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Original Article

MRI of Rheumatoid Arthritis: Comparing the Outcome Measures in Rheumatology Clinical Trials (OMERACT) Scoring and Volume of Synovitis for the Assessment of Biologic Therapy

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The outcome measures in rheumatology clinical trials (OMERACT) scores are the most mature quantitation system for rheumatoid arthritis (RA) on magnetic resonance imaging (MRI). Direct measuring techniques of synovial volume have been reported with good reproducibility, although few reports have demonstrated the changes of these measures in response to treatment. To assess these clinical responses, we evaluated the correlation of the changes of clinical activity score 28-joints disease activity score (DAS28-CRP) with the changes of OMERACT scores and with synovial volume measurements. Eight RA patients who were treated by biologic agents were examined with MRI of the dominant affected wrist and finger joints before and one year after the treatment. The total OMERACT score was reduced from 48.0 to 41.3, and synovial volume was reduced from 15.4 to 8.8 milliliters. Positive correlations were seen between the changes of DAS28-CRP and the changes of OMERACT synovitis score ($r = 0.27$), OMERACT total score ($r = 0.43$) and synovial volume ($r = 0.30$). Limited to synovium assessment, synovial volume showed a better correlation with DAS28-CRP than the OMERACT synovitis score. On the other hand, the OMERACT total score showed a higher correlation with DAS28-CRP than synovial volume, probably because the OMERACT total score includes scores for bone erosion and bone edema as well.

Key words: magnetic resonance imaging, rheumatoid arthritis, outcome measures in rheumatology clinical trials scoring system, direct volume measuring, medical work station

Treatments for rheumatoid arthritis (RA) have changed remarkably since the advent of biologic agents, and the treatment goals have greatly shifted to the achievement of remission and prevention of joint destruction. To evaluate treatment responses, imaging studies are important in addition to clinical evaluations such as the 28-joints disease activity score (DAS28). Magnetic resonance imaging (MRI) allows the assessment of not only bone erosions but also bone marrow edema and synovitis, which are difficult to detect on plain radiographic images.

The outcome measures in rheumatology clinical trials (OMERACT) RA MRI scoring (RAMRIS) scoring system was devised for use in multi-center studies as a method of MRI assessment of the wrist and meta-

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carpophalangeal (MCP) joints [1]. It is utilized in various clinical studies worldwide as a standard assessment method for MRI. It characteristically allows separate scoring of synovitis, bone erosions, and bone marrow edema. However, as a total of 53 sites—7 for synovitis and 23 each for bone erosion and bone marrow edema—are evaluated, its application is time-consuming. In addition, low reproducibility has been recognized as a limitation [2]. Atlases have been published to improve the reproducibility of results obtained with this method, [3, 4]. Nevertheless, even a trained rater needs about 30 min to complete the evaluation, making it difficult to utilize in clinical practice.

Many studies have demonstrated the use of direct measurement of synovial volume and shown its reproducibility. First, a manual outlining technique was developed, but outlining the synovitis manually can take 1–2 h per scan [5, 6]. To reduce analysis times, a semi-automated volume measuring system was developed. Thresholding in combination with rough manual outlining in each plane can substantially reduce analysis times.

These studies have reported good reproducibility, but did not elucidate patients' responses to treatments. In the current study, we developed thresholding in combination with manual outlining in 3D space using a medical workstation, and used it to calculate the synovial volume. To assess the effects of biologic treatments, we evaluated the correlation of the changes of clinical activity score (DAS28-CRP) with the changes of OMERACT scores and synovial volume.

Patients and Methods

Patients and clinical assessments. This research was a retrospective single center study conducted between the dates of January 2008 and December 2013. Inclusion criteria included patients with rheumatoid arthritis, biological therapy, and high-field (1.5-T) MR imaging examinations at baseline and 12 months following the biological therapy. Of the 24 patients undergoing MR imaging before biologic therapy, 16 patients either dropped out of therapy or did not undergo MR imaging at the one-year point. Thus, 8 patients (7 women and 1 man) were included in this study. Clinical assessment was also performed before and 1 year after the initiation of treatment with biological agents. For clinical assessment, the results of the visual analogue scale (VAS) for general health, counts of swollen and tender joints, and levels of C-reactive protein (CRP) and matrix metalloproteinase 3 (MMP-3) were determined. DAS28-CRP was calculated from the results obtained. The study protocol was approved by the Human Ethics Review Committee of Okayama University Hospital.

MRI examination and its protocol. MRI examinations of the more severely-affected-side wrist, MCP and PIP joints were performed at baseline and at 1 year. MRI examinations were performed on a 1.5-T imaging unit (MAGNETOM Avanto, ©Siemens, Erlangen, Germany), utilizing a small flex coil positioned on the dorsum of the wrist. Patients were examined in the prone position with the arm extended and wrist placed in an 8-channel surface-array-coil. The imaging sequence was selected based on the OMERACT core set recommendation [7]. MR images with and without contrast material were acquired; T1-weighted spin-echo (TR 641 ms, TE 11 ms) images, short-time inversion recovery (STIR; TR 3070 ms, TE 91 ms, T1 160 ms) images and contrast-enhanced (3D gradient recalled echo) images were obtained. A bolus of gadolinium (Gd) contrast agent at 0.1 mmol/kg body weight was intravenously injected and images were obtained within 10 min after injection.

Evaluation of MRI findings. Semiquantitative scoring of synovitis, bone marrow edema, and bone erosion, as visualized by MRI, was performed using the European League Against Rheumatism (EULAR)-OMERACT RAMRIS scoring system [8].

Synovial volumes were measured at the wrist and from the 2nd to 5th MCP joints (a total of 5 sites per patient) on Gd-3D images. The volumes were determined according to the method of Tam *et al.* [9], and the enhancement threshold level was set at +2.5 standard deviations (SDs) of the mean intensity of the thenar muscle on enhanced images (Fig. 1). Based on the threshold level, an enhanced area was automatically extracted and a 3D image was constructed. Next, the vascular area was erased manually from the 3D image to obtain a semi-automatically measured synovial volume with high accuracy. Volume measurements were made using the 3D volumetry function of the AZE Virtual Place (AZE Co., Tokyo, Japan) software application (Fig. 2).

One investigator, blinded to the patients' profiles

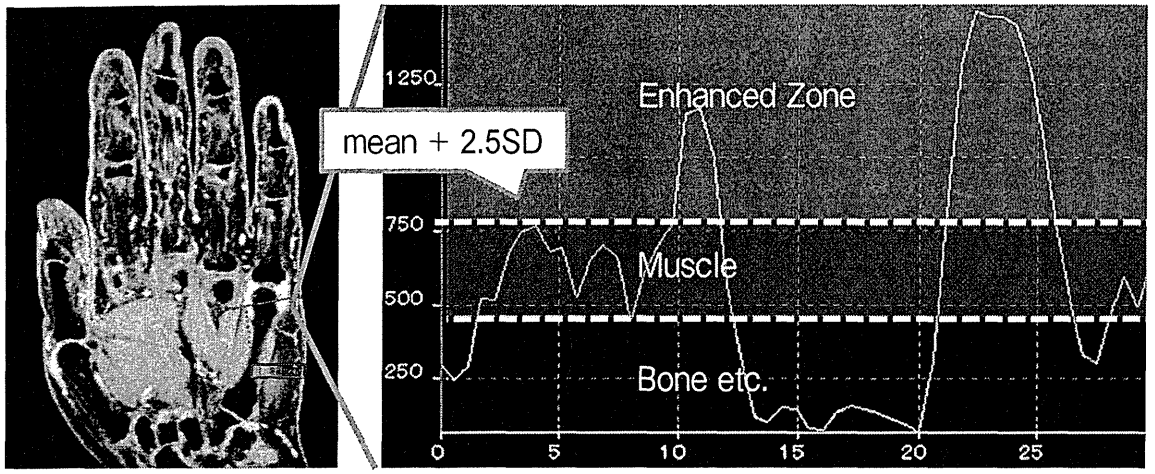

Fig. 1 Enhancement threshold. The enhancement threshold level was set at +2.5 standard deviations (SDs) of the mean intensity of the thenar muscle on enhanced images.

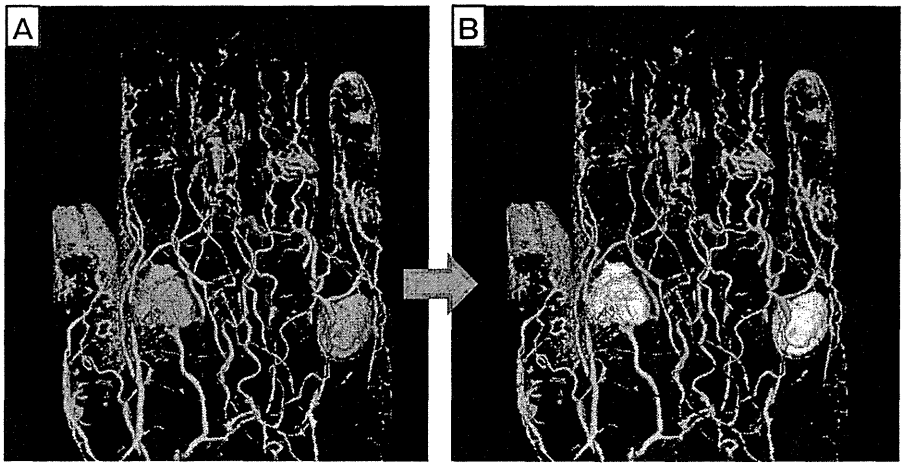

Fig. 2 Semi-automatically measurement on a medical workstation. (A) After thresholding, the synovial area and vascular area were visualized automatically in 3D space. (B) In 3D space, the vascular area was manually erased, and the synovial volume was calculated.

and the chronological order in which the images had been obtained, assessed all images.

