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Concise report

Anatomical location of erosions at the metatarsophalangeal joints in patients with rheumatoid arthritis

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Abstract

Objective. The aim of this study was to identify the anatomical location of erosions at the MTP joints in patients with RA using high-resolution 3T MRI.

Methods. In 24 patients with RA, the more symptomatic forefoot was imaged using 3T MRI. T1-weighted, intermediate-weighted and T2-weighted fat-suppressed sequences were acquired through the MTP joints, together with three-dimensional volumetric interpolated breath-hold examination (3D VIBE) and T1-weighted fat-suppressed post-gadolinium contrast sequences. Images were scored for bone erosion in the distal and proximal part of the MTP joints using the RA MRI scoring (RAMRIS) system. The base of the proximal phalanx and the head of the metatarsal were divided into quadrants to determine the location of erosions (octants) in the dorsal-medial, dorsal-lateral, plantar-medial and plantar-lateral regions.

Results. Seventeen females and seven males with a mean age of 55.5 years and disease duration of 10.6 years (range 0.6–36) were included. Eighteen patients were RF positive, the mean 44-joint DAS for CRP and ESR ($DAS44_{CRP}$ and $DAS44_{ESR}$) were 2.5 (S.D. 0.8) and 2.6 (S.D. 0.9), respectively. In this cohort of patients with RA, irrespective of MTP joint location, octants located in the proximal part (metatarsal) of the joint and the plantar aspect of the joint were more eroded.

Conclusion. This is the first study to report the anatomical location of erosions at the MTP joints in patients with RA. We noted that erosions were more commonly seen on the plantar aspect of the metatarsal head in RA, supporting the hypothesis of a relationship between biomechanical demands and bone changes in the forefoot.

Key words: rheumatoid arthritis, erosion, metatarsophalangeal joint, magnetic resonance imaging, RAMRIS.

CLINICAL SIENCE

Introduction

The forefoot is described as the most common site for symptoms in the foot and ankle of patients with RA [1, 2]. The majority of forefoot pain and the most common site of erosions in the forefoot is at the MTP joints in RA [3, 4]. Bone erosions have been identified as a key component in the destructive process in RA. Imaging techniques to identify erosions are discussed in the background section of the supplementary material, available at *Rheumatology* Online.

Previous studies have observed that erosion-prone sites at the MCP joints in the hands are subject to bony compression from overlying collateral ligaments, suggesting that local anatomic and biomechanical factors may be important in the pathogenesis of early RA [5]. Pressure under the forefoot in patients with RA is significantly increased compared with normal subjects [6]. Deformities of the forefoot and rearfoot have been reported to accentuate forefoot pressures [7]. Subluxation

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and eventually dislocation of the MTP joints occurs in RA as a result of synovitis. The plantar fat pad, which usually lies beneath the MTP joints, is pulled distally, exposing the metatarsal heads to increased pressure. Increased medial forefoot loading has also been detected in RA patients with the typical pes planovalgus deformity. Forefoot peak pressures have been reported to correlate with pain, damage and higher erosion scores at the MTP joints [8–10]. Recent reports have identified damage occurring within the plantar structures, such as the capsule and plantar plate, of the MTP joints in the painful forefoot of patients with RA. This damage has been associated with bone erosion and higher peak plantar pressures, suggesting that altered foot biomechanics or local mechanical effects due to capsule or plantar plate abnormalities may contribute to bone changes [11, 12].

While a tendency towards a radial (lateral) distribution has been noted in the MCP joints in the hands [5] and an ulnar and dorsal distribution in the wrist [13], the location of erosions at the MTP joints has not been reported previously in patients with RA. This exploratory study hypothesized that the majority of erosions at the MTP joints in patients with RA are on the plantar aspect, possibly relating to biomechanical demands in the foot.

Methods

Recruitment of participants

Ethics approval was received from the Leeds (West) Research Ethics Committee and written consent, according to the Declaration of Helsinki, was obtained from all participants. Consecutive patients diagnosed with RA and presenting to the specialist rheumatology foot clinic at Chapel Allerton Hospital with forefoot plantar MTP joint pain were invited to take part in the study. Patients were excluded if they had a diagnosis of multiple morbidities, including diabetes, peripheral vascular disease and other inflammatory arthropathies, a history of forefoot surgery or contraindications to having an MRI or i.v. contrast.

