Comprehensive assessment of rheumatoid hand using cluster analysis involving parameter analysis of three major hand deformities: a cross-sectional and longitudinal study

CURRENT STATUS: UNDER REVIEW

Arthritis Research & Therapy  BMC

Shogo Toyama
Kyoto Furitsu Ika Daigaku

Corresponding Author
shogot@koto.kpu-m.ac.jp
ORCID: https://orcid.org/0000-0002-8626-604X

Ryo Oda
Kyoto Furitsu Ika Daigaku

Daisaku Tokunaga
Kyoto Furitsu Ika Daigaku

Shinji Tsuchida
Kyoto Furitsu Ika Daigaku

Rie Kushida
Marutamachi rehabilitation clinic

Yutaka Kawahito
Kyoto Furitsu Ika Daigaku

Kenji Takahashi
Kyoto Furitsu Ika Daigaku

DOI: 10.21203/rs.3.rs-23686/v1

SUBJECT AREAS
Orthopedics  Rheumatology

KEYWORDS
Rheumatoid arthritis, hand deformity, swan-neck deformity, boutonnière deformity, cluster analysis
Abstract

Background
Although drug therapy in rheumatoid arthritis has recently improved, treating established rheumatoid hand consisting of three major deformities—thumb deformity, finger deformities, and ulnar drift—remains a challenge. Underlying complex pathophysiology makes it difficult to comprehensively understand these deformities, and comprehensive assessment methods require accumulated skill and long learning curves. We aimed to establish an easier composite method of understanding the pathophysiology using data from our cohort and cluster analysis.

Methods
We established a rheumatoid hand cohort in 2004, and clinically evaluated 134 hands (67 patients). We repeated the evaluations in 2009 and 2015, which provided data for 297 hands and 43 hands for cross-sectional and longitudinal analyses, respectively. Thumb deformities, finger deformities (swan-neck and boutonnière deformity), and ulnar drift were semi-quantified and entered as parameters into a two-step cluster (cross-sectional) analysis. Parameter distributions were considered to clarify each cluster’s characteristics. Next, hands with cluster change over the study period were reviewed to clarify deformity progression (longitudinal analysis). We also performed a stratified analysis between the clusters and the affected period to clarify whether long affected period plays an important role in deformity progression.

Results
We identified seven clusters: cluster 1: mild finger deformities; cluster 2: type 1 thumb deformity; cluster 3: type 2 thumb deformity and severe ulnar drift; cluster 4: type 3 or 4 thumb deformity and low or moderate swan-neck deformity; cluster 5: various thumb deformities and severe boutonnière deformity; cluster 6: type 1 thumb deformity and severe swan-neck deformity; and cluster 7: type 6 thumb deformity. The ulnar drift parameters were equally distributed among the clusters except for cluster 3. Larger cluster numbers generally indicated lower function. At the study endpoint, cluster 1 had changed mainly to cluster 2 or 4, cluster 2 changed to cluster 3, and cluster 7 was considered the final morphology with the lowest hand function. Patients affected for > 30 years had increased risk of rapid disability progression.

Conclusions
Our comprehensive assessment indicated seven deformity patterns and a progressive course in rheumatoid hand. Using patterns may provide rheumatologists with easier information for practical interventions and to determine functional prognosis.

**Background**

Rheumatoid hand, which describes the characteristic deformities in rheumatoid arthritis, is typically composed of thumb deformity, finger deformities, and ulnar drift, of varying degrees. Several studies have attempted to quantify hand function using hand space and force-time curves to evaluate hand deformity [1, 2]. Swan-neck deformity, either alone or combined with other deformities, has been reported to affect hand function more. However, it is still difficult to understand patients’ overall pathophysiological conditions such as the presence or absence, and location and severity, of deformity, to determine the most relevant treatment.

A study of early rheumatoid arthritis patients over a 10-year period reported that approximately 50% of hands exhibited combined deformity [3]; however, the authors did not describe the severity of deformity. Another study described severity of deformity from a 5-year observation of established rheumatoid arthritis patients and found that overall deformities worsened with time [4]. The authors evaluated thumb deformity using the Nalebuff classification system (type 1–6) [5], finger swan-neck deformity using the Nalebuff classification (type 1–4) [6], finger boutonnière deformity using the Nalebuff classification (stage 1–3), and ulnar drift by the authors’ new method [7], which quantified ulnar drift by evaluating joint parameters in an extended cohort [8].