To compare the predictability of various MR images for clinical scores, correlations of the DAS28-CRP results with total and synovitis scores of the OMERACT RAMRIS and synovial volumes were evaluated.

The correlation between the synovitis score of the OMERACT RAMRIS and the synovial volume was also analyzed in the wrists and the 2nd to 5th MCP joints.

Statistical analysis. Variables are presented as means ± SDs. The Paired t test was used to compare results at baseline and 1 year. The Pearson product-moment correlation coefficient was used. P values < 0.05 were considered to indicate statistically significant differences.

Results

Patient demographics. The mean age was 58.6 ± 6.4 years and the mean disease duration was 10 ± 8.1 years. The biological agents used were infliximab (n = 3), etanercept (n = 3), and adalimumab (n = 2). The disease modified anti-rheumatic-drugs (DMARDs) used were salazosulfapyridine (SASP; n = 3), bucillamine (BUC; n = 2), and tacrolimus (TAC; n = 1). The mean weekly dose of methotrexate was 6.5 mg. The mean weekly dose of prednisolone was 3.1 mg (Table 1).

Clinical assessment. Clinical parameters pre- and post-treatment are shown in Table 1. Symptom improvements were seen in all 8 patients. The following reductions in clinical parameters were obtained: the swollen joint count, from 4.75 to 1.75; the tender joint count, from 4.50 to 1.13; the VAS score, from 41.8 to 16.3; the CRP level (mg/l), from 2.51 to 0.22; DAS28-CRP, from 3.75 to 1.92.

MR imaging assessment. The OMERACT RAMRIS synovitis, bone marrow edema, and bone erosion scores changed from 12.1 to 6.6, from 6.8 to 4.4, and from 29.0 to 30.2, respectively. The synovial volume was reduced from 15.4 ± 7.4 ml to 8.8 ± 6.3 ml (Table 2). It took 30 to 40 min per patient to complete scoring by the OMERACT system while approximately 20 min were required to measure the synovial volume.

Correlation. Changes in synovial volume and DAS28-CRP are shown in Fig. 3. Changes in the OMERACT RAMRIS score and DAS28-CRP are shown in Fig. 4. Positive correlations were seen between the DAS28-CRP and the OMERACT synovitis score (r = 0.67), OMERACT total score (r = 0.37) and synovial volume (r = 0.66). The changes in the OMERACT RAMRIS total score (r = 0.43), OMERACT RAMRIS synovitis score (r = 0.27), and synovial volume (r = 0.30) showed positive correla-

Table 1 Patients' background

Characteristics	Baseline
Age (years)	58.6 ± 6.4
Gender	F7, M1
Disease duration (years)	10 ± 8.1
Biologic agents	INF 3, ETN 3, ADA 2
DMARDs	SASP 3, BUC 2, TAC 1
Methotrexate (mg/week)	6.5 ± 2.0
Prednisolone (mg/day)	3.1 ± 1.7

ENT, etanercept; IFX, infliximab; ADA, adalimumab; SASP, sulfasalazine; BUC, bucillamine; TAC, tacrolimus.

Table 2 Changes of clinical parameters

	Baseline	1 year
DAS28-CRP	3.7 ± 0.8	1.9 ± 0.5*
Synovial volume (ml)	15.4 ± 7.4	8.8 ± 6.3*
OMERACT RAMRIS	48.0 ± 33.8	41.3 ± 36.3*
synovitis score	12.1 ± 5.3	6.6 ± 5.3*
edema score	6.9 ± 6.9	4.4 ± 6.1
erosion score	29.0 ± 27.7	30.3 ± 27.8

DAS, disease activity score; paired *t* test < 0.05.

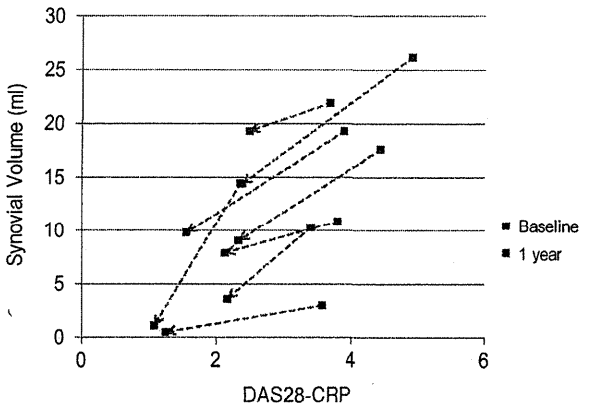

Fig. 3 Changes in volume and DAS28-CRP. Plot of changes in synovial volume and DAS28-CRP.

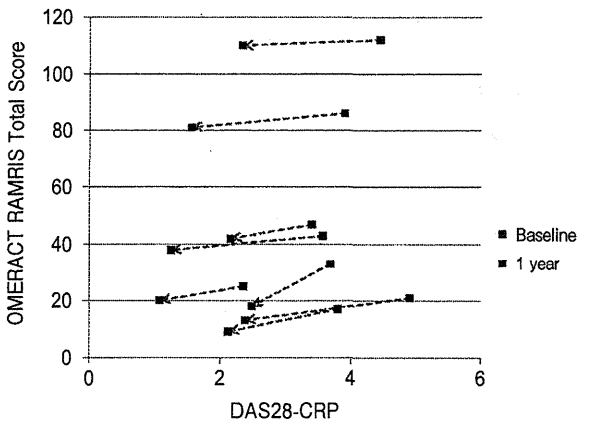

Fig. 4 Changes in OMERACT RAMRIS score and DAS28-CRP. Plot of changes in OMERACT RAMRIS score and DAS28-CRP.

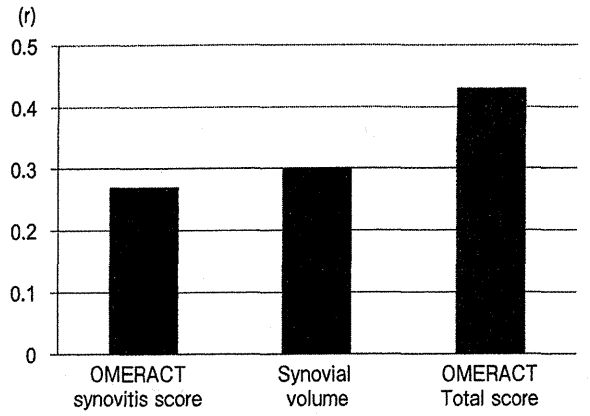

Fig. 5 Correlation with change of DAS28-CRP. The changes in the OMERACT RAMRIS total score (r = 0.43), OMERACT RAMRIS synovitis score (r = 0.27), and synovial volume (r = 0.30) showed positive correlations with DAS28-CRP changes.

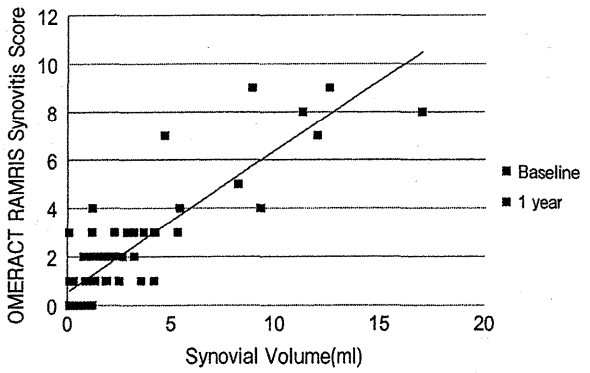

Fig. 6 Volume of each joint and OMERACT RAMRIS synovitis score. The synovial volume of each joint and the OMERACT RAMRIS synovitis score showed a good correlation (r = 0.88).

tions with DAS28-CRP changes (Fig. 5).

Correlations between the synovial volume of each joint and the OMERACT RAMRIS synovitis score are presented in Fig. 6. In each joint, synovial volume showed a good correlation (r = 0.876) with the OMERACT RAMRIS synovitis score.

