured alternately in the dominant hand and the nondominant hand three times, and the mean of the three measurement values from each hand was used. Average values of the 10-second uninterrupted grip were obtained, as previously described (15). Average grip force values of the dominant hand at inclusion and at the 1-year and 5-year follow-up visits were compared with 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 (35). Grip force values for each patient were expressed as a percentage of the expected based on the reference values.

Statistics. Potential baseline predictors of reduced grip force (defined as less than 50% of the expected) at 5 years were examined using logistic regression analysis. In addition, the impact of baseline disease parameters on grip force over time was examined. Differences in the percentage of expected grip force values over the study period and differences in change over time by baseline disease parameters were estimated using mixed linear-effect models. The intercept corresponded to the estimated mean grip force at baseline based on the regression line. Presence versus absence of synovitis of individual joints or joint groups of the dominant arm and continuous disease severity measures (per SD) were included as covariates. Furthermore, patients in...
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Each of the three higher quartiles of baseline disease activity (28-joint Disease Activity Score [DAS28]), disability (HAQ-DI), and pain (VAS) were compared with those in the lowest quartile. Quartiles of each of the subcomponents in the DAS28 (ie, SJC, TJC, ESR, and patient global assessment [VAS-global]) were compared in the same manner.

RESULTS

In an inception cohort of 233 patients with early RA, a subcohort of 200 patients (70% women, mean age of 59.8 years, 62% RF-positive, 56% anti–CCP2-positive, median symptom duration of 7 months) (Table 1) were observed for 5 years and had available

Table 1. Characteristics at inclusion of the early RA cohort

| Inclusion | All Patients With Grip Force Dataa | Patients With Data on Grip Force at the 5-y Follow-up | 5-y Follow-up |
|-----------|----------------------------------|-----------------------------------------------------|---------------|
| N         | 200                              | 173                                                 | 173           |
| Female sex, % (n) | 70 (140)               | 71 (123)                                           | 71 (123)       |
| Age, mean (SD), y | 59.8 (14.7)                 | 60.4 (14.6)                                         | 64.6 (14.3)    |
| Symptom duration at inclusion, median (IQR), mo | 7 (5-10)                        | 7 (5-10)                                            | 7 (5-10)       |
| RF-positive at inclusion, % (n) | 62 (125)                     | 65 (113)                                            | 65 (113)       |
| Anti–CCP-positive at inclusion, % (n) | 56 (99)                      | 59 (89)                                             | 59 (89)        |
| DAS28 (0-10), mean (SD) | 4.6 (1.4)                    | 4.6 (1.4)                                           | 3.6 (1.4)      |
| HAQ (0-3), mean (SD) | 0.85 (0.63)                  | 0.86 (0.63)                                         | 0.76 (0.66)    |
| Patient global assessment (VAS: 0-100), mean (SD) | 42 (26)                       | 44 (27)                                             | 34 (25)        |
| Pain (VAS: 0-100), mean (SD) | 41 (27)                      | 41 (26)                                             | 30 (24)        |
| SJC (out of 28), mean (SD) | 7.9 (5.0)                    | 7.8 (5.0)                                           | 5.2 (4.9)      |
| TJC (out of 28), mean (SD) | 6.3 (6.4)                    | 5.9 (6.0)                                           | 3.0 (5.1)      |
| Methotrexate treatment, % (n) | 54 (108)                      | 54 (93)                                             | 61 (106)       |
| Other DMARDs, % (n) | 31 (62)                       | 32 (56)                                             | 24 (42)        |
| Glucocorticoid treatment, % (n) | 40 (79)                       | 37 (64)                                             | 30 (51)        |
| CRP, median (IQR), mg/l | 9 (<9-23.5)                  | <9 (<9-28)                                          | <9 (<9-10)     |
| ESR, median (IQR), mm/h | 20.5 (10-42)                 | 21 (11-44)                                          | 16 (10-25)     |

Synovitis on dominant side

| Shoulder, % (n) | 7 (13)               | 8 (14)                                             | 1 (2)          |
| Elbow, % (n) | 8 (16)               | 9 (16)                                             | 4 (7)          |
| Wrist, % (n) | 64 (127)             | 64 (109)                                           | 34 (59)        |
| ≥1 MCP joint, % (n) | 79 (156)              | 76 (130)                                           | 67 (116)       |
| ≥1 PIP joint, % (n) | 53 (105)              | 53 (90)                                            | 26 (45)        |
| No. of MCP joints, median (IQR) | 2 (1-3)              | 2 (1-3)                                            | 1 (0-3)        |
| No. of PIP joints, median (IQR) | 1 (0-2)              | 1 (0-2)                                            | 0 (0-1)        |

