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Assessing forefoot bursitis in rheumatoid arthritis: a comprehensive approach with ultrasound, MRI, and baropodometry

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Abstract

Aim: In rheumatoid arthritis (RA), forefoot bursitis is prevalent, with limited studies comparing ultrasonography (US) and Magnetic Resonance Imaging (MRI). This study aims to evaluate these bursae, providing a comparative analysis of US and MRI, and explore associations with demographic, disease-related factors, pain, clinical examination, and baropodometry in RA patients. **Material and methods:** Participants with RA were recruited from the day-hospital clinic. The forefeet were assessed clinically, and the selected foot was examined by US and MRI to evaluate intermetatarsal (IMB) and submetatarsal bursitis (SMB). Baropodometry assessed plantar pressures and contact surfaces. **Results**: Thirty-five RA patients were enrolled, 85.7% females, mean age 59.2 (11.3) years, mean body mass index (BMI) 26.5 (5.7) kg/m^2, median disease duration of 36.0 (16.5-114.0) months, and 34.3% with painful forefoot. A total of 140 intermetatarsal and 175 submetatarsal spaces were evaluated. Agreement between US and MRI was high (PA=97.14%, k=0.801, p<0.001), and interobserver reliability for both modalities was excellent (US: PA=98.73%, k=0.888, p<0.001; MRI: PA=98.41%, k=0.900, p<0.001). IMB was negatively associated with disease duration (the only independent predictor) and linked to clinical signs like the opening toes sign and hammer toe deformity. SMB showed an association with BMI and erosions. Baropodometric analysis indicated no significant differences in plantar pressures for IMB, and larger contact surfaces in SMB regions. **Conclusions:** US and MRI are valuable tools for forefoot bursitis evaluation. IMB is associated with disease duration (negative association), the opening toes sign, and hammer toe deformity, while SMB correlates with BMI, erosions, and foot architectural deformity. Baropodometry revealed larger contact surfaces in regions with SMB.

Keywords: intermetatarsal bursitis; submetatarsal bursitis; rheumatoid arthritis; ultrasound; MRI

Introduction

The forefoot region houses two types of bursae, the intermetatarsal and submetatarsal bursae, which play crucial roles in mitigating mechanical stress and friction. The former, categorized as real bursae, situated between the interosseous tendons, are lined with a synovial membrane. The latter, considered adventitial or accidental bursae, reside within the fat pad beneath the metatarsal heads [1] – fat pad that serves to absorb mechanical shock and redistribute forces and pressure effectively [2]. There are no communications between the bursae and the adjacent metacarpophalangeal (MTP) joints [3]. Inflammation of the intermetatarsal bursa, leading to synovial membrane proliferation and fluid accumulation, is termed intermetatarsal bursitis (IMB), being more an inflammatory lesion. The accumulation of fluid within the fat pad located beneath a metatarsal head is termed submetatarsal bursitis (SMB) representing a mechanical lesion [1].

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In rheumatoid arthritis (RA) patients, forefoot bursitis (FFB) is a more prevalent occurrence compared to healthy individuals, particularly manifesting in the third [4-6] or forth intermetatarsal space [7,8]. The incidence of IMB tends to surpass that of SMB [5,9], and is independently associated with and specific to early RA [5]. Previous observations indicate that FFB in RA correlates with foot limitation of activity and functional impairment [9,10], potentially contributing to a diminished quality of life.

Ultrasonography (US) and Magnetic Resonance Imaging (MRI) serve as valuable imaging modalities for identifying FFB [11,12]. Previous studies have demonstrated good interobserver agreement for US assessments [11], while for MRI, only intraobserver agreement has been reported, indicating a very good agreement [5]. Baropodometry is a technique used to measure pressures of the soles when in contact with the ground during standing or walking [13]. In RA patients it has been found that forefoot peak plantar pressures were increased resulting from a pain avoidance type of gait with decreased ankle power [14] and heel pressures [15]. This is a very important finding since wearing therapeutic insoles and foot orthoses could decrease forefoot pressure and pain [16-21].