Discussion

The OMERACT RAMRIS system has been used in many clinical studies because the results correlate with clinical scores of disease activity such as DAS28 and it is useful for evaluating drug efficacy. Although the OMERACT RAMRIS total score is usually used, the synovitis score, bone marrow edema score, or bone erosion score alone reportedly correlates with clinical assessment parameters. The synovitis and bone marrow edema score reportedly correlate with the degree of inflammation on scintigraphic images as well as with levels of CRP and the erythrocyte sedimentation rate (ESR) [10]. Several studies have demonstrated that bone erosion, bone marrow edema, or the synovitis score alone predicts the progression of bone erosion [11, 12].

As the OMERACT RAMRIS system has limitations associated with low reproducibility and its time-consuming nature, synovial volumes were measured in the present study to determine whether this method provides better reproducibility as well as reduced reading time. Measurement of synovial volumes has advantages over the RAMRIS score not only in reducing reading time and enhancing reproducibility but also in improving the ability to assess clinical disease activity. Synovial volumes are reportedly useful for evaluating treatment efficacy because they correlate not only with clinical scores [9, 13] but also with changes in clinical scores from pretreatment values [14]. They have also been reported to correlate with histological inflammation [15] and bone erosion progression [16].

Unlike computed tomography (CT) images, MRI is frequently affected by inherent imaging distortions and unevenness. Therefore, manual outlining is regarded as the area selection method yielding the highest reproducibility. However, a higher-field MR scanner has become available and extremity coils have been developed, the resolution has improved and distortion has decreased. In recent years, it has been possible to set an enhancement threshold level in order to extract an enhanced area, thereby allowing differentiation of the synovial area from the vascular area. This semi-automated measurement method has been widely used. Because MRI can be obtained with thin slices, and as many as 90 images are obtained during one 3D imaging session, manual outlining has become time-consuming and cumbersome to perform.

It is challenging to set an enhancement threshold level for extracting an enhanced area. Several studies have proposed determining this threshold relative to muscle tissue [9, 17] or employing dynamic contrast-enhanced intensities [9]. In the present study, dynamic

MRI was not performed in all 8 patients and the threshold level for extracting an enhanced area was set relative to the enhancement of muscle tissue (+2.5 SDs of the mean thenar muscle enhancement). In addition to the intra-articular synovium, an enhanced area contains blood vessels, tenosynovitis, and bone marrow edema, all of which must be erased. This procedure is performed only manually, and is therefore referred to as a semi-automated measurement. Although the blood vessels, edema, and tenosynovitis have thus far been erased manually on a one-by-one basis, at present a medical workstation for 3D analysis of CT images would allow 3D reconstruction of the extracted images and detection of the synovium in the 3D space, resulting in improved accuracy of extraction and a reduction in reading time. With these measures, nearly 15 min were required to measure synovial volumes in each of the patients in this study.

Since distinguishing synovial fluid from synovial tissue is difficult with non-contrast MR imaging, administration of contrast medium is necessary for measurement of synovial volumes. Synovial volumes measured using unenhanced images are reportedly larger than those measured from enhanced images [18]. Thus, administration of contrast material is considered to be useful for accurate volume measurement. The timing of administration of the medium is also important. In one study, MR images of the knee were acquired every 1.75 min after administration of contrast material. After 11 min, the boundary between the synovial tissue and fluid reportedly became obscure [19]. Thus, the present study protocol specified that 3D images were to be taken within 10 min after injection of contrast medium.

Since the OMERACT RAMRIS synovitis score in each joint correlated strongly with synovial volume, measurement of synovial volumes is considered to be useful for clinically assessing the disease state. The change in synovial volume from pretreatment levels correlated with the change in DAS28-CRP, and the correlation coefficient was higher than that of the change in the OMERACT RAMRIS synovitis score but lower than that of the change in the OMERACT RAMRIS total score. Even though we assessed only 8 subjects in this study, the present results might suggest that synovial volume was more useful for the evaluation of treatment response than the OMERACT RAMRIS synovitis score alone; however, it was inferior to the OMERACT RAMRIS total score, which includes scores for bone erosion and bone marrow edema.

There were several limitations in this study: (i) the sample size was small, which may have limited the statistical power; (ii) all patients had high disease activity at baseline and all patients clinically responded to therapy, so low-disease-activity patients and poor responders to therapy were not evaluated.

In conclusion, measurement of synovial volumes showed higher reproducibility, reduced reading time and a better correlation with DAS28-CRP than the OMERACT RAMRIS synovitis score. However, this method can be said to be less accurate than the OMERACT RAMRIS total score at evaluating clinical disease activity because the correlations with clinical parameters were poorer than those with the OMERACT RAMRIS total score.

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ORIGINAL ARTICLE

Risk factors for surgical site infection and delayed wound healing after orthopedic surgery in rheumatoid arthritis patients

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Abstract

Objective: To investigate the prevalence and the risk factors of surgical-site infection (SSI) and delayed wound healing (DWH) in patients with rheumatoid arthritis (RA) underwent orthopedic surgery.

Methods: We reviewed the records of 1036 elective orthopedic procedures undertaken in RA patients. Risk factors for SSI and DWH were assessed by logistic regression analysis using age, body mass index, disease duration, pre-operative laboratory data, surgical procedure, corticosteroid use, co-morbidity, and use of conventional synthetic disease-modifying anti-rheumatic drugs (csDMARDs) and biological DMARDs (bDMARDs) as variables.

Results: SSI and DWH were identified in 19 cases and 15 cases, respectively. One case of SSI and three cases of DWH were recorded among 196 procedures in patients using bDMARDs. Foot and ankle surgery was associated with an increased risk of SSI (odds ratio (OR), 3.167; 95% confidence interval (CI), 1.256–7.986; $p = 0.015$). Total knee arthroplasty (TKA; OR, 4.044; 95% CI, 1.436–11.389; $p = 0.008$) and disease duration (OR, 1.004; 95% CI, 1.000–1.007; $p = 0.029$) were associated with an increased risk of DWH.

Conclusions: Our results indicated foot and ankle surgery, and TKA and disease duration as risk factors for SSI and DWH, respectively. bDMARDs was not associated with an increased risk of SSI and DWH.

Key Words

Biological DMARDs, Delayed wound healing, Orthopedic surgery, Rheumatoid arthritis, Surgical-site infection

History

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Introduction

Rheumatoid arthritis (RA) is a systemic disease characterized by inflammations in multiple joints with destruction of bone and cartilage [1]. Pharmacological treatment of RA has made great progress over the last two decades. Biological disease-modifying anti-rheumatic drugs (bDMARDs) have been reported to improve the symptoms of RA and delay destruction of bone and joint, especially if combined with methotrexate (MTX) [2]. Recommendations for RA management set by the European League Against Rheumatism (EULAR) in 2013 stated that MTX or other conventional synthetic disease-modifying anti-rheumatic drugs DMARDs (csDMARDs) were the first choice to control RA. In patients responding insufficiently to MTX and/or other csDMARDs strategies, bDMARDs should be commenced with MTX [3]. The Japanese Ministry of Health, Labor and Welfare issued approvals for the first bDMARD, infliximab, in 2003. Seven bDMARDs are now available in Japan: tumor necrosis factor (TNF)-α inhibitors (infliximab, etanercept, adalimumab, golimumab, and certolizumab), an interleukin (IL)-6 inhibitor (tocilizumab), and a cytotoxic T-lymphocyte-associated protein 4-immunoglobulin (CTLA4-Ig) immunoconjugate (abatacept).

Despite the dramatic anti-inflammatory effects of new agents, several reports have shown bDMARDs to increase the risk of serious infection in RA patients [4–8]. Moreover, the risk of serious infection of skin and soft tissue has been shown to increase in TNF inhibitor-treated patients [9]. It has been suggested that perioperative use of bDMARDs in RA patients carries potential risks for surgical-site infection (SSI) and delayed wound healing (DWH) due to their immunosuppressive effects. However, the risk of SSI and DWH with perioperative use of bDMARDs has not reached a general consensus [10–27]. In most guidelines, surgeons are recommended to discontinue bDMARDs during the perioperative period to reduce the risk of SSI and DWH. The recommended perioperative discontinuation periods of bDMARDs differ slightly among rheumatology societies [28–33]. In this retrospective study, we reviewed the prevalence of SSI and DWH in RA patients undergoing orthopedic surgery, and statistically examined to identify the risk factors for SSI and DWH.

Patients and methods

In this retrospective study, we investigated medical records of all RA patients underwent elective orthopedic procedures between January 2004 and December 2012 in two centers; Okayama

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University Hospital (Okayama, Japan) and Kurashiki Sweet Hospital (Kurashiki, Japan). The procedures for infection were excluded due to the object of this study, and remaining 1036 surgical procedures were included. All patients fulfilled the 1987 revised American College of Rheumatology (ACR) criteria for RA [34]. The study was approved by the ethics committee of our institute, and all subjects gave their written informed consent (approval number 251).

