

ORIGINAL

Changes in foot function, disease activity, and disability after forefoot resection arthroplasty in patients with rheumatoid arthritis

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Abstract : The purpose of this study was to investigate the changes in foot function, disease activity, and disability in patients with RA after resection arthroplasty of the forefoot (arthroplasty). Arthroplasty was performed on 11 patients with RA. All study patients underwent clinical assessment to measure disease activity (Disease Activity Score in 28 Joints-C-reactive protein, DAS28-CRP), disability (Health Assessment Questionnaire-Disability Index, HAQ-DI) and foot function (Foot Function Index, FFI) at the following stages : preoperatively and 1, 3, and 12 months after surgery. Following arthroplasty, foot function improved significantly, as assessed by FFI total and subscales (pain, disability, and limitation of activity) ($P < 0.001$, $P < 0.001$, $P < 0.001$, and $P = 0.002$, respectively). Disease activity was significantly improved in relation to DAS28-CRP and its subscales of number of swollen joints and patient global assessment (PtGA) ($P = 0.033$, $P = 0.008$, and $P = 0.038$, respectively). There was no significant difference in disability, as assessed by the HAQ-DI and its subscale, HAQ-walking ($P = 0.150$ and $P = 0.597$, respectively). Foot function improved significantly after arthroplasty, and was maintained at 12 months postoperatively. Additionally, our study showed that disease activity and its subscale PtGA improved after arthroplasty. *J. Med. Invest.* 63 : 38-44, February, 2016

Keywords : rheumatoid arthritis, resection arthroplasty of the forefoot, foot function

INTRODUCTION

Rheumatoid arthritis (RA) is a systemic and inflammatory autoimmune disease (1). Uncontrolled RA causes joint damage, disability, increases the risk of cardiovascular and other co-morbidities, and can result in a lower quality of life (2). In most cases, the metacarpophalangeal and proximal interphalangeal joints of the fingers, the interphalangeal joints of the thumbs, the wrists, and the metatarsophalangeal (MTP) joints of the toes are affected in the early stages of the disease (3, 4). Other joints of the upper and lower limbs, such as the elbows, shoulders, ankles, and knees, are also commonly impaired. Although the foot is commonly affected by RA (5-10), it is rarely addressed in routine clinical practice (11). Foot deformity and pain adversely affect activities of daily living by limiting the person's ability to walk (12, 13), and also have an adverse effect on the quality of life (14). Hence, resection arthroplasty is often performed to treat deformities of the forefoot in patients with RA (15, 16).

The Disease Activity Score in 28 Joints (DAS28) (17) is frequently used as an indicator of disease activity in RA. However, one limitation of DAS28 is the inclusion of only the knee joint in the evaluation of affected joints of the lower extremities. van der Leeden *et al.* (18) evaluated the forefoot of patients with RA who were classified as in remission based on DAS28 during the first 8 years after disease onset, and reported that pain or swelling were present in at least one of the MTP joints in 40% of patients.

Wechalekar *et al.* (19) evaluated the ankle and foot joints of patients with RA who met the criteria for remission according to DAS28 and reported that synovitis of the forefoot was found in 43% of patients.

The Health Assessment Questionnaire-Disability Index (HAQ-DI) (20) has been widely used to evaluate disability in patients with RA (21), and has also been used as an indicator of functional remission (HAQ remission) (22). Rojas-Villarraga *et al.* (23) reported that movement pain in the forefoot was associated with disease activity (DAS28) and disability (HAQ-DI).

The Foot Function Index (FFI) (24) is commonly used to evaluate foot-related disorders such as RA (25-27). Bal *et al.* (28) reported that the HAQ-DI was the most important correlate of FFI and its subscales.

It is unclear how improvement of foot function in patients with RA who undergo resection arthroplasty affects disease activity and disability. Therefore, the purpose of this study was to investigate the changes in foot function, disease activity, and disability in patients with RA after resection arthroplasty.

