Original Article

Influence of Disease Activity on Finger Deformity and Impairment Worsening in Rheumatoid Arthritis

Shogo TOYAMA, Ryo ODA, Daigo TANIGUCHI, Ryosuke IKEDA, Daisaku TOKUNAGA, Hiroyoshi FUJIWARA, Toshikazu KUBO

Department of Orthopaedics, Graduate School of Medical Science, Kyoto Prefectural University of Medicine

*Correspondence to:
Ryo ODA, MD, PhD
Department of Orthopaedics, Graduate School of Medical Science, Kyoto Prefectural University of Medicine
465 Kajii-cho, Kamigyo-ku, Kyoto-city, Kyoto pref, 602—8566, Japan
Tel: +81—75—251—5549
E-mail: shogot@koto.kpu-m.ac.jp (First author: Shogo TOYAMA)

Abstract

Introduction: Finger involvement is highly prevalent in rheumatoid arthritis, and when deformity affects these fingers through joint destruction, it can markedly impact the activities of daily living. Progress in pharmacotherapy has dramatically improved disease activity control, but residual synovitis may still continue to affect the fingers of many patients. We previously reported that deformities and dysfunction progresses in such cases. However, no apparent correlations have been established between disease progression and disease activity. We therefore investigated how disease activity affected progression of finger deformity and dysfunction over time.

Methods: Between 2009 and 2015, we analyzed 37 patients with 63 hands affected by rheumatoid arthritis available for follow-up. Swan-neck deformity of the fingers were classified according to Nalebuff’s type classification. Boutonnière deformity of the fingers were classified according to Nalebuff’s stage classification. Hand function and upper extremity function was assessed based on a modified Kapandji index (MKI) and Disabilities of the Arm, Shoulder and Hand (DASH) score. Changes in disease activity from 2009 through 2015 were used to divide the patients into the following four groups: “improved”, “low disease activity maintained”, “high disease activity maintained”, and a “worsening” group.

Results: There were 22, 9, 16, and 16 hands in the improved, low disease activity maintained, high disease activity maintained, and worsening groups, respectively. Finger deformities progressed in all four groups with a statistically significant worsening observed in all groups, except for the low disease activity maintained group. MKI was only maintained in the low disease activity maintained group. DASH improvement during the study period was only seen in the low disease activity maintained and improved groups, while marked worsening was noted in the high disease activity main-
tained group and worsening group.

**Discussion:** Goals in treating rheumatoid arthritis include clinical, structural, and functional remission, but until now, it has been unknown whether pharmacotherapy would be effective in achieving the latter two forms of remission. This study clarifies that although finger deformity does progress regardless of disease activity control, finger function can be maintained by keeping disease activity low over the long term. With the use of appropriate pharmacotherapy, it is possible to achieve these treatment goals.

**Conclusion:** Physicians who treat rheumatoid disease must continue their efforts in daily clinical practice to preserve finger function by suppressing disease activity to as low as possible.

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**Introduction**

Since the advent of rheumatoid arthritis pharmacotherapy with methotrexate and biologic agents, many patients can now achieve good disease control\(^1\). However, if the patient is of advanced age or suffers complications, it may be difficult to institute aggressive drug treatment. In those patients, residual synovitis cannot be avoided, even after remission. Previously, we reported that deformities and functional impairment can progress in the finger joints of such patients\(^2\). However, no studies to date have looked at how disease activity may influence finger outcomes, and there is no information on which patients with what levels of disease activity suffer progression of deformities and impaired function. In order to elucidate the pathogenesis of finger deformities and functional impairment, we have continued to follow a cohort of patients with finger deformities since 2004. In this study, we investigated how changes in disease activity affected the development of finger deformities and progressive impairment of function.

**Methods**

**Patients**

Since 2004, we have followed a cohort of patients with rheumatoid arthritis at our institution who have finger deformity involvement. Follow-up evaluations were conducted every 5 years, and 3 evaluations have been carried out thus far in 2004, 2009, and 2015. Unfortunately, disease activity was not assessed in 2004 and so the subjects of this study comprised the 37 patients with 63 hands who were available for a 6-year follow-up survey between 2009 and 2015.