Tenderness on dominant side

| Shoulder, % (n) | 30 (60)               | 34 (57)                                            | 18 (32)        |
| Elbow, % (n) | 12 (23)               | 11 (18)                                            | 2 (4)          |
| Wrist, % (n) | 45 (88)               | 45 (76)                                            | 13 (23)        |
| ≥1 MCP joint, % (n) | 54 (106)              | 49 (83)                                            | 30 (52)        |
| ≥1 PIP joint, % (n) | 42 (82)               | 40 (68)                                            | 22 (39)        |
| No. of MCP joints, median (IQR) | 1 (0-2)              | 0 (0-2)                                            | 0 (0-1)        |
| No. of PIP joints, median (IQR) | 0 (0-2)              | 0 (0-2)                                            | 0 (0-0)        |

Abbreviation: CCP, cyclic citrullinated peptide; CRP, C-reactive protein; DAS28, 28-Joint Disease Activity Score; DMARD, disease-modifying antirheumatic drug; ESR, erythrocyte sedimentation rate; HAQ, Health Assessment Questionnaire; IQR, interquartile range; MCP, metacarpophalangeal; PIP, proximal interphalangeal; RA, rheumatoid arthritis; RF, rheumatoid factor; SJC, swollen joint count; TJC, tender joint count; VAS, visual analogue scale.

*aAverage values of the dominant hand at any time point.
data on grip force. Most patients were started on methotrexate and/or other disease-modifying antirheumatic drugs (DMARDs) less than 1 year after symptom onset (Table 1). A total of 17% initiated treatment with a biologic DMARD within 5 years. Baseline characteristics of the patients included in the present study and the original cohort were similar (Supplementary Table 1). The right hand was dominant in 187 patients (93.5%).

At inclusion, 53% had synovitis of one or more proximal interphalangeal (PIP) joint in the dominant hand, whereas synovitis of metacarpophalangeal (MCP) joints, wrist, elbow, and shoulder joints in the dominant extremity was observed in 79%, 64%, 8%, and 7%, respectively. Five years after diagnosis, 76 patients (44%) had reduced grip force (less than 50% of the expected). The mean value for the average grip force of the dominant hand increased from 40% of expected at baseline to 57% at the 5-year follow-up. There was also improvement in standard clinical disease measures (Table 1).

Baseline characteristics that predicted reduced grip force at 5 years included high HAQ-DI scores (odds ratio [OR] 1.54 per SD; 95% confidence interval [CI] 1.13-2.11) and high scores for pain (OR 1.36 per SD; 95% CI 1.00-1.86) and patient global assessment (OR 1.41 per SD; 95% CI 1.03-1.92), but laboratory markers of inflammation (CRP level and ESR), the DAS28, RF, anti-CCP levels, and 28-joint SJCs and TJs were not predictive of reduced grip force (Table 2). Furthermore, baseline synovitis involvement of individual joints in the dominant upper extremity did not predict reduced grip force at 5 years (Table 2). The higher the baseline grip force (percentage of the expected value), the lower the risk of reduced grip force at 5 years (OR 0.41 per SD; 95% CI 0.27-0.62) (Table 2).

| Table 2. Baseline predictors of reduced grip force (<50% of expected; average grip force values of the dominant hand) at 5 years in the early rheumatoid arthritis cohort |
|-----------------------------------------------|----------------|------------------|
| **Odds Ratio** | **95% Confidence Interval** |
| Female sex | 1.79 | 0.90-3.55 |
| RF-positive | 0.76 | 0.41-1.43 |
| Anti-CCP-positive | 0.99 | 0.52-1.90 |
| DAS28 (per SD) | 1.16 | 0.85-1.57 |
| HAQ (per SD) | 1.54 | 1.13-2.11 |
| Pain (VAS) (per SD) | 1.36 | 1.00-1.86 |
| Patient global assessment (VAS) (per SD) | 1.41 | 1.03-1.92 |
| SJC (out of 28) (per SD) | 0.86 | 0.63-1.17 |
| TJC (out of 28) (per SD) | 1.11 | 0.80-1.54 |
| ESR (per mm/h) (per SD) | 0.96 | 0.71-1.29 |
| CRP (≥9 mg vs <9 mg/l) | 0.72 | 0.39-1.32 |
| Grippit average score, dominant hand (% of predicted) (per SD) | 0.41 | 0.27-0.62 |
| **Synovitis on dominant side** |
| Shoulder | 1.29 | 0.43-3.87 |
| Elbow | 0.98 | 0.35-2.78 |
| Wrist | 0.99 | 0.53-1.86 |
| ≥1 MCP joint | 0.95 | 0.47-1.95 |
| ≥1 PIP joint | 0.94 | 0.51-1.71 |
| No. of MCP joints (per joint) | 0.94 | 0.76-1.17 |
| No. of PIP joints (per joint) | 1.02 | 0.82-1.26 |