Based on these findings, we hypothesized that a semi-quantitative approach using the type/stage and the new method would provide a comprehensive understanding of the rheumatoid hand. The aim of this study was to perform a comprehensive assessment and clarify the progressive patterns of hand function and deformity in patients with rheumatoid arthritis.

**Methods**

**Patients**

The data collection began in 2004 for patients with rheumatoid arthritis with any hand deformity. The study began in 2004 because biological agents were first approved in our country in 2003. We collected repeat data again in 2009 and 2015. At each evaluation, we evaluated patients’ hand
deformity and functional assessments. A total of 297 hands were available for the cross-sectional analysis, and data for 43 hands were used for the longitudinal analysis, according to the cross-sectional analysis results (Fig. 1).

**Deformity evaluation**
Thumb deformity, all four digits' swan-neck deformity or boutonnière deformity, and ulnar drift were assessed according to the Nalebuff classification of thumb deformity (type 1-6)[5]; the Nalebuff classification of swan-neck deformity (Type 1-4) and boutonnière deformity (stage 1-3) for the fingers[6, 7]; and ulnar drift (total score 0-8). The ulnar drift total score was calculated by adding scores for the four parameters for the metacarpophalangeal joints (deviation, subluxation, reduction, and bone destruction) and was scored from 0 to 2 for each parameter. The severity of ulnar drift was evaluated according to the sum of each parameter’s score, and scores increased with worsening of the ulnar drift[8].

**Functional evaluation**
Patient-rated subjective indicators that evaluate unilateral hand function are better for polyarticular diseases such as rheumatoid arthritis. Therefore, evaluation methods such as the Michigan Hand Outcomes Questionnaire are currently considered the best tools [9]; however, this questionnaire was not used in our cohort, and the Kapandji index was used instead[10]. The Kapandji index evaluates finger extension (20 points), finger flexion (20 points), and thumb opposition (10 points), with a maximum of 50 points. The Kapandji index evaluates unilateral hand function within minutes independent of impact from the elbow and shoulder joint. As in a previous study, we chose this functional evaluation method [11].

**Cross-sectional analysis**
A comprehensive understanding of the rheumatoid hand regarding the characteristic deformities was derived from the cluster analysis according to the described clinical parameters. The numerical values for thumb deformity (0-6) were entered as nominal variables because, to our knowledge, no studies have compared function between each deformity type. Finger deformities exist independently from the index to little finger with varying severity, and the presence of swan-neck deformity or boutonnière deformity also varies; therefore, several parameters should be considered and entered...
into the analysis (which finger, type of deformity, and severity). Because the thumb has the most important functional role in both rheumatoid hands and normal hands[12, 13], we considered that the evaluated parameters should be minimized to weight the impact from thumb deformity in the cluster analysis. Therefore, the score for finger deformity according to the Nalebuff classification (swan-neck deformity: 0–4, boutonnière deformity: 0–3) were totalled separately from the swan-neck deformity score and the boutonnière deformity score from the index to the little finger. We entered the values for only these two scores as ordinal variables.

Ulnar drift score was an ordinal variable and was entered directly into the analysis[8].

We performed two-step cluster analysis because one of the parameters was a nominal variable. The final number of clusters was seven after weighting the importance of thumb deformity, and the characteristics of each cluster were determined according to the distributions of the entered parameters. We used Student’s t-test for two-group comparisons for continuous variables and analysis of variance and the post-hoc Tukey’s test for multiple comparisons.

**Longitudinal analysis**
We used data for hands that had changed to a different cluster category at each evaluation point, in the longitudinal analysis. Using changes in hand characteristics over time, we determined the patterns of deformity progression over time.

**Relationship between affected period and cluster**
To determine the influence of the affected duration on hand deformities, we calculated the proportions of each cluster by affected period category (almost every 5 years).

**Results**

**Patients’ demographics**

Patients’ demographics at each endpoint are shown in Table 1. Drug therapy was performed in accordance with the treatment guidelines/recommendations of the European League Against Rheumatism and the American College of Rheumatology, which changed several times during the follow-up period. Therefore, disease activity generally improved over time, despite the fact that patients aged.