**Clinical evaluation**

To conduct a longitudinal assessment of the effects of disease activity on finger deformities, we needed to take fluctuations in disease activity into consideration. Disease activity score 28 (DAS28) was used to assess disease activity\(^3\), and a DAS28 value over 3.2 indicated high to moderate disease activity or the "high activity group," while a DAS28 value of 3.2 or lower indicated low disease activity or in remission states and were in the "low activity group." Participating patients were divided into 4 groups based on how their disease activity changed over the course of the study period. Those whose levels changed from high to low were considered improved (I), those who maintained low disease activity levels at both time points were designated the "low maintained (LM)" group, those whose levels remained high were called "high maintained (HM)" and those whose disease activity levels rose from low to high were designated wors-
Deformities were assessed according the Nalebuff classification, checking for swan-neck deformity and boutonniere deformity in 4 digits (index finger to little finger)\(^4\)\(^-\)\(^6\). To assess the entire hand, the deformity score was calculated by simply adding the scores of these 4 digits. Finger function was assessed using a modified Kapandji index (MKI)\(^7\), while activities of daily living (ADL) were evaluated based on Disabilities of the Arm, Shoulder and Hand (DASH) scores\(^8\),\(^9\). MKI is a method of determining unilateral finger mobility. It is primarily used in Europe and is said to correlate with hand function. It comprises the thumb opposition test (10 points), finger flexion test (20 points), and finger extension test (20 points), for a maximum score of 50 points. The higher the score, the better the mobility. DASH is a patient-based assessment questionnaire about the arms that can be used as an indicator of ADL using both upper limbs and is composed of 30 questions on daily activities. With a maximum score of 100 points, it calculates the disability score. The higher the score, the worse the disability.

**Procedure**

Deformity score, MKI, and DASH results from 2009 and 2015 were compared for each group with a Student’s \(t\)-test, while an analysis of variance with a *post-hoc* Tukey’s test was used to compare differences (\(\Delta\)defect score, \(\Delta\)MKI, \(\Delta\)DASH) among the 4 groups. Statistical analysis was performed using statistical software R version 3.2.2 (R Foundation for Statistical Computing, Vienna, Austria). A 5% level of significance was used.

**Ethical considerations**

Participants were provided with oral explanations of the study at both the 2009 and 2015 assessments, and written informed consent was obtained before enrollment in this study. This study protocol was approved by the institutional review board of 4 institution (Approval No.: ERB-C-555-1).

**Results**

**Patients**

Participants comprised 2 men with 4 hands, and 35 women with 59 hands. The mean age in 2009 was 64.4 years (range: 40–81 years), and mean disease duration was 22.7 years (range: 10–46 years). No statistically significant differences in patient background were noted between 2009 and 2015 with regard to blood biochemistry test results (Table 1).

Patients were classified based on changes in disease activity as Group I, Group LM, Group HM, and Group W with 22, 9, 16, and 16 hands in each group, respectively. Patient characteristics did not differ significantly among these groups except for disease activity.

**Clinical evaluation**

In a comparison between the 2009 and 2015 data, a statistically significant worsening of deformity scores was noted in the I, HM, and W groups. Although aggravation did not reach statistical significance in the LM group, worsening of scores was noted in this group as well (Table 2). MKI only worsened in the HM group, while no changes were noted in the remaining 3 groups. DASH did not differ significantly between the I and LM groups, but while these 2 groups both improved, the HM and W groups showed statistically significant worsening.

A comparison of all 4 groups looked at the degree of change during the observation period for deformity score, MKI, and DASH. For all items evaluated, the LM group had the least amount of aggravation. This was followed
by the I group with a poorer MKI than the LM group, but aggravation of both deformity score and DASH were still adequately suppressed (Fig. 1). In the W group that showed worsening of disease activity during the study period, DASH score significantly deteriorated compared to that in the I and LM groups.

Table 1  Patient Characteristics

<table>
<thead>
<tr>
<th></th>
<th>2009</th>
<th>2015</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRP (n=37)</td>
<td>0.83 (1.09)</td>
<td>0.78 (1.22)</td>
<td>N.S.</td>
</tr>
<tr>
<td>(mg/dL)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ESR (n=34)</td>
<td>29.0 (24.2)</td>
<td>34.6 (22.8)</td>
<td>N.S.</td>
</tr>
<tr>
<td>(mm/hr)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MMP-3 (n=33)</td>
<td>150.0 (144.0)</td>
<td>171.4 (188.7)</td>
<td>N.S.</td>
</tr>
<tr>
<td>(ng/dL)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DAS28 (n=30)</td>
<td>2.99 (0.91)</td>
<td>3.00 (1.22)</td>
<td>N.S.</td>
</tr>
</tbody>
</table>

Numbers express means (S.D.) for each clinical assessment. CRP: C-reactive protein, ESR: erythrocyte sedimentation rate, MMP-3: matrix metalloprotease-3 DAS28: disease activity score 28, N.S: not significant