**Abbreviation:** CCP, cyclic citrullinated peptide; CRP, C-reactive protein; DAS28, 28-joint Disease Activity Score; DMARD, disease-modifying antirheumatic drug; ESR, erythrocyte sedimentation rate; HAQ, Health Assessment Questionnaire; MCP, metacarpophalangeal; PIP, proximal interphalangeal; RF, rheumatoid factor; SJC, swollen joint count; TJC, tender joint count; VAS, visual analogue scale.
Baseline estimates of average grip force (percentage of the expected value) were lower in patients with synovitis of each of the individual joints or joint groups compared with the corresponding joint or joint group (Table 3). The greatest differences, with nonoverlapping CIs, were seen in those with one or more MCP joint and those with a swollen wrist (Table 3). Patients with one or more swollen MCP joint or with wrist synovitis had lower grip force over time, whereas there were no such differences for synovitis of the shoulder, elbow, or PIP joints (Table 3). Improvement of grip force was significantly greater in those with wrist or MCP synovitis compared with those without swelling in these joints. No such differences were observed for synovitis of other joints of the dominant arm (Table 3).

There were negative associations for disease severity parameters (ie, Health Assessment Questionnaire [HAQ], DAS28, VAS-pain, VAS-global, SJC, TJC, and ESR) at baseline with estimated baseline grip force and grip force over time (Table 4). Higher baseline HAQ score, DAS28, SJC, TJC, and ESR were also associated with significantly greater improvement in grip force over time, whereas there were no such associations for VAS-pain (estimated difference in change per year; 0.4% of the expected grip force per SD; 95% CI −0.3% to 1.0%) and VAS-global (Table 4).

Patients with baseline parameters in the three higher quartiles had significantly lower mean grip force values over time compared with patients in the lowest quartiles (Table 5). Patients in the highest quartile of the DAS28 had significantly greater improvement compared with patients in the lowest quartile (Table 5). By contrast, there was no difference in improvement for those in the highest quartiles of VAS-pain or the HAQ (Table 5) compared with those in the lowest quartiles. Mean grip force values at each follow-up visit by quartile of the DAS28, VAS-pain, and HAQ are illustrated in Figures 1A-C.

Patients with RA with baseline subcomponents of the DAS28 in the highest quartiles had lower mean grip force values over time compared with those in the lowest quartiles (Supplementary Table 2). Patients in the highest quartiles of SJC, TJC, or ESR had significantly greater improvement in grip force compared with patients in the lowest quartile (Supplementary Table 2). There was no difference in improvement for those in the highest quartiles of VAS-pain or the HAQ compared with those in the lowest quartiles. Mean grip force values at each follow-up visit by quartile of the DAS28, VAS-pain, and HAQ are illustrated in Figures 1A-C.

### Table 3. Average grip force (% of expected value) over time (from baseline to 5 y), by joint involvement in early RA (mixed model analysis)