PATIENTS AND METHODS

We identified 12 patients who fulfilled the American College of Rheumatology (ACR) revised criteria for rheumatoid arthritis (29), who had marked forefoot deformities and pain, and underwent resection arthroplasty of the forefoot (30) at the Utazu Hama Clinic (currently Utazu Hospital), Kagawa Prefecture, Japan, between July 2008 and January 2012. One patient was excluded from the study because the patient was admitted to another hospital 1 year after the surgical procedure. The resection arthroplasty of the forefoot is composed of excision of all metatarsal heads through

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incision of the medial site of the hallux and the planta. Figure 1 shows the plain radiographs before and after the forefoot resection arthroplasty. Written informed consent was obtained from each patient and the study protocol was approved by the ethics committee of Tokushima University Hospital.



Figure 1. Plain radiographs before (A) and after (B) the forefoot resection arthroplasty

Patient characteristics, including age, gender, body mass index (BMI), disease duration, and prescribed drugs, were obtained from medical records.

All study patients underwent clinical assessment for foot function, disease activity, and physical function, preoperatively and 1, 3, and 12 months after surgery.

Dysfunction in the foot was evaluated using the FFI, which uses a visual analog scale for pain, disability, and limitation of activity. The scale consists of 23 items divided into three subscales: pain (9 items), disability (9 items), and limitation of activity (5 items). Patients were asked to record the most appropriate score for each condition on a line. To calculate the subscale scores, the sum of the values for each item was calculated and divided by the number of items that were applicable to each individual patient. By calculating the average of the three subscale scores, the total FFI score (FFI total) was determined. Each score ranges from 0 to 100, with higher scores corresponding to more severe pain and disability, and greater limitation of activity. These calculations were carried

out by physicians and trained physical therapists.

Disease activity was assessed using DAS28-C-reactive protein (CRP) (31-32). The DAS28-CRP score was calculated using the number of tender joints and swollen joints out of 28 joints, the Patient Global Assessment (PtGA) score, and CRP level.

Disability was evaluated using the HAQ-DI, which is composed of eight categories: dressing and grooming; arising; eating; walking; hygiene; reach; grip; and activities. There are two to three questions per category, with a total of 20 questions. Patients report the amount of difficulty they have in performing these activities: "without any difficulty", "with some difficulty", "with much difficulty", and "unable to do", with 0, 1, 2, or 3 points assigned, respectively. The overall HAQ-DI score is obtained by dividing the sum of the highest points of each category by 8 (range: 0-3 points).

Statistical analysis

Descriptive statistics were presented using median (range) and mean \pm standard deviations for continuous variables. Qualitative data were presented as frequencies and percentages. Repeated measures analysis of variance was used to evaluate the effects of resection arthroplasty of the forefoot on changes in foot-related function, disease activity, and disability. If the null hypothesis was rejected, the paired t-test was used to compare foot function, disease activity, and disability preoperatively and 1, 3, and 12 months after surgery. In this analysis, $P < 0.017$ (0.05/3) was considered to be statistically significant using the Bonferroni method. To investigate the correlations between foot function, disease activity, and disability, we analyzed the correlation between the extent of change preoperatively and 1, 3, and 12 months after surgery using Spearman's rank correlation coefficient. In this analysis, $P < 0.05$ was considered statistically significant.

Statistical analyses were performed using the PASW Statistics version 18 (IBM Co., Armonk, NY, USA) and SAS software version 8.2 (SAS Institute, Cary, NC).

RESULTS

Patient characteristics are presented in Table 1. Eleven patients (nine women and two men, with a mean age of 65.3 years) participated in the study. The mean BMI was 21.9 kg/m², and mean disease duration of RA was 20.3 years. Disease-modifying anti-rheumatic drugs (DMARDs) and non-steroidal anti-inflammatory drugs (NSAIDs) were prescribed in approximately 50% of patients. Methotrexate (90.9%) and corticosteroids (81.8%) were the most commonly prescribed drugs in the study group. Biologic drugs were prescribed in 27.3% of patients; tocilizumab (Actemra) was not licensed for use at the time of the study. There were no substantial changes in the prescribed drugs during 12 months after the surgery. Seven patients underwent bilateral forefoot resection arthroplasty; four patients underwent unilateral forefoot resection arthroplasty, of which, two had previously undergone a similar procedure on the contralateral foot.

