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Original Article

Radiographic factors associated with painful callosities after forefoot surgery in patients with rheumatoid arthritis

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ABSTRACT

Objectives: Operative procedures for rheumatoid forefoot deformities have gradually changed from arthrodesis or resection arthroplasty to joint-preserving surgery. Although joint-preserving arthroplasty has yielded good outcomes, painful plantar callosities may occur post-operatively. This study aimed to reveal the radiographic factors associated with painful callosities after joint-preserving surgery for forefoot deformities in patients with rheumatoid arthritis (RA).

Methods: We retrospectively evaluated 166 feet in 133 patients with RA who underwent forefoot joint-preserving arthroplasty, including proximal rotational closing-wedge osteotomies of the first metatarsal, between January 2012 and December 2015. Logistic regression analysis was performed with the objective variable set as the presence/absence of painful plantar callosities at the final observation and the explanatory variables set as several radiographic factors, including post-operative relative first metatarsal length (RML), amount of dorsal dislocation of the fifth metatarsal (5DD), and arc failure of the lesser toes.

Results: At the final follow-up, 42 of the 166 feet (25.3%) had painful callosities under the metatarsal heads post-operatively. Logistic regression analysis showed that the RML, 5DD, and lesser toes' arc failure were significantly associated with painful callosities.

Conclusions: We identified that RML, 5DD, and arc failure of the lesser toes were associated with painful plantar callosities after the surgery.

KEYWORDS: Examination; forefoot deformities; forefoot joint-preserving arthroplasty; osteotomy; post-operative painful callosities; rheumatoid arthritis

Introduction

Rheumatoid arthritis (RA) is a chronic inflammatory autoimmune disorder that damages multiple joints. Potent disease-modifying antirheumatic drugs (DMARDs), such as biologic DMARDs (bDMARDs) and targeted synthetic DMARDs, have greatly improved outcomes in RA. In a Japanese RA cohort, over 50% of the patients achieved clinical remission, while only 1.5% were classified as having high disease activity based on the disease activity score in 28 joints [1].

Foot symptoms are reported as the first signs of the disease in 20–53% of patients with RA [2–5], and painful foot deformities are prevalent in 80–90% of patients in the course of the disease [6]. When non-operative therapies for forefoot deformities fail, various operative procedures are considered [7–10]. Recently, operative procedures for rheumatoid forefoot deformities have gradually changed from arthrodesis or resection arthroplasty to joint-preserving surgery. Although joint-preserving arthroplasty has yielded good outcomes [10–12], painful plantar callosities may occur post-operatively [13, 14]. Therefore, we focused on painful plantar callosities as an assessment of post-operative outcomes.

There are some possible risks for painful plantar callosities after joint-preserving arthroplasty for the rheumatoid forefoot. The procedure often involves changing the length of the metatarsals. A large difference in the height of the second metatarsal head relative to the first might create new or residual callosities under the second metatarsal head [15–17]. Similarly, the occurrence of painful callosities is related to arc failure of the lesser toes that have no smooth curve with the second metatarsal head at the apex [16, 18, 19]. For rheumatoid forefoot arthroplasty, the recommended technique is to form a smooth curve, making the residual second metatarsal bone the longest, followed by the first, third, fourth, and fifth (the Lelievre formula; $1 < 2 > 3 > 4 > 5$) [20]. Dorsal dislocation of the distal fragment of the fifth metatarsal after metatarsal osteotomy can also lead to a transverse arch collapse, a potential risk factor for the occurrence of callosities [21, 22]. Increased first-fifth inter-metatarsal-angle (M1M5A) also leads to splay foot, resulting in transverse arch collapse [23]. An increased hallux valgus angle (HVA) and first-second inter-metatarsal angle (M1M2A), as well as the recurrence of dislocation/subluxation of the metatarsophalangeal (MTP)