The literature review revealed a limited number of studies dedicated to assessing forefoot bursae in RA patients [4-12,22-32]. Among these, two were comprehensive reviews focusing on US [31] and MRI [12], two were case reports [23,26], seven were US studies [7-11,27,28], and eight were MRI studies [4-6,22,24,25,29,30]. None of these studies conducted a comparative analysis between US and MRI findings. Furthermore, only one study correlated US with baropodometry [32]. This underscores the current gap in the literature regarding the comparative evaluation of US and MRI outcomes and the limited exploration of their correlation with baropodometric data.

This study aims to comprehensively evaluate forefoot bursae in RA patients using US and MRI, offering a comparative analysis of these imaging techniques. Additionally, the associations between FFB, demographic and disease related factors, pain, clinical examination, and baropodometry was explored.

Material and methods

Participant selection

Consecutive RA patients were recruited from our day-hospital clinic between April and December 2018, meeting the 2010 American College of Rheumatology (ACR)/ European League Against Rheumatism (EULAR) classification criteria [33]. Exclusion criteria comprised unstable treatment in the past 3 months, history of forefoot surgery or trauma, overlapping with other rheumatological diseases, local steroid injection in the past 3 months, and absolute contraindications for MRI. Prior to enrollment, all participants provided informed consent, and the study was approved by the University's Ethics Committee.

Data collection

A rheumatologist collected general demographics and disease-related data, conducted forefoot pain interviews, selected the foot for further assessment (the dominant foot in asymptomatic and the most painful foot in symptomatic patients), and performed clinical examination assessing flat foot, mallet, hammer, and claw toes, the opening toes sign ("V sign"), and the presence of pain during palpation of each MTP joint and intermetatarsal space. Disease activity was evaluated using the Clinical Disease Activity Index (CDAI) [34] and Disease Activity Score with 28 joint count and C-reactive protein (DAS28-CRP) [35]. Baropodometry, US and MRI of the selected foot were performed on the same day.

For US examination, a GE Logiq S7 ultrasound machine (GE Healthcare, Chicago, USA) with an L8-18i-D linear array hockey stick transducer was utilized. Patients were positioned according to EULAR standardized procedures [36]. Gain, focus, and frequency settings were adjusted based on the examined region. In Power Doppler (PD) mode, the gain was set at the minimal level with minimum noise artifact, frequency was set at 9 MHz and the Pulse Repetition Frequency (PRF) at 0.6-0.8 kHz. The examination encompassed the longitudinal dorsal aspect of MTP joints, the dorsal and plantar aspect of intermetatarsal spaces (transvers and longitudinal) and the plantar aspect (transvers and longitudinal) of metatarsal regions corresponding to the metatarsal heads. For each joint, the presence or absence of synovitis and erosions, following EULAR definitions [37,38], were recorded. IMB and SMB were also recorded as present or absent. IMB was considered when a well-defined hypoechoic area within the intermetatarsal spaces (between the distal heads of two adjacent metatarsal bones), with or without anechoic areas, compressible and displaceable (corresponding to fluid collection), with or without PD signal [8,10,28,39]. SMB was documented when a well-defined or ill-defined hypoechoic, anechoic, or heterogenous area or collection was identified within the fat pad under the metatarsal heads, with or without PD signal [10,28,39]. Two blinded examiners, with 5-year and 20-year experience in musculoskeletal US (MSUS), performed the examination, and images for each evaluated structure were stored. Disagreements were resolved by a third examiner with over 15 years experience who reviewed the images.

For the MRI examination, a 1.5T MRI equipment (Signa Explorer, GE Healthcare, France) was employed.