Imaging

The more symptomatic forefoot was imaged using a 3T Verio scanner (Siemens Healthcare, Erlangen, Germany); MRI acquisition protocols (Methods section) and images are provided as supplementary material and Figs S1–S4, available at *Rheumatology* Online. Images were scored for bone erosion at each MTP joint using the RA MRI scoring (RAMRIS) system defined by the OMERACT group [14]. MRI bone erosion is defined as a sharply marginated bone lesion, with correct juxta-articular localisation, which is visible in two planes with a cortical break seen in at least one plane.

The base of the proximal phalanx and the head of the metatarsal (1 cm from the articular surface) were divided into quadrants to determine the location of erosions in the dorsal-medial, dorsal-lateral, plantar-medial and plantar-lateral regions. MRIs were read by two experienced consultant musculoskeletal radiologists (R.J.H. and A.J.G.) and consensus was reached for the RAMRIS system score and the location of erosions was determined by an experienced consultant rheumatologist (P.S.H.). Standard antero-posterior radiographs were taken to identify the severity of RA at each lesser MTP joint using the Larsen method [15].

Statistical analysis

To investigate the associations between the location of erosions at the MTP joints in patients with RA, the primary unit was an octant; eight RAMRIS system scores were recorded in each of the five MTP joints per patient [dorsal–medial, dorsal–lateral, plantar–medial and plantar–lateral for both the proximal (metatarsal) and distal (phalanx) aspect of the joint]. This was therefore considered a three-level, cross-sectional, multilevel model with the patient at level 3, the MTP joint at level 2 and the octant at level 1. A full explanation of the multilevel model is provided in the Methods section of the supplementary material, available at *Rheumatology* Online.

Results

Demographic and disease characteristics

Twenty-four consecutive patients with RA [17 females and 7 males with a mean age of 55.5 years (S.D. 10.5) and disease duration of 10.6 years (S.D. 8.6) (range 0.6–36)] participated in the study. Eighteen of the 24 patients were RF positive, the mean 44-joint DAS using CRP or ESR ($DAS44_{CRP}$ and $DAS44_{ESR}$) were 2.5 (S.D. 0.8) and 2.6 (S.D. 0.9), respectively. Twenty-three (96%) patients were taking a DMARD, 15 patients (63%) were taking a biologic therapy and one patient was taking oral corticosteroids. The mean 100-mm visual analogue scale (VAS) forefoot pain score was 43.4 (S.D. 27.9). The median Larsen score at the MTP joints was 0.0 [interquartile range (IQR) 0.0–1.0] at the first MTP joint, 1.0 (0.0–1.75) at the second MTP joint, 1.0 (0.0–3.0) at the third MTP joint, 1.0 (0.0–2.75) at the fourth MTP joint and 1.0 (0.25–2.75) at the fifth MTP joint.

Barefoot peak plantar pressures (in kilopascals) were measured at each MTP joint using the emed pressure platform system (Novel, Munich Germany). The mean peak pressure was 581.5 kPa (S.D. 379.6) at the first MTP joint, 651.5 (311.1) at the second MTP joint, 644.4 (282.0) at the third MTP joint, 334.3 (202.4) at the fourth MTP joint and 355.2 (242.0) at the fifth MTP joint.

Erosions on MRI

In total, 120 MTP joints were examined by MRI. MRI data are missing for the third MTP joint in one patient, as it was not possible to visualize the joint. Bone erosion, scored using the RAMRIS system, was reported proximally (metatarsal) in 85 MTP joints (first MTP joint $n = 19$, second MTP joint $n = 16$, third MTP joint $n = 17$, fourth MTP joint $n = 14$, fifth MTP joint $n = 19$) and distally (proximal phalanx) in 57 MTP joints (first MTP joint $n = 13$, second MTP joint $n = 11$, third MTP joint $n = 11$, fourth MTP joint $n = 10$, fifth MTP joint $n = 12$).