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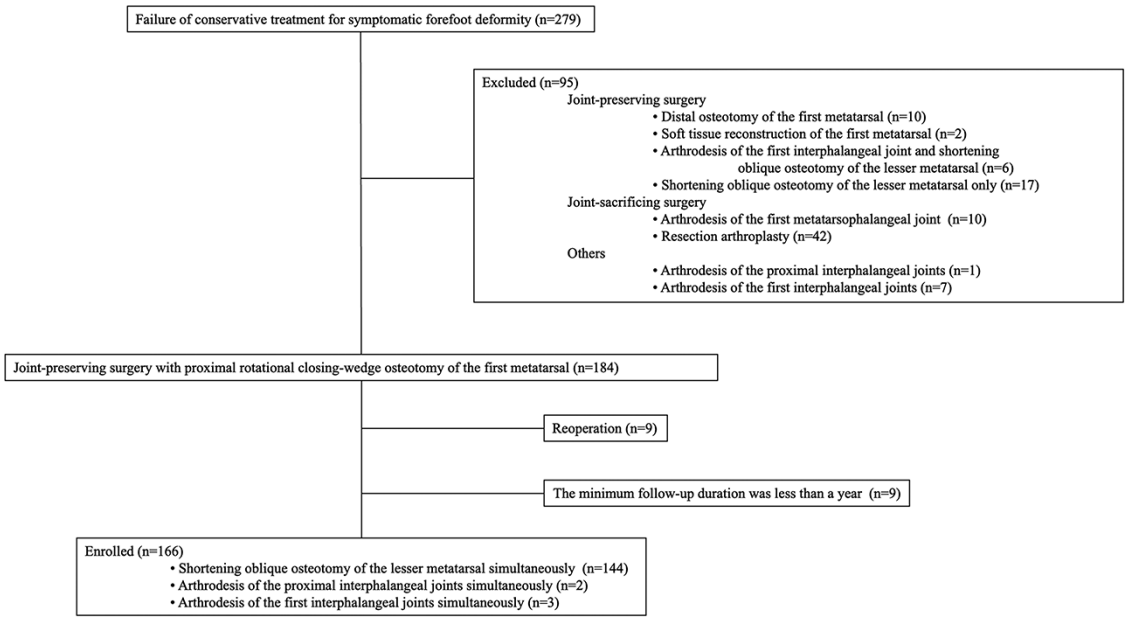

Figure 1. Flow diagram showing the enrolment process.

joints, are also risk factors for the occurrence of callosities post-operatively [14, 24, 25].

This study aimed to reveal the radiographic risk factors of painful callosities after joint-preserving surgery for forefoot deformities in patients with RA.

Patients and methods

This study was approved by our institutional review board (approval number: 3314-R2). In this retrospective study, we included 166 feet in 133 patients with RA who underwent forefoot joint-preserving arthroplasty (including proximal rotational closing-wedge osteotomies of the first metatarsal) from January 2012 to December 2015 (Figure 1) [11]. These patients had symptomatic hallux valgus (HV) treated by non-operative therapies with no previous operative intervention. The minimum follow-up duration of the patients included in this study was 1 year and the mean follow-up duration was 5.2 (range, 1.0–8.8) years. Simultaneously modified shortening oblique osteotomies of the lesser metatarsals were performed in 144 feet. In addition, arthrodesis of the interphalangeal joints of the hallux was performed simultaneously in 3 feet, and the Akin procedure for the first proximal phalanx was performed in 2 feet.

Information on the presence of painful plantar callosities under the metatarsal at the last follow-up was obtained from the patients' medical records. Information on patient demographics (i.e. age, sex, disease duration, disease activity score in 28 joints, prednisolone [PSL] use, PSL dose, methotrexate [MTX] use, MTX dose, bDMARDs use, the number of previously used bDMARDs, and complications of diabetes mellitus) was also obtained from the records.

Surgical technique

Joint-preserving surgery was performed and included a proximal rotational closing-wedge osteotomy of the first metatarsal and modified shortening oblique osteotomies of the lesser metatarsals, as previously reported [10, 12].

Radiographic evaluation

The HVA, M1M2A, and M1M5A were measured on standard full weightbearing anterior-posterior radiographs. Dislocation/subluxation of MTP joints were defined as displacement of the articular surfaces, either with partial joint surface-to-surface contact (subluxation) or without surface-to-surface contact (dislocation) visible on standard oblique or weightbearing lateral radiographs. The pre-operative MTP joint destruction was graded according to the Larsen system on a scale of 0 to V [26]. Relative first metatarsal length (RML) was measured on a standard full weightbearing anterior-posterior radiograph obtained pre-operatively, 3 months post-operatively and at the last follow-up. The RML was defined as the distance between the tops of the first and second metatarsal heads on a vertical line drawn perpendicular to the long axis of the second metatarsal (Figure 2) [17]. The smooth arc of the lesser toes was defined as a smooth curve connecting the second metatarsal head at the apex, followed by the third, fourth, and fifth ($2 > 3 > 4 > 5$) on a standard full weightbearing anterior-posterior radiograph. The lack of a smooth arc was defined as an arc failure of the lesser toes. The amount of dorsal dislocation of the fifth metatarsal (5DD) can be determined by comparing the distance from the centre of the metatarsal head from the dorsal margin of the metatarsal shaft (Figure 3). Since measuring 5DD on the weightbearing lateral foot radiograph could not identify the fifth metatarsal head due to an overlap with the other toes in flat feet, a standard oblique radiograph was used pre-operatively, 3 months post-operatively and at last follow-up. For the analysis of interobserver reliability, each radiograph was independently interpreted by two board-certified orthopaedic surgeons. For the analysis of intraobserver reliability, one orthopaedic surgeon resident interpreted twice. The observers did not have