Demographics of each cluster
The demographics of each cluster regarding patients’ background characteristics are shown in Table 2. We found almost no difference in age when comparing the clusters. In contrast, the affected period lengthened as the cluster number increased. The Kapandji index in clusters 1, 2, and 4 was > 30 points, but in cluster 3, the index was similar to that in cluster 5 and 6. Cluster 7 had the lowest Kapandji index score.

The distributions of patients in each cluster for each parameter are also shown in Table 3. Because clustering aimed to emphasize differences regarding thumb deformity, patients with each type of thumb deformity were clearly clustered except for cluster 5, as follows: cluster 1: no thumb deformity, low or moderate swan-neck deformity and boutonnière deformity, variable ulnar drift; cluster 2: type 1 thumb deformity, low or moderate swan-neck deformity and boutonnière deformity, variable ulnar drift; cluster 3: type 2 thumb deformity, low swan-neck deformity and boutonnière deformity, severe ulnar drift; cluster 4: type 3 or 4 thumb deformity, low or moderate swan-neck deformity, almost no boutonnière deformity, variable ulnar drift; cluster 5: various types of thumb deformity, almost no swan-neck deformity, severe boutonnière deformity, variable ulnar drift; cluster 6: type 1 thumb deformity, severe swan-neck deformity, almost no boutonnière deformity, variable ulnar drift; and cluster 7: type 6 thumb deformity. Interestingly, the distributions were scattered regarding the ulnar drift scores in every cluster except cluster 3.

Cluster changes over time
Cluster changes in the longitudinal study are shown in Fig. 2. Because cluster 1 had no thumb deformity, its transitions were mainly to cluster 2 or 4, which have thumb deformity and low-grade finger deformity. Cluster 2 changed to cluster 3, 5, and 6, meaning that type 1 thumb deformity worsened to type 2 thumb deformity and was associated with variable degrees of finger deformity. No hands changed to cluster 7 during the study.

Stratified analysis by affected period
The proportions of each cluster by the affected period are shown in Fig. 3. Although hands in cluster 3 or higher constituted less than approximately 10% of the hands if the affected period was shorter than 10 years, the proportion of these patients rapidly increased to approximately 30% of all hands, if the affected period was longer than 10 years. Moreover, if the affected period was longer than 35
years, the proportion of hands in cluster 3 or higher and the proportion of severely deformed hands increased to > 70% of all hands.

Discussion

Our findings suggest that rheumatoid hand phenotypes and disease progression represent several specific patterns (Fig. 4). In the early phase, hands with type 1 thumb deformity were the most common phenotype, and patients had minimal disability, implying that type 1 thumb deformity is the mildest and first hand deformity we encounter clinically. Other hands developed type 3 or 4 thumb deformity first. In the middle phase, several progression paths appeared. Some hands with type 1 thumb deformity progressed to type 2, some hands developed severe boutonnière deformity, and other hands developed severe swan-neck deformity. In the terminal phase, despite the fact that no hands progressed to cluster 7 from other clusters, in this study, if disease activity remains high, any thumb deformity would progress to type 6.

Originally, the Nalebuff classification for thumb deformity divided thumbs into six types by the initially affected joint and its appearance[14, 15], and type change over time was not considered. Additionally, to our knowledge, no studies have compared hand function by type and none have quantified the impact of deformity type on hand function. Our results showed that type 1, 3, and 4 are the primary phenotypes of the thumb deformity, and type 2 is a secondary lesion of type 1. In type 2, the carpometacarpal joint was initially involved, and flexion contracture of the metacarpophalangeal joint was secondary; however, type 3 also initially involves the carpometacarpal joint. The underlying mechanisms influencing this phenotype difference are unknown. Some hands with type 1 thumb deformity progressed to type 2 in this study, suggesting that type 2 involves the metacarpophalangeal joint, first, followed by the carpometacarpal joint.