The discontinuation protocol of bDMARDs was based on guidelines set by the Japan College of Rheumatology (JCR) [28–30]. Those guidelines recommend that TNF inhibitors (including infliximab, etanercept, adalimumab, and golimumab) should be withheld 2–4 weeks before surgery. Infliximab and golimumab was withheld 4 weeks before surgery, and adalimumab was withheld 2 weeks before surgery. Etanercept was withheld once (patients of one injection/week) or twice (patients on two injections/week) before surgery, which was based on our previous report [35]. As the discontinuation period for tocilizumab and abatacept was not referred to in the JCR guidelines, tocilizumab was withheld 4 weeks, and abatacept was withheld 2 weeks before surgery. Infliximab was restarted 4 weeks after surgery, and etanercept, adalimumab, tocilizumab, and golimumab were restarted after healing of surgical wounds.

In our protocols for "stress dose steroids", hydrocortisone was administered intravenously in a dose of 100 mg twice daily at the day of the surgery for the patients who received prednisolone more than 5 mg/day. Identification of SSI was done based on the 1999 guidelines for the prevention of SSI [36]. Cases in which suture removal was longer than 2 weeks after surgery or which required re-suturing were regarded as DWH.

Statistical analyses

Risk factors for SSI and DWH were assessed by univariate logistic regression analyses and multivariate logistic regression analyses between age, the body mass index (BMI), disease duration, surgical procedure, corticosteroid use, diabetes mellitus, hypertension, csDMARDs, and bDMARDs. First, univariate logistic regression analysis was undertaken for these factors and factors with $p<0.20$ were selected. In addition, multivariate logistic regression analysis with method of increasing variables of likelihood ratio was carried out for the selected factors. $p<0.05$ was considered significant.

Results

A total of 840 procedures involved csDMARDs and 196 procedures involved bDMARDs group. Table 1 shows patients' background at the time of surgical procedure. The patients with corticosteroid use were 624 cases (74.3%, including 95 cases more than 5 mg/day) in csDMARDs group and 120 cases (61.2%, including 5 cases more than 5 mg/day) in bDMARDs group. Surgical procedures were: hand and wrist surgeries (286 procedures); foot and ankle surgeries (204); total knee arthroplasty (TKA, 196); total hip arthroplasty (THA, 97); total elbow arthroplasty (TEA, 127); total shoulder arthroplasty (TSA, 8), arthroscopic synovectomy (32); spine surgery (60); others (26) (Table 2). The bDMARDs group comprised: 94 procedures treated with etanercept; 52 with infliximab; 22 with adalimumab; 22 with tocilizumab; 5 with abatacept; and one with golimumab. The mean duration of discontinuation bDMARDs before and after surgery (in days), was 10.2 and 12.8 with etanercept; 31.7 and 31.0 with infliximab; 15.9 and 15.6 with adalimumab; 29.9 and 33.3 with tocilizumab; 17.8 and 18.8 with abatacept; and 29.0 and 25.0 with golimumab, respectively (Table 3).

In 1036 procedures, SSI and DWH were identified in 19 cases (1.83%) and 15 cases (1.45%), respectively. Among patients with SSI, superficial infection and deep infection were identified in 10 cases and 9 cases, respectively. In patients using bDMARDs, one case of superficial infection (0.51%) and three cases (1.53%) of

Table 2. Type of orthopedic procedures.

Surgical procedures	csDMARDs	bDMARDs	Total
Hand and wrist	227	59	286
Foot and ankle	157	47	204
TKA	166	30	196
THA	78	19	97
TEA	111	16	127
TSA	5	3	8
Arthroscopic synovectomy	21	11	32
Spine	54	6	60
Others	21	5	26
Total	840	196	1036

TKA: total knee arthroplasty; THA: total hip arthroplasty; TEA: total elbow arthroplasty; TSA: total shoulder arthroplasty; Others: open reduction and internal fixation for fractures, neurolysis, tumor excision, Hemiarthroprasty for femoral neck fractures; csDMARDs: conventional synthetic disease-modifying antirheumatic drugs; bDMARDs: biological disease-modifying antirheumatic drugs.

Table 1. Patients' background at the time of surgical procedure.

	csDMARDs group (n = 840)	bDMARDs group (n = 196)	p value
Age, years (range)	64.0 (15–88)	59.0 (28–80)	<0.001*
Disease duration of RA, years (range)	18.7 (0.3–63.9)	16.3 (0.8–51.2)	0.001*
Rheumatoid factor, %	75.3	74.8	0.915**
Body mass index, kg/m^2 (range)	21.8 (10.9–38.7)	22.0 (14.6–33.5)	0.624***
Mean pre-operative WBC,/μl (range)	7300 (2180–19,100)	6305 (2640–13,300)	<0.001*
Mean pre-operative CRP, mg/dl (range)	0.72 (0.0–13.2)	0.21 (0–13.5)	<0.001*
MTX use, %	55.0	67.9	0.001**
Mean MTX, mg/week (range)	6.0 (1–16)	6.8 (2–16)	
PSL use, %	74.29	61.2	<0.001**
Mean PSL, mg/day (range)	5.98 (1–40)	3.74 (1–10)	
Hypertension, %	26.0	19.4	0.054**
Diabetes mellitus, %	7.4	6.6	0.878**

csDMARDs: conventional synthetic disease-modifying antirheumatic drugs; bDMARDs: biological disease-modifying antirheumatic drugs; RA: rheumatoid arthritis; WBC: white blood cell; CRP: C-reactive protein; MTX: methotrexate; PSL: prednisolone.
*Mann–Whitney U test.
**Fisher's exact test.
***Independent t-test.

DWH were recorded (Tables 4 and 5). Univariate and multivariate logistic regression analyses revealed procedures in the foot and ankle to be associated with an increased risk of SSI [odds ratio (OR), 3.167; 95% confidence interval (CI), 1.256–7.986; $p=0.015$; Table 6]. TKA (OR, 4.044; 95% CI, 1.436–11.389; $p=0.008$) and disease duration (OR, 1.004; 95% CI, 1.000–1.007; $p=0.029$) were associated with an increased risk of DWH (Table 7). Pre-operative use of bDMARDs was not an independent risk factor for SSI (OR, 0.234; 95% CI, 0.031–1.765; $p=0.159$) and DWH (OR, 1.073; 95% CI, 0.300–3.838; $p=0.914$).

Table 3. Discontinuation periods of bDMARDs.

bDMARDs	Pre-operation	Post-operation days (range)
Etanercept ($n=94$)	10.2 (5–22)	12.8 (5–27)
Infliximab ($n=52$)	31.7 (26–47)	31.0 (14–94)
Adalimumab ($n=22$)	15.9 (8–23)	15.6 (12–23)
Tocilizumab ($n=22$)	29.9 (14–45)	33.3 (14–105)
Abatacept ($n=5$)	17.8 (13–21)	18.8 (9–33)
Golimumab ($n=1$)	29.0	25.0

bDMARDs: biological disease-modifying antirheumatic drugs.

Discussion

The current retrospective study suggested that surgery of the foot and ankle was a risk factor for SSI, and TKA and disease duration were risk factors for DWH. Pre-operative use of bDMARDs was not an independent risk factor for a significant increase in the prevalence of SSI and DWH.

Previous studies identified foot and ankle surgery as a potential risk of infection by Broeder et al. (OR: 3.2; 95% CI: 1.6–6.5) [12], Kubota et al. (OR: 19.27; 95% CI: 4.67–79.45) [16] and foot surgery by Momohara et al. (OR: 3.06; 95% CI: 1.009–9.327) [17]. Corticosteroid use has been recognized to be a major risk factor for infection in RA patients [37–39], but corticosteroid use was not an independent risk factor in this study. This finding might be due to relatively small dose (mean, 6 mg/day) of corticosteroid in our study as compared with previous studies [37–40]. Statistical analyses revealed TKA and disease duration to be associated with an increased risk of DWH (Table 7). Previous reports suggested TKA for connective disease has a potential risk of wound complication, such as skin necrosis, wound dehiscene [41,42]. Disease duration was also identified as a risk factor of DWH in this study, partly because longer chronic inflammation or steroid use might induce thinner and weaker connective tissue including skin structure.

Table 4. Characteristics of patients with SSI.

Patient	Gender	Age (years)	Disease duration (years)	SSI	Surgical procedures	PSL (mg/day)	csDMARDs	bDMARDs
1	F	37	7.7	Superficial	Toe plasty	5	MTX	Etanercept
2	F	59	31.5	Superficial	Toe plasty	5	MTX	–
3	F	69	37.0	Superficial	Ankle arthrodesis	–	–	–
4	F	58	18.1	Superficial	Toe plasty	8	MTX	–
5	F	70	30.0	Superficial	TKA	–	–	–
6	M	76	3.5	Superficial	TKA	5	TAC	–
7	F	75	4.1	Superficial	TKA	5	SASP	–
8	F	64	31.8	Superficial	Toe plasty	2	MTX, TAC	–
9	F	80	20.3	Superficial	Toe plasty	3	BUC	–
10	F	57	21.4	Superficial	Toe plasty	–	MTX, TAC	–
11	F	73	36.4	Deep	Tumor excision	5	Auranofin	–
12	M	68	12.5	Deep	THA	10	MTX	–
13	F	72	12.9	Deep	TEA	5	BUC	–
14	F	58	18.3	Deep	TFA (MP joints)	10	MTX	–
15	F	76	9.1	Deep	THA	8	MTX	–
16	F	67	3.5	Deep	Toe plasty	–	MTX, TAC	–
17	F	67	17.7	Deep	TKA	5	BUC, Auranofin	–
18	F	69	28.8	Deep	TFA (MP joints)	5	MTX	–
19	F	57	5.6	Deep	TKA	3	SASP	–

SSI: surgical site infection, PSL: prednisolone, TKA: total knee arthroplasty, THA: total hip arthroplasty, TEA: total elbow arthroplasty, TFA: total finger arthroprasty, MTX: methotrexate, TAC: tacrolimus, SASP: salazosulfapyridine, BUC: bucilamine.