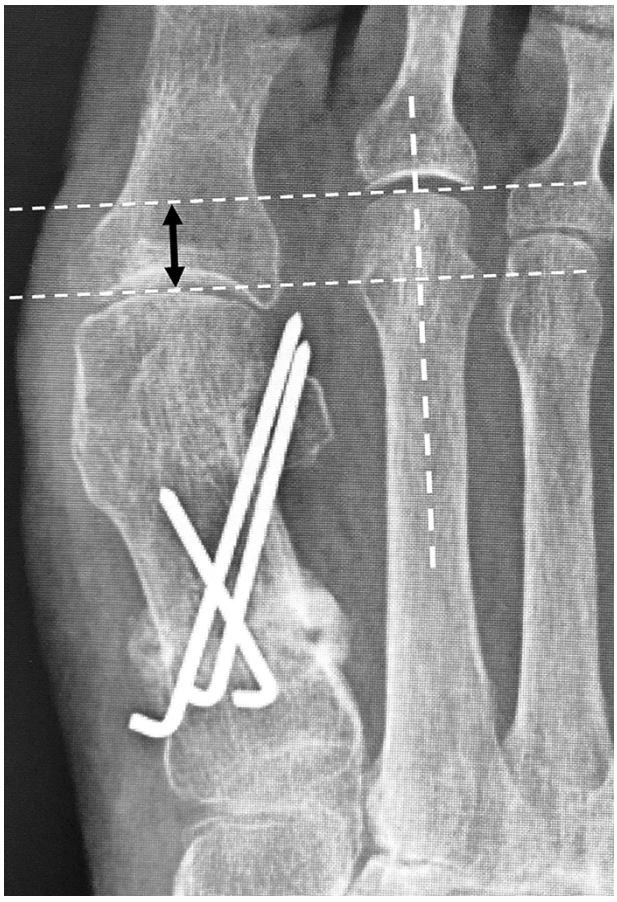

Figure 2. Measurement of the relative first metatarsal length (RML). RML (black arrow) was defined as the distance between the tops of the first and second metatarsal heads under a vertical line drawn perpendicular to the long axis of the second metatarsal. A negative index implied when the first metatarsal was shorter than the second and vice versa.

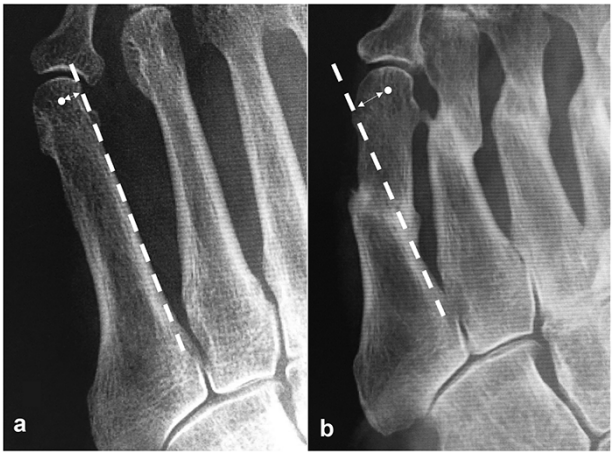

Figure 3. Measuring the amount of the dorsal dislocation of the fifth metatarsal (5DD). 5DD (white arrows) can be determined by comparing the distance from the centre of the metatarsal head (white dots) from the reference line (white dotted lines), dorsal margin of the metatarsal shaft, pre- (a) and post-operatively (b).

access to their own previous readings or those of the other observers.