Quantifying finger deformities, specifically swan-neck deformity and boutonnière deformity, was challenging in this study. Anatomically, the index to little fingers have different roles. The index and middle fingers are mainly used in extension for reach behaviours, in contrast with the ring and little fingers, which work in flexion while grasping. Therefore, the affected finger should be considered when interpreting our results. A previous study evaluated each affected finger separately[16], but the
authors did not evaluate the proximal interphalangeal joint and did not describe the finger deformity phenotypes. Another study reported the results of a stratified analysis by finger among patients who underwent surgery with silicone arthroplasty. The authors reported that the ring and little finger had larger extension lags[17], but the authors did not describe hand function. A study evaluating finger deformity separately showed an almost even distribution for the characteristic finger deformities from the index to little fingers[4]. However, to our knowledge, no patient-rated subjective indicator evaluating hand function assesses fingers separately; therefore, the absence of weighting impact on function difference by each finger would have minimal impact on the results.

In this study, the swan-neck deformity scores and boutonnière deformity scores were treated equally and entered into the cluster analysis. Several studies have shown that swan-neck deformity indicates more severe disability than boutonnière deformity[1, 2, 18]. This suggests that scores from swan-neck deformity should be weighted; however, our previous study showed that both deformities contribute equally to hand function. Therefore, we used the same quantification method, in this study. The ulnar drift scores were equally dispersed across the clusters except for cluster 3, indicating that ulnar drift may occur independently from other deformities. Ulnar drift arises mainly from metacarpophalangeal joint involvement, but clinically, many other causes dictate its course[19]. As a result, ulnar drift should be managed separately from other deformities when rheumatologists consider referring a patient for surgery. Silicone arthroplasty for ulnar drift can provide excellent relief from the cosmetic effects and poor hand function related to rheumatoid arthritis[17, 20].

Our stratified analysis showed that hands affected for ≤ 10 years constituted only approximately 10% of clusters 3 or higher (middle or terminal phase). In contrast, hands affected for more than 10 years constituted 30% of clusters 3 and higher, suggesting that a 10-year affected period could be a meaningful threshold indicating increasing risk of rapid disability progression.

This study includes several limitations. First, our cluster analysis prioritized the impact of thumb deformity to determine the seven clusters. Therefore, the characteristics of all clusters were influenced by thumb deformity. Given that thumb deformity provides the main impact on disability, our cluster classification could be very useful in determining daily medication therapy, but it remains
unclear which deformities and what degree of severity influence disability. Second, the cluster analysis assigned hands to each cluster group retrospectively. Therefore, our clusters are explanatory research and cannot necessarily be applied to new single hands; additional studies are needed. Third, we used the Kapandji index as a functional evaluation, and our results should be verified using patient-reported outcome measures.

Conclusions
Our clustering of rheumatoid hand characteristics could be a useful tool, even for rheumatologists unfamiliar with patients with impaired activities of daily living.

Declarations
Ethics approval and consent to participate
This study received full ethical approval from the institutional review board of Kyoto Prefectural University of Medicine (approval number: ERB-C-351-4), and the study was performed in accordance with the principles of the Declaration of Helsinki.

Consent for publication
All patients provided oral and written informed consent at each evaluation point.

Availability of data and materials
Not applicable

Competing interests
The authors declare that they have no competing interests.

Funding
Not applicable

Authors' contributions
TS, the first author, contributed to gathering, analyzing, and interpreting the data, and writing the manuscript. OR, TD, and KY contributed to the clinical evaluation and data interpretation. KR contributed independently to the functional assessments and clinical evaluations as an occupational therapist. TS contributed to the data analysis. TK contributed to the design of this study.

Acknowledgements
The authors thank all the rheumatologists who treated the patients included in our cohort. The lead author thanks his family members, Kaori Toyama and Ryosuke Toyama, for their support. We thank Jane Charbonneau, DVM, from Edanz Group (www.edanzediting.com/ac) for editing a draft of this manuscript.

References

1. Dias JJ, Smith M, Singh HP, Ullah AS. The working space of the hand in rheumatoid arthritis: its impact on disability. J Hand Surg Eur Vol. 2009;34(4):465–70.

2. Dias JJ, Singh HP, Taub N, Thompson J. Grip strength characteristics using force-time curves in rheumatoid hands. J Hand Surg Eur Vol. 2013;38(2):170–7.

3. Johnsson PM, Eberhardt K. Hand deformities are important signs of disease severity in patients with early rheumatoid arthritis. Rheumatology. 2009;48(11):1398–401.