Table 5. Characteristics of patients with delayed wound healing.

Patient	Gender	Age (years)	Disease duration (years)	Surgical procedures	PSL (mg/day)	csDMARDs	bDMARDs
1	F	62	31.8	Toe plasty	5	TAC	Tocilizumab
2	F	70	7.8	THA	3	–	Adalimumab
3	F	59	29.8	TKA	–	BUC	Adalimumab
4	F	67	20.3	TKA	5	SASP	–
5	F	42	32.0	TKA	8	–	–
6	F	66	15.4	Toe plasty	3	MTX	–
7	F	72	43.1	TKA	7	Minocycline	–
8	F	62	12.6	ORIF (humerus)	3	MTX	–
9	F	78	45.3	THA	3	MTX	–
10	F	74	15.4	TKA	1	BUC	–
11	F	73	20.3	Toe plasty	–	–	–
12	F	58	13.6	TKA	4	MTX, SASP	–
13	F	72	17.7	TKA revision	5	MTX	–
14	F	53	53.3	TEA revision	5	TAC	–
15	F	70	34.7	THA	1	SASP	–

PSL: prednisolone, ORIF: open reduction and internal fixation, THA: total hip arthroplasty, TKA: total knee arthroplasty, TEA: total elbow arthroplasty, TAC: tacrolimus, MTX: methotrexate, BUC: bucilamine, SASP: salazosulfapyridine.

Table 6. Univariate and multivariate logistic regression analysis of risk factors for SSI.

	Univariate			Multivariate		
	OR	95%CI	*p* value	OR	95%CI	*p* value
Age (per year)	1.038	0.991–1.088	0.114	n.e.		
BMI (kg/m^2)	1.047	0.932–1.176	0.441			
Disease duration (per months)	0.999	0.996–1.002	0.569			
Preoperative WBC (/μl)	0.843	0.680–1.045	0.118	n.e.		
Preoperative CRP (mg/dl)	0.957	0.728–1.259	0.756			
Rheumatoid factor	0.545	0.129–2.302	0.409			
Type of procedures						
Hand and wrist	0.302	0.069–1.316	0.111	n.e.		
Foot and ankle	3.066	1.217–7.724	0.017	3.167	1.256-7.986	0.015
TKA	1.545	0.550–4.340	0.41			
THA	1.142	0.260–5.017	0.861			
TEA	0.393	0.052–2.968	0.365			
TSA	n.c.					
Arthroscopic synovectomy	n.c.					
Spine	n.c.					
Drug						
PSL	1.481	0.488–4.501	0.488			
MTX	0.821	0.331–2.037	0.67			
csDMARDs except MTX	1.481	0.597–3.675	0.397			
bDMARDs	0.234	0.031–1.765	0.159	n.e.		
Comorbidity						
Hypertension	1.409	0.530–3.745	0.492			
Diabetes mellitus	0.708	0.093–5.377	0.738			

Multivariate logistic regression analysis with method of increasing variables of likelihood ratio was performed. n.c.: not countable (No SSI case); n.e.: not entered (the factors is not significant); SSI: surgical site infection; BMI: Body mass index; WBC: white blood cell; CRP: C-reactive protein; TKA: total knee arthroplasty; THA: total hip arthroplasty; TEA: total elbow arthroplasty; TSA: total shoulder arthroplasty; PSL: prednisolone; MTX: methotrexate; csDMARDs: conventional synthetic disease-modifying antirheumatic drugs; bDMARDs: biological disease-modifying antirheumatic drugs.

Table 7. Univariate and multivariate logistic regression analysis of risk factors for delayed wound healing.

	Univariate			Multivariate		
	OR	95%CI	*p* value	OR	95%CI	*p* value
Age (per year)	1.031	0.980–1.085	0.243			
BMI (kg/m^2)	0.945	0.811–1.100	0.464	n.e.		
Disease duration (per months)	1.003	1.000–1.006	0.04	1.004	1.000–1.007	0.029
Preoperative WBC (/μl)	0.933	0.748–1.165	0.542			
Preoperative CRP (mg/dl)	0.745	0.453–1.223	0.244			
Rheumatoid factor	0.877	0.230–3.386	0.847			
Type of procedures						
Hand and wrist	n.c.					
Foot and ankle	1.026	0.287–3.671	0.968			
TKA	3.852	1.380–10.753	0.01	4.044	1.436-11.389	0.008
THA	2.465	0.684–8.892	0.168	n.e.		
TEA	0.507	0.066–3.891	0.514			
TSA	n.c.					
Arthroscopic synovectomy	n.c.					
Spine	n.c.					
Drug						
PSL	2.579	0.578–11.498	0.214			
MTX	0.365	0.124–1.076	0.068	n.e.		
csDMARDs except MTX	1.521	0.547–4.227	0.421			
bDMARDs	1.073	0.300–3.838	0.914			
Comorbidity						
Hypertension	2.045	0.721–5.802	0.179	n.e.		
Diabetes mellitus	1.998	0.442–9.022	0.368			

Multivariate logistic regression analysis with method of increasing variables of likelihood ratio was performed. n.c.: not countable (No delayed wound healing case); n.e.: not entered (the factors is not significant); BMI: Body mass index; WBC: white blood cell; CRP: C-reactive protein; TKA: total knee arthroplasty; THA: total hip arthroplasty; TEA: total elbow arthroplasty; TSA: total shoulder arthroplasty; PSL: prednisolone; MTX: methotrexate; csDMARDs: conventional synthetic disease-modifying antirheumatic drugs; bDMARDs: biological disease-modifying antirheumatic drugs.

Accumulating reports have evaluated the perioperative risk of the use of bDMARDs, but have not reached a general consensus. Several reports have suggested that treatment with bDMARDs increases the risk of SSI [10,13,14,19,21], whereas other studies have reported that use of bDMARDs is not associated with SSI [11,12,15–18,20,22–27]. One of the possible reasons for this discrepancy might be that the criteria for defining SSI among these studies were different. Some studies reported the patients with infectious signs or who were given additional antibiotics according to the judgments of the surgeon were identified as being SSI, and

all these reports suggested that bDMARDs increased the risk of SSI [10,13,14,19,21]. However, this definition of SSI carries a potential risk of overestimation of SSI. Kawakami et al. described a situation in which infection cases were recorded if surgeons diagnosed or "suspected" a surgical infection, and antibiotics were given prophylactically. In the TNF inhibitor group, seven cases were identified by surgeons as having post-operative superficial infections that necessitated antibiotic use. If the definition of infection is purulent drainage from a deep incision, or an abscess found upon direct examination, then there was only one case of infection in the TNF inhibitor group [19]. In this study, patients who had additional antibiotics given prophylactically were not included as SSI. As a result, only one case of superficial SSI after foot surgery with etanercept was observed, and the risk of SSI with bDMARDs was not significant. The prevalence of infection in patients being treated with bDMARDs and csDMARDs was 0.5 and 2.1% in our study, which was not higher than reports regarding SSI and treatment using csDMARDs (1.2–3.3%) [43–45]. Suzuki et al. reported, using a lager dataset accumulated by a questionnaire survey, that the chance of having bDMARDs treatments was more than two-fold greater in patients with SSI compared with the chance of having csDMARDs treatments [21]. The prevalence of infection of their reports in the foot surgery and TKA was 5.1 and 2.6%, respectively, which was higher than the 2.1% observed in all joint arthroplasties in our study. They cautioned to pay a careful attention to the surgery at both sites. The limitations of their study were that the response rate to the questionnaire was only 61.7%, differences in surgical conditions (classification of "clean room", experience of the surgeon), and lack of statistical analyses for confounders.

The risk of DWH with bDMARDs treatment is also controversial. In this study, 15 cases of DWH included three cases with bDMARDs. The prevalence was 1.45% in total and 1.53% in patients using bDMARDs. Studies [45,46] on DWH with csDMARDs have reported a prevalence of 4.9–5.1%, and our findings were not higher. Bibbo et al. [11] and Kubota et al. [25] reported that use of bDMARDs in pre-operative periods in RA patients was not associated with DWH. Hirano et al. [20] reported that controlled use of TNF inhibitors caused no complications in surgical wounds, and could improve recovery from post-operative anemic conditions due to anti-TNF effects upon bone marrow. Conversely, Broeder et al. [12] suggested that TNF inhibitors could be associated with impaired wound healing. However, they compared effects between continuation and discontinuation of TNF inhibitors in the perioperative period. Therefore, the risk of DWH remains unclear if bDMARDs are stopped during the relevant periods.