Statistical analysis

A comparison of the 5DD with a standard oblique and a weightbearing lateral radiograph was made in patients in whom there was no difficulty identifying the fifth metatarsal head to evaluate the validity of using an oblique radiograph for the measurement. A correlation coefficient of 0.7 or higher was considered as a strong positive correlation. Correlation analysis was performed using the Pearson product–moment correlation coefficient. A logistic regression analysis was performed to determine the risks of painful plantar callosities at the final observation after forefoot surgeries. Dependent variables for the analysis were HVA, M1M2A, M1M5A, the recurrence of dislocation/subluxation of MTP joints, the RML, arc failure of the lesser toes, and 5DD. The Mann–Whitney U-test was performed to compare continuous variables, and the Fisher exact test was used to compare grouping variables that were significantly associated with the occurrence of painful plantar callosities in logistic regression analysis. A receiver operating characteristic (ROC) analysis was performed to determine the cut-off value of the occurrence of painful plantar callosities in possible predictors detected by logistic regression analysis. Interobserver and intraobserver correlation analysis was performed using the Spearman correlation coefficient. A post hoc power analysis was performed as needed. The level of statistical significance was set at $\alpha = .05$. The statistical analyses were performed using the R software package (https://www.r-project.org/).

Results

The demographic characteristics of the patients included in this study are shown in Table 1. At the final follow-up, 42 of the 166 feet (25.3%) had painful plantar callosities under the metatarsal heads after surgery. Some patients had multiple painful plantar callosities on a single foot. There were 12 feet with callosities under the first metatarsal head, 10 feet under the second metatarsal head, 22 feet under the third metatarsal head, 8 feet under the fourth metatarsal head, and 4 feet under the fifth metatarsal head, respectively. The HVA, M1M2A, and M1M5A significantly improved after surgery (Table 2). The recurrence of dislocation/subluxation of MTP joints was found in 25 feet (15.1%), and 16 of the 25 feet had no painful callosities. RML, 5DD, frequency of arc failure of the lesser toes, and dislocation/subluxation of MTP joints did not change significantly between the 3-month post-operative visit and the latest follow-up.

The fifth metatarsal head of 37 feet could be easily identified on weightbearing lateral radiographs. A strong positive linear relationship of the 5DD using lateral and oblique radiographs was observed in patients with a correlation coefficient of 0.84, confirming the validity of measuring 5DD using the oblique view (Figure 4).

Intraobserver correlation coefficients using the Spearman test for RML and 5DD were 0.951 and 0.978, respectively. Interobserver correlation coefficients for RML and 5DD were 0.935 and 0.886, respectively.

Logistic regression analysis showed that RML, 5DD, and arc failure of the lesser toes were significantly associated with the occurrence of painful plantar callosities, while HVA, M1M2A, M1M5A, and the recurrence of dislocation/subluxation of MTP joints were not (Table 3).

Table 1. Characteristics of the included patients ($n = 166$).

Age, years, median (IQR)	68.0 (58.3, 72)
Female sex, *n* (%)	163 (98.1)
Disease duration, years, median (IQR)	23.0 (17.0, 28.0)
DAS28-ESR, median (IQR)	3.0 (2.2, 3.8)
PSL use, *n* (%)	65 (39.2)
PSL dose, mg/day, median (IQR)	0 (0, 3.0)
MTX use, *n* (%)	106 (63.9)
MTX dose, mg/week, median (IQR)	8.0 (0, 10.0)
Biologic DMARDs use, *n* (%)	43 (25.9)
Biologic DMARDs, *n*	IFX: 8, ETN: 22, ADA: 2, GLM: 2, TCZ: 4, ABT: 3, CZP: 2
Complications of diabetes mellitus, *n* (%)	4 (2.4)
Larsen grade of the first and fifth MTP joints, *n*	First, 0: 0, I: 9, II: 77, III: 68, IV: 12, V: 0 Fifth, 0: 0, I: 54, II: 57, III: 43, IV: 12, V: 0

Abbreviations: IQR, interquartile range; DAS28, disease activity score using 28 joint counts; ESR, erythrocyte sedimentation rate; PSL, prednisolone; MTX, methotrexate; DMARD, disease-modifying antirheumatic drug; IFX, infliximab; ETN, etanercept; ADA, adalimumab; GLM, golimumab; TCZ, tocilizumab; ABT, abatacept; CZP, certolizumab pegol; MTP, metatarsophalangeal.

The median RML in 42 feet with painful callosities was −4.48 mm (interquartile range [IQR]: −2.88, −6.46), while that in 124 feet without painful callosities was −2.13 mm (IQR: −0.65, −4.0), indicating a significant association ($p < .01$, Figure 5). The ROC analysis showed that the cut-off values for the RML in the occurrence of painful plantar callosities was −3.42 mm, with a sensitivity of 66.7%, a specificity of 67.7%, and an area under curve (AUC) of 0.69 (Figure 6).