| Joint Involvement | Intercept (95% CI) | Estimated Mean Difference Over Time (95% CI) | Change/Year (95% CI) | Difference in Change/Year (95% CI) |
|-------------------|-------------------|---------------------------------------------|---------------------|----------------------------------|
| Swollen shoulder  | 42.5% (30.4% to 54.7%) | −3.7% (9.2% to −16.7%) | 2.5% (0.5% to 4.5%) | −0.5% (−2.9% to 2.0%) |
| No swollen shoulder | 45.6% (41.9% to 49.3%) | ... | 2.9% (2.2% to 3.6%) | ... |
| Swollen elbow     | 39.2% (27.3% to 51.0%) | −6.0% (6.2% to −18.2%) | 3.1% (1.2% to 5.0%) | 0.2% (−2.0% to 2.4%) |
| No swollen elbow  | 45.6% (41.9% to 49.3%) | ... | 2.9% (2.2% to 3.6%) | ... |
| Swollen wrist     | 40.6% (36.6% to 44.5%) | −9.3% (−2.5% to −16.2%) | 3.5% (2.7% to 4.3%) | 1.7% (0.4% to 3.0%) |
| No swollen wrist  | 53.1% (46.5% to 59.8%) | ... | 1.8% (0.8% to 2.8%) | ... |
| ≥1 swollen MCP joint | 42.0% (38.2% to 45.8%) | −11.0% (−3.1% to −18.9%) | 3.2% (2.5% to 4.0%) | 1.5% (0 to 3.0%) |
| No swollen MCP joint | 56.0% (47.4% to 64.5%) | ... | 1.7% (0.3% to 3.2%) | ... |
| ≥1 swollen PIP joint | 44.2% (39.3% to 49.1%) | −0.9% (5.8% to −7.6%) | 3.2% (2.3% to 4.0%) | 0.5% (−0.8% to 1.8%) |
| No swollen PIP joint | 46.1% (40.9% to 51.2%) | ... | 2.6% (1.7% to 3.6%) | ... |

Abbreviation: CI, confidence interval; MCP, metacarpophalangeal; PIP, proximal interphalangeal; RA, rheumatoid arthritis.

### Table 4. Relation between baseline disease severity parameters and average grip force (dominant hand; % of expected value) over time (from baseline to 5 y) in early RA (mixed model analysis)

| Parameter             | Estimated Mean Difference at Baseline per SD (95% CI) | Estimated Mean Difference Over Time per SD (95% CI) | Difference in Change/Year per SD (95% CI) |
|-----------------------|------------------------------------------------------|--------------------------------------------------|---------------------------------------------|
| HAQ                   | −12.0% (−15.2% to −8.8%)                             | −10.7% (−13.7% to −7.8%)                         | 0.7% (0.05% to 1.3%)                        |
| Pain (VAS)            | −8.0% (−11.5% to −4.6%)                              | −7.4% (−10.6% to −4.1%)                         | 0.4% (−0.3% to 1.0%)                        |
| Patient global assess- | −8.5% (−11.9% to −5.1%)                              | −8.0% (−11.1% to −4.8%)                         | 0.3% (−0.4% to 0.9%)                        |
| ment (VAS)            |                                                      |                                                  |                                             |
| DAS28                 | −11.5% (−14.8% to −8.2%)                             | −9.3% (−12.4% to −6.2%)                         | 1.2% (0.6% to 1.8%)                         |
| SJC (out of 28)       | −8.1% (−11.7% to −4.6%)                              | −5.6% (−8.9% to −2.2%)                         | 1.4% (0.7% to 2.0%)                         |
| TJC (out of 28)       | −9.3% (−12.8% to −5.7%)                              | −7.4% (−10.8% to −4.1%)                         | 1.0% (0.4% to 1.7%)                         |
| ESR (per mm/h)        | −5.8% (−9.3% to −2.3%)                               | −4.5% (−7.7% to −1.2%)                         | 0.7% (0.1% to 1.4%)                         |

Abbreviation: CI, confidence interval; DAS28, 28-joint Disease Activity Score; ESR, erythrocyte sedimentation rate; HAQ, Health Assessment Questionnaire; RA, rheumatoid arthritis; SJC, swollen joint count; TJC, tender joint count; VAS, visual analogue scale.
had reduced grip force at 5 years. The results of this study under-
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tive treatment, in particular, in patients with a severe early

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sibly, the lack of association between traditional prognostic mark-

ard measures of disease activity were not predictive of reduced

outcome measures (PROMs) at baseline (ie, high HAQ-DI scores

In this study of patients with early RA, poor patient-reported

of disease activity with grip force (% of expected value) over time, by quartile

Table 5. Relation of baseline patient-reported outcomes and disease activity with grip force (% of expected value) over time, by quartile