Table 2 summarizes the values for FFI total and subscale scores (FFI pain, FFI disability, FFI limitation of activity) at each assessment stage. The scores for FFI total, FFI pain, FFI disability, and FFI limitation of activity scores for the affected foot showed significant improvements ($P < 0.001$, $P < 0.001$, $P < 0.001$, and $P = 0.002$, respectively). The differences in scores were significant in all but one pair when preoperative parameters were compared with those at 1, 3, and 12 months after surgery. The exception was the change in FFI limitation of activity score preoperatively and at 1 month after surgery.

The changes in DAS28-CRP and its subscales are presented in Table 3. There were significant improvements in DAS28-CRP,

Table 1. Clinical characteristics of patients with rheumatoid arthritis at baseline (n=11)

Characteristics	Value
Age (years) ^a	65.3±7.2 (51-72)
Sex (women/men) ^b	9/2
Body mass index (kg/m ²) ^a	21.9±2.1 (17.9-25.6)
Duration of disease (years) ^a	20.3±8.0 (5-33)
Medication (%) ^c	
NSAIDs	54.5
DMARDs	45.5
Methotrexate	90.9
Corticosteroid	81.8
Biologics	27.3 (tocilizumab=0)
Forefoot resection arthroplasty ^b	
Bilateral	7
Unilateral	4
History of prior arthroplasty (done/none)	2/2
CRP (mg/dl) ^a	0.53±0.53 (0.06-1.47)
FFI ^a	49.25±17.83 (23.40-76.90)
DAS28-CRP ^a	3.87±0.87 (2.68-5.03)
HAQ-DI ^a	1.28±0.68 (0-2.38)

NSAIDs, non-steroidal anti-inflammatory drugs ; DMARDs, disease-modifying antirheumatic drugs ; CRP, C-reactive protein ; FFI, foot function index ; DAS28, disease activity score in 28 joints ; HAQ-DI, health assessment questionnaire-disability index.

^amean± standard deviation (range).

^bnumber.

^cpercentage.

Table 2. Values of the FFI total and its subscale in patients with rheumatoid arthritis

Variable	Mean±SD	Median (range)	P-value	
			repeated measures ANOVA	paired t-test
FFI total			P< 0.001	
preoperative	49.25±17.83	53.76 (23.40-76.90)		
postoperative 1 month	28.80±11.11	35.04 (14.10-44.24)		P< 0.001
postoperative 3 months	18.83±9.26	15.33 (6.90-35.10)		P< 0.001
postoperative 12 months	16.87±19.15	11.70 (1.86-67.65)		P=0.001
FFI pain			P< 0.001	
preoperative	50.16±21.59	51.10 (13.71-86.10)		
postoperative 1 month	21.69±13.99	22.57 (0.71-48.57)		P< 0.001
postoperative 3 months	10.39±6.26	10.14 (1.88-26.29)		P< 0.001
postoperative 12 months	12.90±23.07	2.14 (0-74.30)		P=0.001
FFI disability			P< 0.001	
preoperative	57.48±23.50	56.67 (17.44-85.70)		
postoperative 1 month	38.58±14.28	42.00 (18.67-68.22)		P=0.002
postoperative 3 months	28.17±13.77	30.78 (8.89-53.11)		P=0.001
postoperative 12 months	22.25±20.83	18.00 (1.89-74.56)		P=0.003
FFI activity limitation			P=0.002	
preoperative	32.64±19.59	35.60 (0-54.00)		
postoperative 1 month	21.64±17.01	15.40 (0-45.80)		P=0.086
postoperative 3 months	14.18±13.13	13.80 (0-35.20)		P=0.007
postoperative 12 months	13.85±15.62	11.00 (0-47.20)		P=0.015

SD, standard deviation ; ANOVA, analysis of variance ; FFI, foot function index.