A subgroup analysis was undertaken using the patients who had undergone modified shortening oblique osteotomies of the fifth metatarsal ($n = 98$) to evaluate 5DD as a risk factor for post-operative callosities. The 5DD in 19 feet with painful callosities was 7.19 mm (IQR: 3.87, 8.61), while that in 79 feet without painful callosities was 1.66 mm (IQR: 0.10, 5.76), indicating a significant association ($p < .01$, Figure 7). The ROC analysis showed that the cut-off value for the 5DD in the occurrence of painful plantar callosities was 5.74 mm, with a sensitivity of 68.4%, a specificity of 74.7%, and an AUC of 0.80 (Figure 8).

Arc failure of the lesser toes was found in 19 feet (11.4%), and 12 of the 19 feet had painful callosities, while only 30 feet had painful callosities in 147 feet without arc failure of the lesser toes ($P < 0.01$).

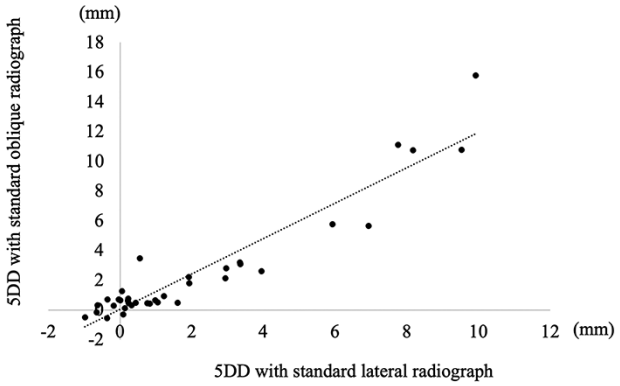

Figure 4. Correlation between dorsal dislocation of the fifth metatarsal (5DDs) using oblique and weight-bearing lateral radiographs. 5DD was measured in the 37 feet in which the fifth metatarsal could be identified by standard lateral and oblique radiographs pre- and post-operatively. It showed a strong positive correlation with a correlation coefficient of 0.84 ($y = 1.19x + 0.03$).

Discussion

We examined the radiographic factors associated with painful callosities after joint-preserving surgery for forefoot deformities in patients with RA. As a result, we identified that RML, 5DD, and arc failure of the lesser toes were associated with painful callosities after surgery.

Excessive shortening of the first metatarsal was a reported risk factor for post-operative callosities [15, 17, 27, 28]. Additional shortening of the lesser toes has been recommended when excessive shortening of the first metatarsal was needed to repair HV. The adequate RML was previously reported to be ≥−3 mm to avoid post-operative metatarsalgia, while our cut-off value was −3.42 mm [17]. These data suggest that an excessive decrease in the RML may be associated with painful plantar callosities after surgery.

The coronal position of the metatarsal head is important when considering callosity formation, and collapse of the anterior transverse arch is considered a risk factor for the occurrence of callosities [21, 22, 29]. We especially focused on the fifth metatarsal head, which is the cornerstone for the transverse arch. The 5DD was measured by standard oblique radiographs, and the validity was confirmed with standard lateral radiographs. Although the association with 5DD and

Table 2. The pre- and post-operative radiographic data ($n = 166$).

	Pre-operative	3 months post-operatively	Latest follow-up
RML, mm	−2.17 (−0.86, −3.76)	−2.45 (−0.86, −4.23)	−2.82 (−0.82, −4.89)
5DD, mm[a]	0	3.32 (0.54, 6.41)	3.20 (0.47, 6.46)
Arc failure of the lesser toes, *n* (%)	0 (0.0)	18 (10.8)	19 (11.4)
HVA, degree, median (IQR)	46.7 (37.7, 53.9)	15.6 (8.9, 22.3)	17.3 (9.7, 24.9)
M1M2A, degree, median (IQR)	15.9 (12.8, 18.7)	7.0 (3.5, 10.4)	7.3 (3.9, 10.9)
M1M5A, degree, median (IQR)	35.3 (30.4, 40.1)	21.6 (16.9, 25.4)	22.4 (17.4, 26.7)
Dislocation/subluxation of MTP joints, *n* (%)	119 (71.7)	14 (8.4)	25 (15.1)

[a]Limited to the patients who were treated with oblique osteotomies of the fifth metatarsal ($n = 98$).
Abbreviations: RML, the relative first metatarsal length; 5DD, the amount of the dorsal dislocation of the fifth metatarsal; HVA, hallux valgus angle; IQR, interquartile range; M1M2A, first/second inter-metatarsal angle; M1M5A, first/fifth inter-metatarsal-angle; MTP; metatarsophalangeal.