|                | Intercept (95% CI) | Estimated Mean Difference (95% CI) | Change/Year (95% CI) | Difference in Change/Year (95% CI) |
|----------------|-------------------|-----------------------------------|----------------------|-----------------------------------|
| **DAS28**      |                   |                                   |                      |                                   |
| Quartile I (0.8-3.6) | 61.4% (53.4% to 69.4%) | Reference                         | 1.3% (0.02% to 2.6%) | Reference                         |
| Quartile II (3.7-4.7) | 48.2% (41.8% to 54.5%) | -10.7% (-20.0% to -19.4%)        | 2.6% (1.4% to 3.9%)  | 1.3% (-0.4% to 3.1%)            |
| Quartile III (4.8-5.7) | 41.3% (34.6% to 47.9%) | -16.7% (-7.9% to -25.5%)        | 3.1% (1.9% to 4.4%)  | 1.8% (0% to 3.6%)              |
| Quartile IV (5.8-7.8) | 29.6% (24.1% to 35.1%) | -25.9% (-17.2% to -34.6%)       | 4.4% (3.2% to 5.7%)  | 3.1% (1.4% to 4.9%)            |
| **VAS pain**   |                   |                                   |                      |                                   |
| Quartile I (0.8-3.6) | 59.4% (52.0% to 66.7%) | Reference                         | 1.8% (0.5% to 3.1%)  | Reference                         |
| Quartile II (3.7-4.7) | 45.2% (37.6% to 52.9%) | -11.3% (-2.2% to -20.4%)        | 3.4% (2.0% to 4.7%)  | 1.5% (0.3% to 3.4%)            |
| Quartile III (4.8-5.7) | 34.7% (29.1% to 40.4%) | -20.8% (-12.2% to -29.5%)       | 3.9% (2.8% to 5.0%)  | 2.1% (0.4% to 3.8%)            |
| Quartile IV (5.8-7.8) | 41.0% (34.2% to 47.8%) | -17.4% (-8.6% to -26.3%)       | 2.3% (0.9% to 3.7%)  | 0.5% (-1.3% to 2.3%)           |
| **HAQ**        |                   |                                   |                      |                                   |
| Quartile I (0.0-0.38) | 62.2% (55.1% to 69.3%) | Reference                         | 2.0% (0.8% to 3.2%)  | Reference                         |
| Quartile II (0.39-0.75) | 43.2% (36.2% to 50.1%) | -17.7% (-9.2% to -26.3%)        | 2.7% (1.4% to 4.0%)  | 0.7% (-1.1% to 2.5%)           |
| Quartile III (0.80-1.25) | 42.6% (36.8% to 48.4%) | -17.0% (-8.8% to -25.1%)       | 3.4% (2.2% to 4.6%)  | 1.4% (-0.3% to 3.1%)           |
| Quartile IV (1.30-2.75) | 28.8% (22.8% to 34.8%) | -30.6% (-22.0% to -39.2%)       | 3.5% (2.0% to 5.0%)  | 1.5% (-0.3% to 3.4%)           |

Abbreviation: CI, confidence interval; DAS28, 28-joint Disease Activity Score; HAQ, Health Assessment Questionnaire; VAS, visual analogue scale.

There was no such difference for those in the highest quartile of VAS-global (Supplementary Table 2).

**DISCUSSION**

In this study of patients with early RA, poor patient-reported outcome measures (PROMs) at baseline (ie, high HAQ-DI scores and high scores for pain and patient global assessment) predicted reduced grip force at 5 years. Seropositivity and the standard measures of disease activity were not predictive of reduced grip force. This contrasts with the well-documented association between these parameters and radiographic progression, which has also been demonstrated in this patient population (10). Possibly, the lack of association between traditional prognostic markers and long-term reduced grip force may reflect results of early intensive treatment, in particular, in patients with a severe early phenotype. However, a major proportion of the patients (44%) still had reduced grip force at 5 years. The results of this study underline the importance of using PROMs in the assessment of patients with RA, which is an important part of modern management (36).

Baseline synovitis involvement of individual joints in the dominant upper extremity did not predict reduced grip force at 5 years. As expected, the higher the baseline grip force (percentage of the expected value), the lower the risk of reduced grip force at 5 years.

Patients with synovitis of each of the individual upper extremity joints or joint groups had lower baseline estimates of average grip force (percentage of the expected value) compared with the corresponding joint or joint group. The greatest differences were seen in those with more than one MCP joint and those with a swollen wrist. Over 5 years, patients with more than 1 swollen MCP joint or with wrist synovitis had lower grip force, whereas there was no such difference for synovitis of the shoulder, elbow, or PIP joints. Patients with wrist or MCP synovitis had significantly greater improvement of grip force during the follow-up compared with those without swelling in these joints.

Disease severity parameters at baseline were negatively associated with estimated baseline grip force and grip force over 5 years. Higher baseline levels of disease activity were also associated with greater improvement in grip force over 5 years, whereas there were no such associations for VAS-pain and VAS-global.