Perioperative discontinuation period of bDMARDs could influence the prevalence of SSI and DWH. Several reports [10–27] related to bDMARDs use in the perioperative period have demonstrated duration of discontinuation of drugs based on the guidelines of each country or society, but the pre-operative and post-operative discontinuation period among guidelines differ [28–33]. In our institutes, the perioperative discontinuation periods of bDMARDs were based on JCR guidelines except for etanercept, as we reported previously [35]. That report suggested that the discontinuation period of etanercept before surgery could be <2 weeks based on measurements of the serum concentration of etanercept. Etanercept was withheld in average 10.2 days, and this duration was shorter than that recommended by the JCR. The duration of discontinuation of tocilizumab was not referred to in JCR guidelines [30]. In our protocol, tocilizumab was withheld 4 weeks before surgery and was restarted after healing of surgical wounds. Momohara et al. [17] reported that the period from the final infusion of tocilizumab to the surgical procedure was 23.5 days, and the period from the surgical procedure until reinfusion was 24.8 days. Greater vigilance with respect to infectious complications is need for RA patients being treated by tocilizumab because monitoring of levels of C-reactive protein is masked due to drug efficacy. We experienced disease flare-up in only four patients. More than 14 days of discontinuation of etanercept before surgery in the early periods of this study was noted in three patients. In one case with golimumab, post-operative restarting of golimumab treatment was postponed due to re-operation not related to SSI or DWH (spinal surgery with mal-positioning of a pedicle screw).

In reports focusing on perioperative complications with bDMARDs, most used TNF inhibitors (infliximab, etanercept, and adalimumab). Two studies focused on tocilizumab [17,18], and one study detailing eight orthopedic procedures with abatacept reported a safe 2–3 weeks treatment-free interval before surgery [34]. Our study included 27 procedures (15% in 196 cases) with bDMARDs other than TNF inhibitors, which remains too small to render a robust conclusion. More data for newer bDMARDs such as golimumab, certolizumab, and abatacept would be needed.

Our study had several limitations. First, due to the low prevalence of complications associated with surgery, a larger number of patients would be necessary to detect such complications accurately. Second, our data were collected retrospectively using the medical records of patients who had undergone surgery. The activity and severity characteristics such as DAS 28 might be associated with the risk of SSI and DWH, but the data for DAS 28 was lacking in patients underwent surgery before 2010. As a prospective study including surgical procedures would be difficult due to ethical concerns, larger multicenter studies under the same protocol and definition of SSI and DWH would provide useful information.

Conflict of interest

K. N. has received research funding from Abbvie, Astellas, Chugai, Mitsubishi-Tanabe, Eisai and BMS. T. O. has received research funding from GlaxoSmithKline. For the remaining author, no conflict of interest is declared.

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ORIGINAL ARTICLE

Clinical and radiographic study of partial arthrodesis for rheumatoid wrists

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Abstract

Objectives. To retrospectively investigate the clinical and radiographic results of partial arthrodesis for the wrists with rheumatoid arthritis (RA).

Methods. Forty-one wrists with RA were treated by radiolunate (RL) or radiolunotriquetral (RLT) arthrodesis with ulnar head resection. The average follow-up period after surgery was 7.1 years. Preoperative radiographs of all wrists were classified according to Schulthess classification. We performed RL arthrodesis for all Type II ($n = 26$) and Type III wrists ($n = 7$), and RLT arthrodesis for Type III wrists ($n = 8$). Pre- and postoperative pain score (visual analog scale), grip strength, range of motion, and radiographic parameters were statistically compared.

Results. Pain scores in all groups were significantly improved at final follow-up ($P < 0.05$). Grip strength increased from 5.9 to 12.4 (kg) significantly in Type II wrists ($P < 0.01$), from 7.2 to 9.1 in Type III wrists after RLT arthrodesis, but decreased from 6.9 to 6.0 in Type III wrists after RL arthrodesis. In all groups, the arc of pronation and supination improved significantly ($P < 0.05$), and all radiographic parameters improved.

Conclusions. RL arthrodesis for Type II wrists showed satisfactory clinical results. RLT arthrodesis would be a reliable method in case of unstable wrist joint.

Keywords

Arthrodesis, Rheumatoid arthritis, Wrist joint

History

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Introduction

Rheumatoid arthritis (RA) frequently affects the wrist joints. Wrist joint involvement affects up to 60% of patients within the first 2 years after the onset of RA, increasing to 90% after 10 years during the course of RA [1]. Functional disturbance of the hand is often caused by the pain and instability of the wrist joint [2,3]; therefore, the wrist joint is a key joint in the treatment of loss of hand function in RA [4].

Surgical synovectomy of the wrist has been the main procedure to provide pain relief and good hand function, but many authors reported that synovectomy alone could not prevent radiological deterioration and disease progression [5,6]. Chamay et al. [7] reported that in the wrists with RA, 13% of the cases showed spontaneous partial fusion with good stability and functional motion. They also reported the results of four surgical radiolunate (RL) arthrodeses in the paper [7]. The technique was combined with synovectomy and ulnar head resection (UHR). Subsequently, they showed excellent results of partial wrist arthrodesis on 21 wrists with RA [8]. RL arthrodesis provided excellent pain relief and corrected palmar subluxation and ulnar shift of the carpus, and the carpal height. The modification of carpal height by bone graft between the radius and the lunate theoretically improves the tension of extrinsic muscle–tendon units and the grip strength [9]. Ishikawa et al. [10] reported that wrists with RA maintained good stability with preservation of motion by radiocarpal arthrodesis for more than 10 years.

Simmen and Huber [1] reported on Schulthess classification, which classifies wrists with RA into three types: Type I (ankylosis type), Type II (osteoarthritis type), and Type III (disintegration type). Della Santa and Chamay [11] reported that RL arthrodesis could prevent dislocation of an unstable wrist, and recommended RL arthrodesis for Type II wrists. When the midcarpal joint space and proximal carpal row are preserved, RL arthrodesis with UHR can be applied for Type II and Type III wrists. We previously evaluated the radiographic results of surgical RL arthrodesis in association with preoperative disease activity and the Schulthess preoperative radiographic classification [12]. In that study, we performed RL arthrodesis for both Type II and Type III wrists, and showed that RL arthrodesis for Type II wrists could prevent carpal collapse and preserve functional range of motion (ROM). However, some cases with Type III wrists showed postoperative progression of carpal collapse and ulnar carpal shift. These results suggested that applied additional fixation following RL arthrodesis might be needed for the wrists in which the lunate bone and the distal end of the radius cannot be fixed firmly. Ishikawa et al. reported that it might be better to avoid the scaphoid from arthrodesis because radioscapholunate (RSL) arthrodesis decreases the arc of wrist extension and flexion by half [10]. Therefore, we have applied radiolunotriquetral (RLT) arthrodesis as additional fixation. The

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contraindication to RL or RLT arthrodesis is that there is remarkable midcarpal joint destruction and that there is no sufficient bone stock in the proximal carpal row and the distal end of the radius.

The purpose of this study is to retrospectively investigate the clinical and radiographic results of RL and RLT arthrodesis for Type II and Type III wrists.

Materials and methods

Patients

We reviewed 41 wrists with RA treated by radiocarpal arthrodesis with UHR between 2000 and 2008 (Table 1). There were 40 women and 1 man. Ages at surgery ranged from 28 to 74 (average, 54.1) years. The average follow-up period after surgery was from 2.6 to 11.5 (average, 7.1) years. Before the operations, 36.6% of the patients were treated by methotrexate, 100% by prednisolone, 70.7% by other immunosuppressants or disease-modifying antirheumatic drugs (DMARDs), and 7.3% by biologic DMARDs. Average C-reactive protein (CRP) levels were 0.5 (0.1–2.0) mg/dL.

Preoperative radiographs showed Type II in 26 wrists and Type III in 15 wrists according to Schulthess classification. We selected RL arthrodesis for all Type II wrists and 7 Type III wrists, and RLT arthrodesis for 8 Type III wrists.

The primary radiographic indications of radiocarpal arthrodesis with UHR for RA were as follows: (1) radiocarpal joint space narrowing and erosions, (2) ulnar carpal shift, (3) carpal collapse, (4) dorsal subluxation of the ulnar head, and (5) Type II or Type III in Schulthess classification [9]. Spontaneous fusion of carpal bones, including the midcarpal joint, is possible for Type I wrists, so the functional ROM cannot be expected in the future. Because of this, partial arthrodesis is not indicated for Type I wrists. A sufficient bone stock of the proximal carpal row and the distal end of the radius are required for radiocarpal arthrodesis. We performed RL arthrodesis according to our previously reported procedure [12]. However, some cases with Type III wrists showed postoperative progression of carpal collapse and ulnar shift. We therefore have indicated RLT arthrodesis for Type III wrists in cases where the proximal carpal row and the distal end of the radius cannot be fixed firmly after RL arthrodesis (Figure 1). Total arthrodesis is indicated when carpal bones are severely collapsed.