Table 3. Logistic regression analysis of post-operative painful callosities.

	Standardized regression coefficients	Odds ratio (95% CI)	*p*
RML, mm	−1.16	0.72 (0.62, 0.84)	<.01
5DD, mm	0.84	1.31 (1.13, 1.50)	<.01
Arc failure of the lesser toes	0.93	18.22 (5.10, 65.01)	<.01
HVA, degree	0.16	1.01 (0.97, 1.06)	.52
M1M2A, degree	−0.25	0.95 (0.85, 1.06)	.34
M1M5A, degree	0.22	1.03 (0.96, 1.11)	.43
Dislocation/ subluxation of MTP joints	0.13	1.43 (0.50, 4.14)	.51

Abbreviations: CI, confidence interval; RML, the relative first metatarsal length; 5DD, the amount of the dorsal dislocation of the fifth metatarsal; HVA, hallux valgus angle; M1M2A, first/second inter-metatarsal angle; M1M5A, first/fifth inter-metatarsal-angle; MTP, metatarsophalangeal.

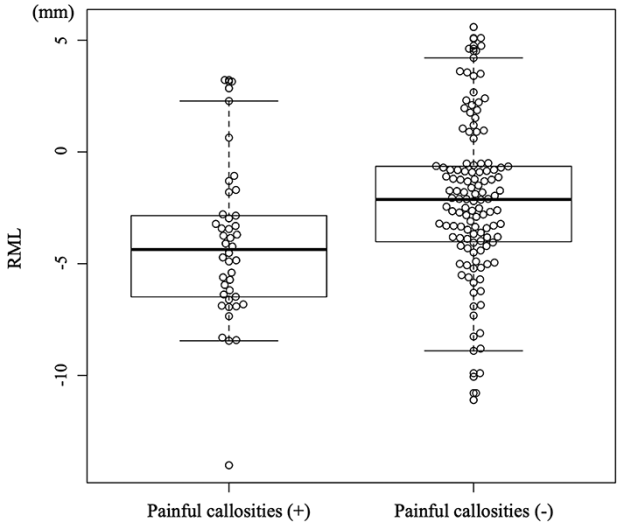

Figure 5. Association between the relative first metatarsal length (RML) and the occurrence of painful callosities. The median values of the RML in patients with painful plantar callosities (−4.48 mm, $n = 42$) was significantly higher than that in patients without plantar callosities (−2.13 mm, $n = 124$) ($p < .01$).

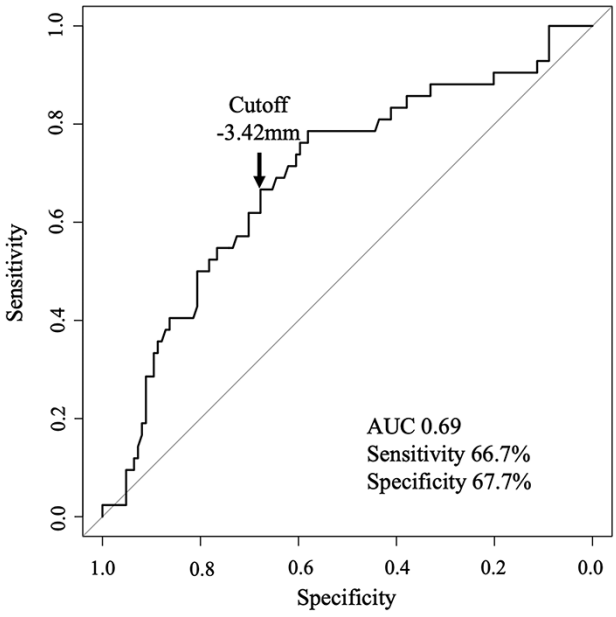

Figure 6. The cut-off value of relative first metatarsal length (RML) for the occurrence of painful callosities. Receiver operating characteristic analysis showed that the cut-off values of the RML for the occurrence of painful plantar callosities was −3.42 mm, with a sensitivity of 66.7%, a specificity of 67.7%, and an area under the curve (AUC) of 0.69.