The locations of erosions at the MTP joints in patients with RA are shown in Table 1. The majority of erosions

TABLE 1 Location of erosions at the MTP joints in RA

	Location of erosions (quadrants)			
	Dorsal-medial	Dorsal-lateral	Plantar-medial	Plantar-lateral
First proximal phalanx	7	3	5	7
First metatarsal	6	4	13	19
Second proximal phalanx	0	1	5	8
Second metatarsal	6	5	9	6
Third proximal phalanx	1	1	6	6
Third metatarsal	3	4	10	8
Fourth proximal phalanx	1	1	6	6
Fourth metatarsal	6	3	12	6
Fifth proximal phalanx	2	4	9	5
Fifth metatarsal	10	11	14	14
Total	42	37	89	75

TABLE 2 Results of the two-way interaction model: coefficients of fixed effects and covariance parameters

Parameter	Coefficient (95% CI)	Significance
Intercept	1.56 (1.19, 1.93)	$t = 8.38$, $P < 0.001$
MTP 1	−0.93 (−1.39, −0.46)	$t = -3.95$, $P < 0.001$
MTP 2	−0.89 (−1.35, −0.42)	$t = -3.78$, $P < 0.001$
MTP 3	−0.65 (−1.12, −0.19)	$t = -2.79$, $P = 0.006$
MTP 4	−0.59 (−1.06, −0.13)	$t = -2.53$, $P = 0.012$
Distal	−1.10 (−1.33, −0.88)	$t = -9.80$, $P < 0.001$
Dorsal	−0.27 (−0.49, −0.05)	$t = -2.41$, $P = 0.016$
Medial	0.06 (−0.03, 0.16)	$t = 1.29$, $P = 0.199$
MTP 1[a] distal	0.85 (0.54, 1.17)	$t = 5.36$, $P < 0.001$
MTP 2[a] distal	0.75 (0.44, 1.06)	$t = 4.71$, $P < 0.001$
MTP 3[a] distal	0.78 (0.46, 1.10)	$t = 4.85$, $P < 0.001$
MTP 4[a] distal	0.60 (0.29, 0.92)	$t = 3.79$, $P < 0.001$
MTP 1[a] dorsal	0.02 (−0.29, 0.33)	$t = 0.13$, $P = 0.896$
MTP 2[a] dorsal	−0.02 (−0.33, 0.29)	$t = -0.13$, $P = 0.896$
MTP 3[a] dorsal	−0.36 (−0.67, −0.04)	$t = -2.23$, $P = 0.026$
MTP 4[a] dorsal	−0.19 (−0.50, 0.13)	$t = -1.18$, $P = 0.239$
Residual	0.61 (0.55, 0.67)	$Z = 20.45$, $P < 0.001$
Within-patient variance	0.16 (0.06, 0.41)	$Z = 2.07$, $P = 0.038$
Within-joint variance	0.43 (0.31, 0.60)	$Z = 5.88$, $P < 0.001$

[a]Interaction. *Z*: Wald test.

(169/243) were seen in the plantar two quadrants of the MTP joints. To identify patterns in the anatomical location of erosions we created a multilevel linear model in which the octant RAMRIS system score was the dependent variable; the model included three factors that specified the location of the octant within the MTP joint and one that specified the MTP joint in which the octant was located. A three-level structure was specified, which accounted for the clustering of octants within MTP joints and MTP joints within patients. The results are displayed in Table 2 relative to the fifth MTP joint, which was used as the reference as it was the most commonly reported site for erosions. The fixed effects results indicated that the first to fourth MTP joints had lower RAMRIS system scores than the fifth MTP joint and that scores were higher in the proximal (metatarsal) ($P < 0.001$) and plantar ($P = 0.016$) aspects of the joint. However, the extent of the differences between octants located proximally or distally, and between those in dorsal or plantar locations, differed depending on the MTP joint position, and vice versa. The largest differences between the proximal and distal joint aspects occurred in the fifth MTP joint, whereas the largest differences between the dorsal and plantar aspects occurred in the third and fourth MTP joints. A full explanation of the interactions is provided in the results section of the supplementary material, available at *Rheumatology* Online.