Again, this suggests that patients with poor PROMs in early RA are at increased risk of persistently impaired hand function. This is compatible with other studies that have demonstrated that poor PROMs predict long-term disability and low levels of physical activity (37). Underlying mechanisms may include poor coping strategies and activity limitation due to severe pain (38,39).

Structured analysis of coping strategies in patients with RA has demonstrated that evasive and emotive strategies are common but often not very effective and that, in particular, emotive strategies are frequently used in patients with severe pain (38). Ineffective coping strategies may further contribute to disability.

Pain in RA is multifactorial (40), often persistent over time (41), and a major predictor of general health perception (42). Particular interventions to improve function and health-related quality of life may be necessary in patients with early RA and severe pain. For the patient, severe pain and extensive disability is a warning sign that indicates increased risk of impaired long-term hand function. The study results indicate that patients with severe VAS for pain and global assessment (in the highest quartiles; VAS score of 64 or higher and 65 or higher, respectively) and severe disability (highest quartile; HAQ-DI score: 1.3 or higher) at diagnosis had particularly
reduced grip force, with limited improvement over time. It is very important for the rheumatology team to identify this category of patients early and initiate appropriate interventions with the purpose of improving grip force. It has been demonstrated that structured rehabilitation programs in RA may improve grip force (19,43) and reduce pain (19,44). Randomized controlled studies have shown that a combination of hand-strengthening and hand-mobilizing exercises for the distal upper extremity may give significant improvements in hand function (19,43). For example, in the Strengthening And stretching for Rheumatoid Arthritis of the Hand (SARAH) trial, a tailored hand-exercise program was shown to improve hand function in patients

Figure 1. Average grip force (percentage of excepted; dominant hand) over time in patients with early rheumatoid arthritis (RA) by quartile of the 28-joint Disease Activity Score (DAS28), visual analogue scale (VAS) pain score, and Health Assessment Questionnaire (HAQ) score. Data are presented as mean values at each visit with 95% confidence intervals. A, Relation between baseline DAS28 and grip force from inclusion to the 5-year follow-up. B, Relation between baseline VAS pain and grip force from inclusion to the 5-year follow-up. C, Relation between baseline HAQ and grip force from inclusion to the 5-year follow-up.
with RA (19). For patients with RA with severe pain, particular coping strategies, such as mind or body techniques for managing pain, may be useful (45).

Limitations of the present study include the lack of a control group of individuals without RA evaluated at our unit. Like in a previous study (15), we used age- and sex-specific reference values from the literature, based on another study from Scandinavia (35), to calculate percentages of expected values of grip force for each individual. Based on this, we estimated the effect of other variables on age- and sex-standardized grip force.

Grip force was measured by several different observers. However, a standardized procedure was used by occupational therapists at our unit during the entire study period (34). All procedures were performed after 9:20 AM to limit the impact of morning stiffness.

PROMs were limited to standard VAS for pain and global assessment of disease activity and to the HAQ-DI; the latter is known to have floor effects in the assessment of disability (46). Newer PROMs, based on item response theory and computerized adaptive testing (46), were not available when this study was initiated. Finally, poor motivation may influence both PROMs and the Grippit measurement (47,48), but no assessment of motivation was available.

Management of RA changed continuously during the study period. The patients were included just before or shortly after the introduction of biologic DMARDs, and a limited number were treated with biologics before the 5-year follow-up. The study results may therefore not apply to patients managed according to a treat-to-target strategy (49), including ready access to biologic DMARDs.

Strengths of this study include the standardized joint assessment performed by the same physician in all cases using a structured protocol. Furthermore, standardized and established methods for assessment of grip force were used in accordance with the recommendations from the American Society of Hand Therapists (50). As recommended, the average of three assessments was used (50).

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

Patients with a severe disease phenotype at baseline had particularly impaired grip force over the first 5 years after RA diagnosis. Patients with high initial disease activity experienced greater improvement in grip force, likely because of successful treatment. Poor patient-reported outcomes at baseline were associated with persistent impairment of grip strength. This underlines the prognostic importance of disability and related symptoms in early RA and suggests that targeted multi-professional interventions may be required in patients with a high HAQ score and severe pain (eg, those with a HAQ-DI score of 1.3 or higher or a VAS-pain score of 64 or higher). Joint counts and the presence of synovitis in individual joints may change rapidly in early RA and may appear to be less predictive of long-term hand function.

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AUTHOR CONTRIBUTIONS

All authors were involved in drafting the article or revising it critically for important intellectual content, and all authors approved the final version to be published. 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.

Study conception and design. Jacobsson, Turesson.

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