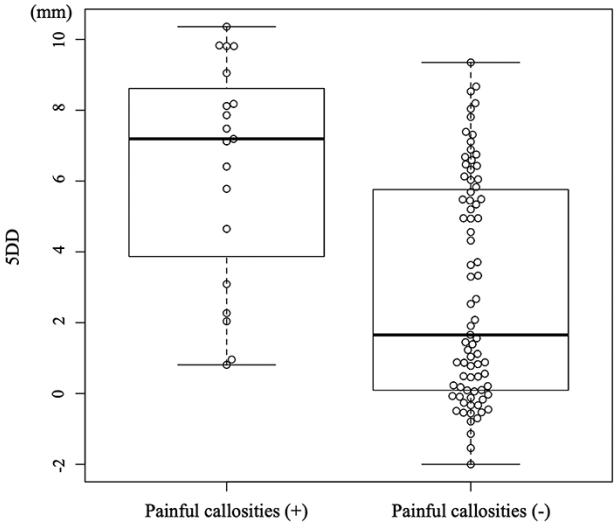

Figure 7. Association between the dorsal dislocation of the fifth metatarsal (5DD) and the occurrence of painful callosities. The median values of the 5DD in patients with plantar callosities (7.19 mm, $n = 19$ feet) were significantly higher than those in patients without plantar callosities (1.66 mm, $n = 79$ feet) ($p < .01$).

the post-operative painful callosities has not been reported in past studies, the present results showed that the presence of painful callosities was associated with large 5DD in standard oblique radiographs.

Arc failure of the lesser toes is due to relative metatarsal length disorders. Excessive shortening of the lesser metatarsal is also a risk factor for transfer painful callosities [16, 18, 19, 30]. Increased weight bearing under the prominent metatarsal head due to a relative metatarsal length disorder might be a risk factor for the occurrence of painful callosities. In this study, arc failure of the lesser toes after joint-preserving surgery was significantly associated with painful callosities, indicating that metatarsal head positioning of the lesser toes requires careful consideration.

Post-operative HVA, M1M2A, and M1M5A are common measures to evaluate forefoot deformity. Previous reports have indicated that painful plantar callosities were improved by HV correction with or without lesser metatarsal osteotomy. When HV is corrected after surgery, the alignment of the first metatarsal is restored, and the plantar flexion force is improved. Therefore, the correction decreases pressure to the lesser metatarsal heads during walking and improves painful plantar callosities [3, 13, 25, 31]. We investigated the association of these endpoints with post-operative callosity formation; however, we could not find any significant differences. Since each of the angles improved significantly after surgery, the risk for painful callosities due to the abnormal angles may not have been evaluated correctly in the study population.

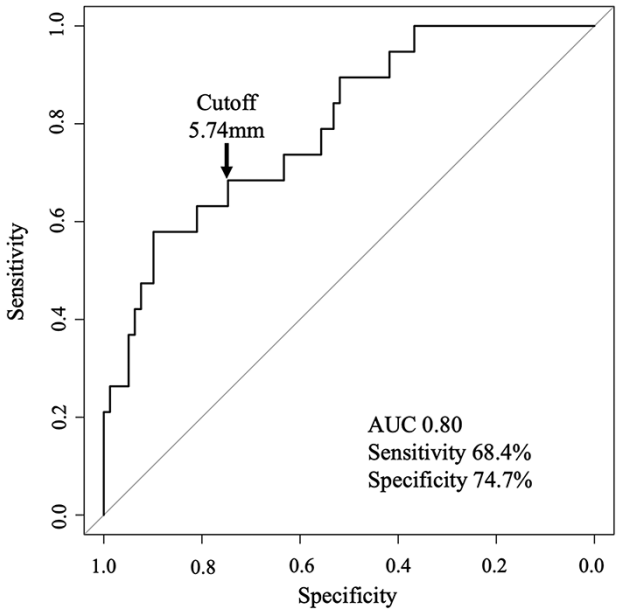

Figure 8. The cut-off value of dorsal dislocation of the fifth metatarsal (5DD) for the occurrence of painful callosities. Receiver operating characteristic analysis showed that the cut-off value of the dorsal dislocation of the 5DD for the occurrence of painful plantar callosities was 5.74 mm, with a sensitivity of 68.4%, a specificity of 74.7%, and an area under the curve (AUC) of 0.80.

Although the recurrence of dislocation/subluxation of MTP joints could be a risk for post-operative painful callosities, we could not detect any significance. If the recurrence of dislocation/subluxation of the MTP joints was a rare event, large sample sizes would be needed to obtain enough statistical power. However, out of 166 feet, there were 25 feet with recurrent dislocation/subluxation of the MTP joints. A post hoc power analysis revealed that having sample sizes of 25 in patients with recurrent dislocation/subluxation and 141 in patients without it achieved 95.8% power to detect an effect size of 0.8 ($\alpha = .05$). One of the possible reasons for this was that the severity of dislocation/subluxation of the MTP joints after surgery in the studied population was not high enough to detect a risk of painful callosities.