Table 3. Values of the DAS28-CRP and its subscale in patients with rheumatoid arthritis

Variable	Mean ± SD	Median (range)	P-value	
			repeated measures ANOVA	paired t-test
DAS28-CRP			<i>P</i> =0.033	
preoperative	3.87 ± 0.87	3.98 (2.68-5.03)		
postoperative 1 month	3.11 ± 1.04	3.28 (1.47-4.70)		<i>P</i> =0.006
postoperative 3 months	3.00 ± 1.31	2.97 (1.28-5.59)		<i>P</i> =0.011
postoperative 12 months	3.47 ± 0.86	3.43 (2.32-4.93)		<i>P</i> =0.202
PtGA			<i>P</i> =0.038	
preoperative	46.45 ± 30.91	47 (4-99)		
postoperative 1 month	25.36 ± 23.74	24 (0-77)		<i>P</i> =0.007
postoperative 3 months	28.18 ± 32.55	9 (0-92)		<i>P</i> =0.066
postoperative 12 months	34.18 ± 31.29	23 (4-99)		<i>P</i> =0.018
CRP			<i>P</i> =0.892	
preoperative	0.53 ± 0.53	0.22 (0.06-1.47)		
postoperative 1 month	0.52 ± 0.46	0.40 (0.03-1.22)		<i>P</i> =0.931
postoperative 3 months	0.42 ± 0.59	0.19 (0.06-1.97)		<i>P</i> =0.535
postoperative 12 months	0.58 ± 0.89	0.28 (0.06-3.13)		<i>P</i> =0.825
Tender joint counts			<i>P</i> =0.492	
preoperative	5.09 ± 3.36	5 (1-13)		
postoperative 1 month	3.45 ± 2.77	4 (0-9)		<i>P</i> =0.111
postoperative 3 months	4.00 ± 3.52	5 (0-10)		<i>P</i> =0.232
postoperative 12 months	4.73 ± 3.77	3 (1-12)		<i>P</i> =0.811
Swollen joint counts			<i>P</i> =0.008	
preoperative	3.64 ± 1.75	4 (1-6)		
postoperative 1 month	2.18 ± 1.66	3 (0-5)		<i>P</i> =0.002
postoperative 3 months	1.45 ± 1.44	1 (0-4)		<i>P</i> =0.002
postoperative 12 months	2.64 ± 1.96	3 (0-5)		<i>P</i> =0.153

SD, standard deviation ; ANOVA, analysis of variance ; DAS28-CRP, disease activity score in 28 joints -C-reactive protein ; PtGA, patient global assessment.

PtGA, and swollen joint counts ($P=0.033$, $P=0.038$, and $P=0.008$, respectively). However, the CRP and tender joint count did not improve significantly ($P=0.892$, and $P=0.492$, respectively). Compared with preoperative values, the postoperative parameters for DAS28-CRP at 1 and 3 months after surgery, PtGA at 1 month after surgery, and postoperative counts of swollen joints at 1 and 3 months after surgery were significantly improved.

The changes in HAQ-DI and HAQ-walking are shown in Table 4. There were no significant changes in HAQ-DI or HAQ-walking ($P=0.150$ and $P=0.597$, respectively).

Finally, we analyzed the correlation for changes in foot function, disease activity, and disability, at 1, 3, and 12 months after surgery compared with preoperative values, using Spearman's rank correlation coefficient. However, there was no significant correlation within any pairs (data not shown).

DISCUSSION

In this study, we investigated the relationship between foot function and changes in the disease activity and disability after resection arthroplasty of the forefoot. The total and all three subscales of foot function were significantly improved after surgery, which is consistent with results from previous studies (33, 34).

The DAS28 is the most widely used method for measuring disease activity in RA. As discussed previously, the inclusion of only 28 joints in DAS28 is controversial. A committee consisting of members of ACR/European League Against Rheumatism (EULAR)

analyzed the data of previous studies regarding the validity of joint counts (35). Its review showed that disease activity often persisted in the foot and foot joint even though patients were judged to be in remission on the basis of the 28 joint score. However, the PtGA was found to be a more reflective measurement of swelling and/or tenderness in the joints not covered by DAS28, as most patients had high scores for the PtGA (35-37). Additionally, our study results showed that the PtGA score improved significantly with improvement of foot function. Although a significant improvement was observed in relation to the number of swollen joints, no significant difference was observed in CRP level or in the number of tender joints after resection arthroplasty. The reason for the significant improvement in the number of swollen joints is unknown. However, our results highlight the importance of verifying changes in the subscales of DAS28. On the other hand, the reason for the lack of significant difference in CRP may be that the levels were rather low even before the surgery, and the amount of postoperative change was expected to be small.