Clinical parameters

The clinical results of this surgical procedure were evaluated by pain score, grip strength (kg), and ROM. Pain scores were recorded on a visual analog scale (VAS: 0–100 mm) by interviewing the patients. ROM included wrist extension, flexion, forearm supination, and pronation before the surgery and at the final follow-up.

Table 1. Baseline characteristics.

Schulthess classification	Type II	Type III		
Fixation method	RL	RL	RLT	Total
No. of wrists (patients)	26 (23)	7 (7)	8 (6)	41 (34)
Female/Male	25/1	7/0	8/0	40/1
Age at operation (average, years)	49.8	61.4	61.9	54.1
Duration of disease (average, years)	9.5	14.0	6.8	9.5
Follow-up (average, years)	7.4	6.5	6.7	7.1
CRP (average, mg/dL)	0.3	0.1	2.0	0.5
Use of Prednisolone (%)	100.0	100.0	100.0	100.0
Daily dose of Prednisolone (average, mg/day)	3.3	4.1	5.2	3.8
Use of DMARD (%)				
Biologic DMARD	7.7	14.3	0	7.3
Methotrexate	26.9	57.1	50.0	36.6
Other antirheumatic drugs	76.9	57.1	62.5	70.7

DMARD disease-modifying antirheumatic drug, *CRP* C-reactive protein.

Radiologic parameters

We evaluated the radiologic parameters just before and after the surgery, and at the final follow-up. Collapse of the carpal bones was evaluated by Youm's carpal height ratio (c/MC) [13]. Ulnar carpal shift was evaluated by Ishikawa's ulnar carpal shift ratio (e/MC) [14] modified from Chamay's ratio. Palmar carpal subluxation was evaluated by Ishikawa's palmar carpal subluxation ratio (h/MC).

c/MC and e/MC were based on posteroanterior views of radiographs of the wrist, and h/MC was based on lateral views (Figure 2).

Statistical analysis

Statistical analysis was performed using paired *t*-test or a one-way analysis of variance (ANOVA) followed by Tukey's test using the free statistical package R for Windows (www.r-project.org). *P* values less than 0.05 were considered statistically significant.

Results

Clinical results

Clinical results (pain score, grip power, and ROM) for Type II and III wrists are shown in Figure 3. Pain scores for both Type II and Type III wrists were significantly improved at the final follow-up (Type II wrists after RL arthrodesis: $P<0.01$, Type III wrists after RL arthrodesis: $P<0.05$, and Type III wrists after RLT arthrodesis: $P<0.01$). Grip strength significantly increased from 5.9 to 12.4 (kg) in Type II wrists ($P<0.01$), and from 7.2 to 9.1 in Type III wrists after RLT arthrodesis. Grip strength tended to decrease from 6.9 to 6.0 (kg) in Type III wrists after RL arthrodesis; however, the decrease was not significant. Although there was no significant difference between the grip strength in Type II and Type III wrists before surgery, Type II wrists had significantly better grip strength than Type III wrists after RL arthrodesis (analyzed by one-way ANOVA followed by Tukey's test). Average preoperative and final follow-up extension/flexion of the Type II wrists were 47.2°/38.8° and 28.3°/15.2°, respectively. Average preoperative and final follow-up extension/flexion of the Type III wrists after RL arthrodesis were 27.0°/32.0° and 19.3°/14.3°, respectively. Average preoperative and final follow-up extension/flexion of Type III wrists after RLT arthrodesis were 28.1°/27.5° and 26.0°/7.0°, respectively. The rotation arc of pronation and supination improved significantly by resection of the distal end of the ulna in both types ($P<0.05$). ROM at the final follow-up was not significantly different among Type II and Type III wrists treated by RL arthrodesis, and Type III wrists treated by RLT arthrodesis (analyzed by one-way ANOVA followed by Tukey's test).

Changes of radiological graphic parameters

The results of radiographic examinations are shown in Table 2. Carpal height ratio (c/MC) improved after the surgery, especially for Type II wrists ($P<0.001$). Ulnar carpal shift ratio (e/MC) improved after the surgery in all groups; however, there were no significant differences between before surgery and at the final follow-up. Palmar carpal subluxation ratio (h/MC) was corrected and improved significantly in Type II wrists treated by RL arthrodesis and Type III wrists treated by RLT arthrodesis. The midcarpal joint space was lost in 3 of 26 (12%) Type II wrists and 9 of 15 (60%) Type III wrists at follow-up.

Complications

There were no surgical-site infections, and no postoperative extensor tendon ruptures. Fibrous nonunion without clinical instability

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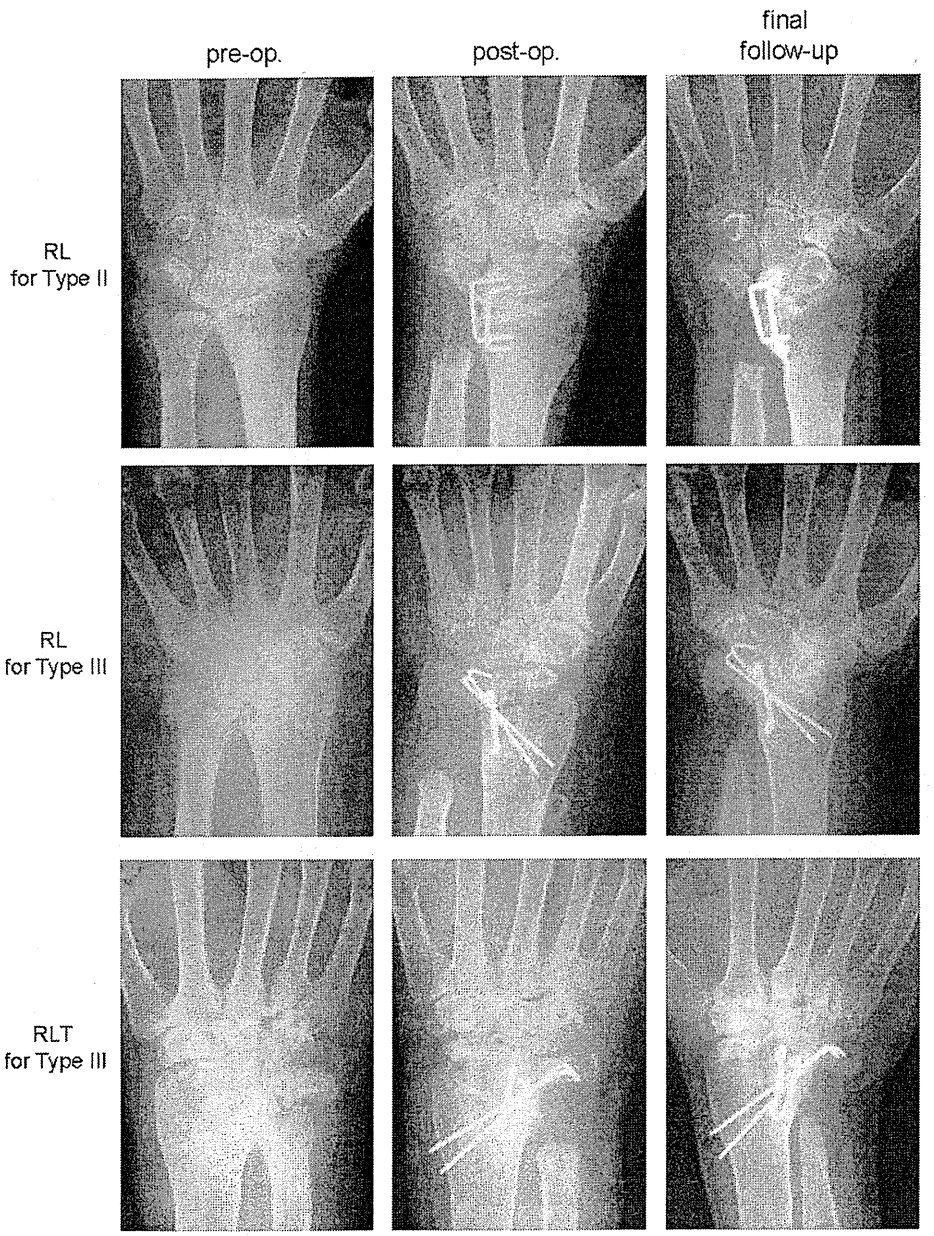

Figure 1. Radiographs of the wrists that underwent radiocarpal arthrodesis with UHR for Type II and Type III wrists.