4. Toyama S, Tokunaga D, Fujiwara H, Oda R, Kobashi H, Okumura H, Nakamura S, Taniguchi D, Kubo T. Rheumatoid arthritis of the hand: a five-year longitudinal analysis of clinical and radiographic findings. Mod Rheumatol. 2014;24(1):69–77.

5. Nalebuff EA. Diagnosis, classification and management of rheumatoid thumb deformities. Bull Hosp Joint Dis. 1968;29(2):119–37.

6. Nalebuff EA, Millender LH. Surgical treatment of the swan-neck deformity in rheumatoid arthritis. Orthop Clin North Am. 1975;6(3):733–52.

7. Nalebuff EA, Millender LH. Surgical treatment of the boutonniere deformity in rheumatoid arthritis. Orthop Clin North Am. 1975;6(3):753–63.

8. Toyama S, Oda R, Tokunaga D, Taniguchi D, Nakamura S, Asada M, Fujiwara H, Kubo T. A new assessment tool for ulnar drift in patients with rheumatoid arthritis using pathophysiological parameters of the metacarpophalangeal joint. Mod Rheumatol. 2019;29(1):113–8.

9. Chung KC, Hamill JB, Walters MR, Hayward RA. The Michigan Hand Outcomes
Questionnaire (MHQ): assessment of responsiveness to clinical change. Ann Plast Surg. 1999;42(6):619-22.

10. Lefevre-Colau MM, Poiraudreau S, Oberlin C, Demaille S, Fermanian J, Rannou F, Revel M. Reliability, validity, and responsiveness of the modified Kapandji index for assessment of functional mobility of the rheumatoid hand. Arch Phys Med Rehabil. 2003;84(7):1032-8.

11. Toyama S, Oda R, Asada M, Nakamura S, Ohara M, Tokunaga D, Mikami Y. A modified Terrono classification for Type 1 thumb deformity in rheumatoid arthritis: a cross-sectional analysis. J Hand Surg Eur Vol. 2020;45(2):187-92.

12. Tsai CL, Lin CF, Lin HT, Liu MF, Chiu HY, Hsu HY, Kuo LC. How kinematic disturbance in the deformed rheumatoid thumb impacts on hand function: a biomechanical and functional perspective. Disabil Rehabil. 2017;39(4):338-45.

13. Harada KMK, Yasuda M, Takeuchi E, Hashimoto H. Radiographic Changes in Rheumatoid Thumb: A radiographic 10 Year Follow-up (in Japanese). J Jpn Soc Surg Hand. 2002;19(4):4.

14. Nalebuff EA. The rheumatoid thumb. Clin Rheum Dis. 1984;10(3):589-607.

15. Stein AB, Terrono AL. The rheumatoid thumb. Hand Clin. 1996;12(3):541-50.

16. Leak RS, Rayan GM, Arthur RE. Longitudinal radiographic analysis of rheumatoid arthritis in the hand and wrist. J Hand Surg Am. 2003;28(3):427-34.

17. Chung KC, Kotsis SV, Wilgis EF, Fox DA, Regan M, Kim HM, Burke FD. Outcomes of silicone arthroplasty for rheumatoid metacarpophalangeal joints stratified by fingers. J Hand Surg Am. 2009;34(9):1647-52.

18. Vliet Vlieland TP, van der Wijk TP, Jolie IM, Zwinderman AH, Hazes JM. Determinants of hand function in patients with rheumatoid arthritis. J Rheumatol. 1996;23(5):835-40.
Patient registration in our hand cohort and the framework for the cross-sectional/longitudinal analyses in this study. The hands contralateral to the surgery side and patients were included in the cohort.
Figure 2

C1–7 in the circle indicate the cluster numbers, and the other numbers indicate patients with changed cluster numbers.
The proportions of each cluster are shown in each column. Hands in cluster 3 or higher constituted more than approximately 30% of the hands if the affected period was longer than 10 years.
Cluster 2 was the most common phenotype and was considered an early phase. Hands in the terminal phase constitute a challenging patient population regarding providing effective treatment; therefore, we recommend considering hand surgery in the middle phase.

Supplementary Files
This is a list of supplementary files associated with this preprint. Click to download.

Table1.xlsx
Table2.tif
Table3.tif