Our results showed that there was no significant difference between pre- and postoperative scores for HAQ-DI and HAQ-walking. Aletaha *et al.* (38), studied the use of HAQ-DI for patients in remission from six clinical trials, and reported that disability in RA, as measured by HAQ-DI, is composed of reversible and irreversible components. As disability is affected by aging (39, 40), scores for HAQ-DI are worse in older patients. Longer disease duration is also associated with impaired foot function and a decrease in walking speed (41). Our study patients had a mean age of 65.3 years, and a long disease duration, mean of 20.3 years. Therefore,

Table 4. Values of the HAQ-DI and its subscale in patients with rheumatoid arthritis

Variable	Mean ± SD	Median (range)	P-value	
			repeated measures ANOVA	paired t-test
HAQ-DI			<i>P</i> =0.150	
preoperative	1.28 ± 0.68	1.38 (0-2.38)		
postoperative 1 month	1.18 ± 0.69	1.25 (0-2.50)		<i>P</i> =0.246
postoperative 3 months	0.99 ± 0.78	0.63 (0-2.38)		<i>P</i> =0.114
postoperative 12 months	1.20 ± 0.73	1.13 (0-2.38)		<i>P</i> =0.422
HAQ-walking			<i>P</i> =0.597	
preoperative	1.00 ± 0.63	1 (0-2)		
postoperative 1 month	1.09 ± 0.94	1 (0-3)		<i>P</i> =0.676
postoperative 3 months	0.82 ± 0.98	1 (0-3)		<i>P</i> =0.441
postoperative 12 months	0.82 ± 0.98	1 (0-3)		<i>P</i> =0.441

SD, standard deviation ; ANOVA, analysis of variance ; HAQ-DI, health assessment questionnaire -disability index.

we believe that improvements in disability were difficult to achieve because of the irreversible components. Additionally, we infer that improvement of foot function had little effect on disability because there is low coverage of lower limb function in the HAQ-DI. Wells *et al.* (42) showed that minimal differences in HAQ-DI, recognized as “somewhat better” by patients (minimal clinically important differences), was 0.22. Our data showed that the difference observed at 3 months postoperatively was only 0.29, and it can be assumed that the patients were not aware of any improvement in disability.

Forefoot involvement has been reported to occur in the early stages of RA following disease onset (10, 43, 44). Although involvement of the foot and ankle joint is common in patients with RA, it is rarely addressed as a clinical problem (45). Therefore, awareness of this involvement is important in order to maintain optimal foot function and prevent disability. Foot function should be evaluated regularly and any problems should be treated appropriately at an early stage. The purpose of treating the foot and foot joints in patients with RA is to provide pain relief and maintain the ability to walk (46).

The first limitation of the present study is that the number of cases was small. The second limitation is that the study included both patients who underwent bilateral surgery and those who underwent unilateral surgery. Because of small numbers, we did not present the results in the bilateral and unilateral surgery groups separately. However, the values of FFI total, FFI pain, FFI disability, FFI activity limitation, PtGA, HAQ-DI and HAQ-walking were somewhat lower in patients who underwent bilateral surgery, especially 12 months after the surgery. The third limitation is that HAQ-DI was not evaluated using the validated Japanese version. However, a strong correlation has been reported (47) between the original index used in the current study and the Japanese version of HAQ-DI ($r=0.993$) ; and we therefore believe that this limitation would have only a small effect on the results. One strength of this study is that patients were evaluated preoperatively and followed up for up to 12 months postoperatively, with a total of four evaluations within this period.

In conclusion, dysfunction of the foot improved significantly after resection arthroplasty of the forefoot, and this improvement had duration of 12 months postoperatively. Significant improvements were also demonstrated for DAS28-CRP, as a measure of disease activity, and its subscales, PtGA and swollen joint count. In comparison, HAQ-DI as a measure of disability and its subscale, HAQ-walking, did not show significant improvements.

CONFLICTS OF INTEREST

The authors declare that there are no conflicts of interest.

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