Table 2  Changes over time and group comparisons

Comparison of assessment between 2009 and 2015

<table>
<thead>
<tr>
<th></th>
<th>2009</th>
<th>2015</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deformity score</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2009</td>
<td>4.1 (2.2–6.0)</td>
<td>6.4 (3.5–9.4)</td>
<td>4.6 (2.4–6.9)</td>
</tr>
<tr>
<td>2015</td>
<td>5.6 (3.6–7.5)</td>
<td>7.6 (4.6–10.5)</td>
<td>8.3 (6.1–10.6)</td>
</tr>
<tr>
<td>P value</td>
<td>0.049*</td>
<td>0.197</td>
<td>0.003**</td>
</tr>
<tr>
<td>MKI</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2009</td>
<td>32.5 (28.3–36.7)</td>
<td>34.1 (27.5–40.8)</td>
<td>25.1 (20.2–27.5)</td>
</tr>
<tr>
<td>2015</td>
<td>31.1 (26.8–35.3)</td>
<td>34.7 (28.0–41.3)</td>
<td>22.5 (17.5–27.5)</td>
</tr>
<tr>
<td>P value</td>
<td>0.306</td>
<td>0.771</td>
<td>0.033*</td>
</tr>
<tr>
<td>DASH</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2009</td>
<td>43.0 (33.9–52.2)</td>
<td>35.2 (21.2–49.2)</td>
<td>65.4 (54.2–76.7)</td>
</tr>
<tr>
<td>2015</td>
<td>40.5 (31.6–49.5)</td>
<td>31.6 (17.6–45.6)</td>
<td>69.7 (59.2–80.2)</td>
</tr>
<tr>
<td>P value</td>
<td>0.902</td>
<td>0.572</td>
<td>0.009**</td>
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Comparison between four groups

<table>
<thead>
<tr>
<th></th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Δdeformity score</td>
<td>1.5 (0.0–2.9)</td>
</tr>
<tr>
<td>ΔMKI</td>
<td>−1.5 (−3.9–1.0)</td>
</tr>
<tr>
<td>ΔDASH</td>
<td>−3.9 (−9.4–1.6)</td>
</tr>
</tbody>
</table>

Numbers express means (95% confidential interval).
DAS28: disease activity score 28, MKI: modified Kapandji index, DASH: Disabilities of the Arm, Shoulder and Hand
I: improved disease, LM: low maintained, HM: high maintained, W: worsened disease, *: P<0.05, **: P<0.01
#: statistically significant difference between groups. post hoc Tukey test revealed a significant difference between the I and W groups
Disease activity control has been improving year over year thanks to progress in the pharmacotherapy of rheumatoid arthritis. However, even now that biologics are available, finger deformities remain a complication that can impair patient ADL and present an issue that remains unsolved. We previously reported that finger deformities increase over time. Therefore, we conducted this study to look at changes in disease activity to determine if finger deformities progress even in cases where disease activity is kept strictly under control.

Since disease activity always fluctuates, some degree of manipulation was necessary to conduct a longitudinal analysis. One reported method determined mean disease activity over a specified interval to determine cumulative disease activity. With this method, disease activity was multiplied to determine area under the curve, so accurate evaluation required frequent disease activity assessment which can become too time-consuming. Instead, it is more common to calculate the mean disease activity over a specified interval, and Pascal et al. use mean disease activity over 6-month periods. Since our study merely compared disease activity in 2009 and 2015, our method may not strictly reflect how disease activity influences outcome when compared with the previously described methods. However, this analysis does provide useful information. Cumulative disease activity was considered to be lowest in the LM group followed by the I group and W group while it...
was highest in the HM group. There are few literature arguing influence of disease activity on rheumatoid hand. Toyohara et al. reported that disease activity using average DAS28 which is calculated in every 3 or 4 months will relate to wrist joint destruction in ten years after\textsuperscript{13}. This, however, could be a first report stating that disease activity have impacts to hand deformities and impairment. This result means that fine observation of rheumatoid hand enables us to estimate patient's disease control with anti-rheumatic drugs from the onset.

In this study, we found that patients with poorly controlled disease activity experienced major progression of deformities, while even in patients where low disease activity levels were maintained, finger deformities still progressed. This leads us to believe that worsening of finger deformities in rheumatoid arthritis will occur beyond a certain degree regardless of whether disease activity is controlled and thus aggravation may be unavoidable. On the other hand, if disease control was good or if improvement was noted, finger mobility was maintained. In cases where disease activity control was difficult, if disease control can be improved at a later point, then it may be possible to preserve finger mobility. ADL worsens not only in cases with poor disease activity control but also in cases that worsen during the course of the study. On the other hand, control tends to be good in patients that show improvement. ADL is believed to parallel disease activity control.

Treatment goals in rheumatoid arthritis include clinical, structural, and functional remission. The Treat-to-Target strategy was proposed to try to achieve these types of remission in all patients\textsuperscript{14,15}. By providing appropriate drug therapy in accordance with this strategy, we can now achieve clinical remission in many patients. However, whether treatment has the potential to achieve structural and functional remission remains slightly less transparent. Results from this study have shown that with regard to finger deformities, maintaining low disease activity levels over the long-term through appropriate pharmacotherapy produces results approaching structural and/or functional remission.

Limitations of this research include the fact that it is based on data from a limited number of participants with only 37 patients and 63 hands, and disease activity was only measured at 2 time points. For more accurate investigation of the effects on disease activity, we will need to look at many more cases and conduct disease assessments more frequently. In addition, we were unable to consider differences among the various types of DMARDs used in this study. Unfortunately, the small number of subjects in this study made it impossible to evaluate whether there were any benefits to using biologics over other drugs. This issue will need to be investigated further in future studies.

Conflict of Interest: None

References

5) Nalebuff EA, Millender LH: Surgical treatment of