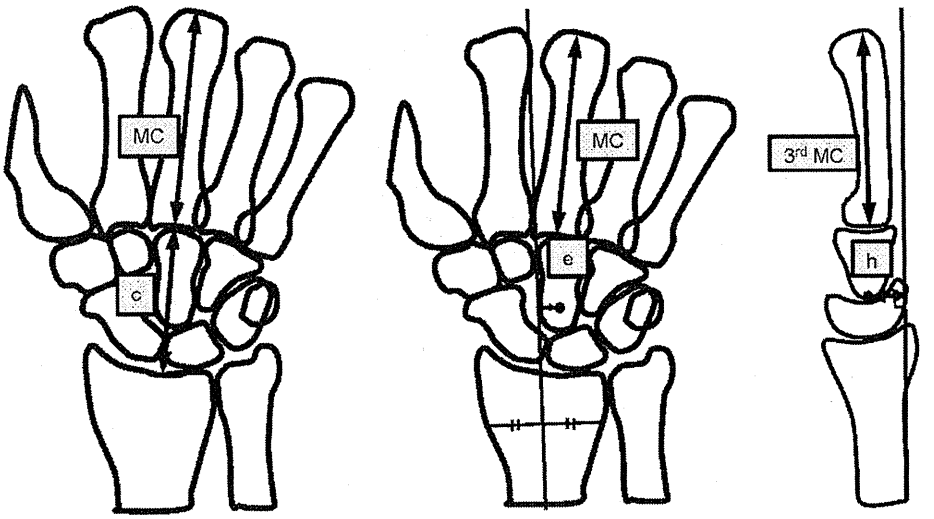

Figure 2. Radiographic parameters used in the present study: carpal height ratio (c/MC), ulnar carpal shift ratio (e/MC), and palmar carpal subluxation ratio (h/MC). c: The distance between the middle point of the base of the third metacarpal and the distal articular surface of the radius measured along the proximal extended line of the longitudinal axis of the third metacarpal bone. e: The distance between the proximal one fourth of the capitate (the center of rotation) and the midaxial line of the radius. h: The distance from the middle point at the most proximal border of the capitate (the rotation center) and the line that was extended parallel with the dorsal cortex of the radial diaphysis. MC: the length of the third metacarpal bone.

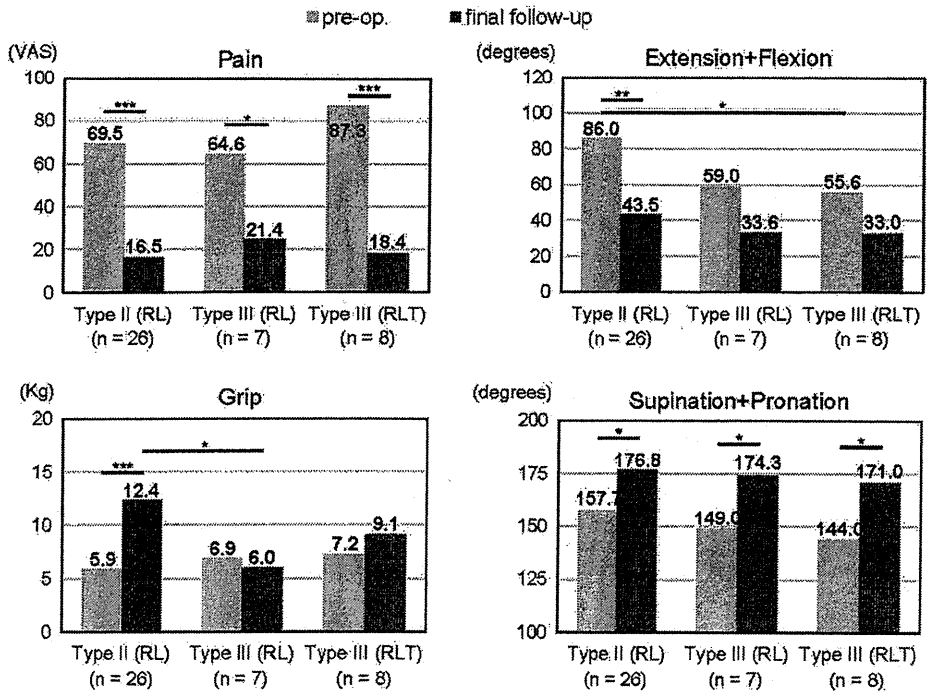

Figure 3. Clinical outcome of RT and RLT partial arthrodesis. *VAS* visual analog scale. Statistical analysis was performed by paired *t*-test to compare the data of pre-op and post-op within the groups. A one-way ANOVA followed by Tukey's test was used to compare the data among Type II and Type III wrists treated by RL arthrodesis, and Type III wrists treated by RLT arthrodesis. $^{*}P<0.05$, $^{**}P<0.01$, $^{***}P<0.001$.

was recognized in three wrists with RL arthrodesis, and one wrist with RLT arthrodesis. However, patients did not complain of wrist pain nor did they require revision surgery.

Discussion

In the present report, we demonstrated that RL arthrodesis for Type II wrists improved pain and grip power and maintained corrected carpal height, palmar carpal subluxation, and ulnar carpal shift. Forearm supination and pronation could be improved by an additional UHR. Although wrist flexion and extension was often reduced after this procedure, the functional ROM was preserved. These results suggest that Type II wrists are a good indication for RL arthrodesis and support our opinion in a previous report [12].

For patients with advanced deterioration of the wrists, total wrist arthrodesis is a reliable method to provide stability. Swelling and pain are better controlled by total wrist arthrodesis than by RL arthrodesis [15]. However, loss of precise functioning in performing personal hygiene and in handling coins and buttons is the frequently reported drawback of total arthrodesis [15,16]. Thus, we consider that total wrist arthrodesis should be avoided for the initial treatment, even for Type III wrists. In RL arthrodesis for Type III wrists, pain improved significantly; however, grip power tended to decrease at the final follow-up. RLT arthrodesis relieved pain and increased grip power, and maintained corrected carpal height, palmar carpal subluxation, and ulnar carpal shift even in Type III wrists. These radiological changes could not be observed in the surgically treated wrist without RLT arthrodesis [17]. It was reported that the additional fixation following RL arthrodesis decreased the ranges of wrist extension and flexion more severely than RL arthrodesis [10], whereas some papers reported that the additional fixation is similar to the results after RL arthrodesis [18,19]. In the present study, the postoperative ROMs of supination, pronation, and combined palmar and dorsal flexion were not significantly different between wrists treated by RL and those treated by RLT arthrodesis (Figure 3).

Table 2. Results of radiographic examinations.

	Schulthess classification	Type II ($n=26$)	Type III ($n=15$)	
	Fixation method	RL	RL ($n=7$)	RLT ($n=8$)
c/MC	pre-op.	0.423	0.442	0.399
	post-op.	0.491***	0.461	0.460***
	final follow-up	0.464***	0.455	0.402
e/MC	pre-op.	0.159	0.151	0.164
	post-op.	0.126**	0.129	0.124*
	final follow-up	0.151	0.155	0.150
h/MC	pre-op.	0.222	0.287	0.239
	post-op.	0.202	0.215	0.186*
	final follow-up	0.196*	0.228	0.221*

Statistical analysis was performed by paired *t*-test relative to pre-op. $^{*}P<0.05$, $^{**}P<0.01$, and $^{***}P<0.001$.

After partial arthrodesis for Type III wrists, the deterioration of the midcarpal joint may cause pain or may decrease the ROM. The midcarpal joint space was lost in 60% Type III wrists at follow-up and resulted in decreased ROM. Taleisnik [20] introduced combined radiocarpal arthrodesis and lunocapitate arthroplasty for wrists severely deteriorated by RA. In this procedure, the motion of the midcarpal joint was preserved by resection of the damaged head of the capitate and replacement with a small implant. In cases with destruction of the midcarpal joint, this method seems to be a useful option.

To classify the wrists according Schulthess classification, it is valuable to examine serial radiographs over a period of at least 6 months, representing progressive changes [13]. We classified each wrist by only the preoperative radiographs in the present study. Some Type II wrists before surgery might change to Type III wrist in the natural course of the disease. However, carpal disintegration did not progress in any of the Type II wrists after RL arthrodesis. These results suggest that RL arthrodesis might alter the natural course and prevent further destruction of wrists with RA.

In the present study, only 7.7% of the patients used biologic DMARDs before surgery, so we could not analyze precisely for the effect of biologic DMARDs. Nowadays, disease activity can be tightly controlled using biologic DMARDs, the joint destruction can be prevented [21], and radiographic remodeling may occur in the joint with RA [22]. The wrist treated by radiocarpal arthrodesis as a joint-preserving procedure may possibly maintain good wrist function under the tight control of the disease.

The present study has several limitations. The first limitation is the relatively small number of patients for analysis in each group. The second is that we evaluated only pain score, grip strength, and ROM. Therefore, the patient-based functional assessment (disabilities of the arm, shoulder, and hand (DASH) or Health Assessment Questionnaire (HAQ)) are needed for precise functional evaluation. The third is that this study is not a randomized controlled clinical trial. We chose RL or RLT arthrodesis according to our indication, hence the results of Type II and III wrists after RL or RLT arthrodesis cannot be compared accurately.

Conflict of interest

None.

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