Discussion

This is the first study to report the anatomical location of erosions at the MTP joints in patients with RA presenting with forefoot pain. Octants in the proximal (metatarsal) and plantar aspects of the MTP joint were most eroded in this cohort of patients with RA, supporting the study hypothesis of a relationship between biomechanical demands and bone changes. Erosions at the MTP joints did not show the predilection for a lateral joint distribution seen in the MCP joints of the hands (radial side of the MCP joint) or the dorsal, ulnar distribution reported in the wrist in RA. Previous small studies, which compared patients with early RA with healthy control subjects, have observed that erosion-prone sites at the MCP joints in the hands are subject to bony compression from collateral ligaments, and suggest that local anatomic and biomechanical factors may be important in the pathogenesis of early RA [5, 16]. Evidence from this current study and previous foot studies suggest that both anatomical and biomechanical factors may be associated with erosion sites at the MTP joints in RA [10, 17].

There is contradictory evidence to suggest that higher erosion scores at the MTP joints are associated with higher peak pressure values in the forefoot of patients with RA. Tuna *et al*. [10] reported that both the highest peak pressure value and highest erosion score in the forefoot were seen at the fifth MTP joint. However, the fifth MTP joint is typically exposed to lower mechanical loads than the second MTP joint in RA [7, 8], as reported in this study. Recent evidence has identified damage to plantar structures, such as the capsule and plantar plate, of the MTP joints to be more common at the fifth MTP joint in the painful forefoot of patients with RA [11, 12]. Damage to these plantar structures has been associated with bone erosion and higher peak plantar pressures, suggesting that altered biomechanics or mechanical effects due to capsule or plantar plate abnormalities may cause bone changes [11, 12]. In this cohort of patients the proximal (metatarsal) part of the joint and the plantar aspect of the joint were more eroded. Anatomically the plantar plate is attached loosely to the plantar aspect of the metatarsal shaft, proposing a relationship between the anatomical location of the plantar plate and bone changes in the MTP joints in RA, which may subsequently lead to biomechanical changes and forefoot pain in patients with RA.

Despite including the MTP joints in the disease activity assessment (DAS44), patients in this study were considered to have low disease activity. There appears to be a discrepancy between clinically reported symptoms in the feet and overall disease activity. These findings are consistent with recent evidence that highlights the presence of tender and swollen MTP joints despite disease remission [18], which may have the potential to drive local disease progression and damage, particularly in the presence of contributing mechanical factors.

The primary limitation of this exploratory observational study was the small sample size ($n = 24$). Furthermore, the range of disease duration was wide (0.6–36 years) and patients predominantly had non-active RA. Further studies would benefit from differentiating between patients with active disease and those in disease remission, and determining the duration and morphology of erosions, particularly in light of 15 of the patients in the sample receiving biologic therapies.

The evidence from this study suggests that both inflammatory and mechanical factors have a role to play in determining the severity of pathology at the MTP joints in patients with RA. Conservative strategies to manage foot disease in patients with RA include therapies to target inflammatory disease, such as steroid injections, as well as mechanical therapies such as foot orthoses and footwear. It has been recognized that residual disease can be present in the feet of patients with RA otherwise deemed to be in clinical remission, putting patients at risk of ongoing damage particularly when assessments of the feet are not undertaken [19]. Therapies should be aimed at detecting early inflammatory foot disease and targeting therapy to prevent progression of disease severity (erosions), which ultimately results in forefoot pathology. A recent systematic review of foot orthoses for RA concluded that the current evidence suggests that custom orthoses are beneficial for the treatment of pain and elevated forefoot pressures in RA [20], hence therapies should also aim to target peak forefoot pressures early with the use of foot orthoses when considering mechanical management strategies for forefoot pain and deformity.

Although MRI is considered the gold standard for detecting erosions, US is commonly used in clinical practice for diagnosing disease and identifying pathology. The anatomical location of erosions at the MTP joints in RA provides evidence to support US imaging of the plantar aspect as well as the dorsal aspect of the MTP joints.

In conclusion, erosions were more commonly seen on the plantar aspect of the metatarsal head in RA, supporting the hypothesis of a relationship between biomechanical demands and bone changes in the forefoot. Longitudinal studies are needed to establish the sequence of events and determine the relationship between forefoot pain, deformity and raised plantar pressures with the location of erosions at the MTP joints in patients with RA.

Rheumatology key messages

- Erosions were more common on the proximal and plantar aspect of the MTP joints in RA.
- In patients with RA, erosions at the MTP joints may be mechanically mediated.

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Supplementary data

Supplementary data are available at *Rheumatology* Online.

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