This study has some limitations. First, because the study design was retrospective, we could not obtain all relevant clinical and radiographic data from the study patients. Second, because the purpose of the study was to reveal the risks for post-operative painful callosities after joint-preserving surgery for rheumatoid forefoot deformity, we did not focus on the position of painful callosities and the relationship of the possible risks for them. Sub-analysis is needed for a more precise evaluation of each risk factor on each position of the callosities. For example, RML could be a risk factor for the painful plantar callosities under the second metatarsal head and 5DD could be a risk factor for the callosities under the fourth or third metatarsal head. Third, since it was difficult to obtain pre- and post-operative computed tomography data in most patients in the retrospective study, we used standard oblique radiographs to measure 5DD. However, we showed a strong positive linear relationship of the 5DDs measured by lateral and oblique radiographs. Fourth, the dorsal dislocation of the metatarsal heads after oblique osteotomy of the fifth metatarsal would have been better assessed on weightbearing radiographs. However, since measuring 5DD on the weightbearing lateral foot radiograph could not identify the fifth metatarsal head due to an overlap with other toes in flat feet, 5DD was measured on a standard non-weightbearing oblique radiograph in this study. Fifth, although the axial plane was evaluated by RML and arc failure of the lesser toes, the coronal plane was only evaluated by 5DD. In particular, the first metatarsal, which is important for the transverse arch, was not evaluated. This is due to the difficulty in measuring first metatarsal dorsal dislocation on the weightbearing lateral foot radiograph since there is overlapping of the first metatarsal head and other toes. Furthermore, unlike the 5DD, the proximal fragment of the first metatarsal was too small to detect the post-operative proximal reference line with a standard oblique radiograph, resulting in low reproducibility of the measurement. Future studies would benefit from more rigorous study designs using computed tomography to further elucidate the risks for post-operative painful callosities after joint-preserving surgery for rheumatoid forefoot deformity. Sixth, the timing of the final follow-up was not at a fixed time point but was at the most recent follow-up. As the duration of follow-up of the patients after surgery ranged from 1.0 to 8.8 years, the radiographic factors that we tested may have deteriorated over time, unrelated to the success of the treatment. However, radiographic factors, including RML, 5DD, and arc failure of the lesser toes were not significantly different between the 3-month post-operative visit and the most recent follow-up. Seventh, as we did not collect data on disease activity of RA and medication use during the follow-up period, we were unable to evaluate the effect of disease activity or medication on radiographic deterioration.

We detected the RML, 5DD, and arc failure of the lesser toes as significant risk factors for post-operative painful callosities after joint-preserving surgery for rheumatoid forefoot deformity. It is necessary to maintain an RML within the standard range, maintain the arc of the lesser toes, and prevent 5DD to reduce the occurrence of post-operative painful callosities. Consideration of our findings while performing surgery may reduce the occurrence of painful callosities and greatly improve post-operative patient satisfaction.

Conflict of interest

K.Y. has received speakers bureau and consulting fee from Eisai, AbbVie, Astellas, Mochida, Bristol-Meyers, Chugai, Janssen Pharmaceutical, Pfizer, Tanabe-Mitsubishi, Asahi-Kasei, and Gilead. K.I. has received speakers bureau and consulting fee from AbbVie, Astellas, Ayumi, Bristol-Meyers, Chugai, Daiichi Sankyo, Janssen Pharmaceutical, Lilly, Pfizer, Takeda, Tanabe-Mitsubishi, and UCB. Division of Multidisciplinary Management of Rheumatic Diseases is an endowment department supported with an unrestricted grant from Ayumi Pharmaceutical Corporation, Chugai Pharmaceutical Co., Ltd., Mitsubishi Tanabe Pharma Co., Mochida Pharmaceutical Co., Ltd., Nippon Kayaku Co., Ltd., and Teijin Pharma Ltd. Division of Multidisciplinary Management of Rheumatic Diseases is an endowment department supported with an unrestricted grant from Ayumi Pharmaceutical Corporation, Chugai Pharmaceutical Co., Ltd., Mitsubishi Tanabe Pharma Co., Mochida Pharmaceutical Co., Ltd., Nippon Kayaku

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