Patients were positioned in the supine position with feet flexed at 90° and flattened, pointing toward the magnet (feet first supine). The coil (HD T/R Knee/Foot Coil by Invivo) was appropriately placed and locked over the foot, and the laser beam localizer was centered over the foot. MRI sequences included coronal Short-TI Inversion Recovery (STIR) with a field of view (FoV) of 180x180 mm, matrix size 256x160, slice thickness 3 mm (TR 2314 ms, TE 43 ms, TI 150 ms), axial STIR with a FoV of 260x210 mm, matrix size 192x152, slice thickness 3 mm (TR 3017 ms, TE 46,5 ms, TI 150 ms), coronal 3 dimensional T1-weighted fast spoiled gradient echo (FSPGR) sequence with a FoV of 180x108 mm, matrix size 192x192, slice thickness 1 mm (TR 6,8 ms, TE 3,2 ms) prior to and after intravenous injection of 0.2 ml/kg body weight of Gadolinium-DTPA (Omniscan). Additionally, the reconstruction of three-dimensional T1-weighted FSPGR sequences of the foot in axial and sagittal planes was performed. For each MTP joint, the presence or absence of synovitis and erosions were recorded according to MRI-OMERACT definitions [40,41]. IMB was considered when a well-defined mass in the intermetatarsal space appeared as low signal intensity on T1-weighted images and high signal intensity on STIR sequences with peripheral enhancement following intravenous contrast administration [39]. SMB was recorded when a well-defined or ill-defined homogenous or heterogenous mass was found within the submetatarsal fat pad, presenting as a signal alteration of the fat pad with low signal intensity on T1-weighted sequences and high signal intensity on STIR sequences with peripheral contrast enhancement, with or without central non-enhancing areas [39,42]. Two radiologists independently interpreted the MRI images, and the disagreements were resolved by a third radiologist, all with over 10 years experience. The sum of IMB found in each foot generated a patient score, ranging from 0 to 4. A parallel scoring system was applied to SMB. The combined scores produced a total FFB score ranging from 0 to 9 for each patient.

Baropodometric measurements were conducted using a P-WALK platform (BTS S.p.A., Milan, Italy). Each patient, barefoot and positioned upright, stood in the middle of the platform with their feet slightly outlying (at an approximate angle of 30°), ensuring equal distance of the heels from the midline. The patient was instructed to maintain a stationary stance, fixating their gaze forward, while measurements were captured over a duration of 10 s. Within each metatarsal regions of the forefoot, assessment included maximum and mean pressures (expressed in kiloPascals or kPa) and the corresponding contact surface area quantified in square centimeters (cm^2).

Statistical analysis

The distribution of continuous variables was assessed using the Shapiro-Wilks test. Descriptive statistics are reported as mean (standard deviation), median (interquartile range – IQR) or number (percent), as appropriate. Interobserver and US-MRI agreement were determined by Cohen's kappa coefficient (k), categorized as poor (0–0.20), fair (0.20–0.40), moderate (0.40–0.60), good (0.60–0.80), and excellent (0.80–1). Percent of Agreement (PA) between US and MRI was also calculated, dividing the number of concordances with the total number of cases and multiplying by 100, categorized as poor (<40%), moderate (40-60%), good (60-80%), and excellent (>80%). Sensitivity (Se) and specificity (Sp) of US for visualizing FFB, considering MRI as the "gold standard" were also calculated. Mean and median differences were assessed using T-test for Independent Samples and Mann-Whitney U test for Independent Samples, respectively. Association between categorical variables was assessed using the Chi-square test or Fisher's Exact test, and correlations through Spearman's coefficients. Multivariable logistic regression models were built to predict IMB and SMB entering body mass index (BMI), flat foot, disease duration, seropositivity, disease stage, disease activity, concomitant synovitis, erosions and bone edema in at least one adjacent joint. Multiple linear regression models were built to predict plantar pressures and contact surfaces entering SMB, IMB and concomitant synovitis, erosions and bone edema of at least one adjacent joint. Statistical significance was set at $p<0.05$, and SPSS Statistics v.23 (IBM, Armonk, New York, USA) was used for analysis.

Results

Thirty-five RA patients were enrolled in the study, 85.7% females, with mean age 59.2 (11.3) years, mean BMI 26.5 (5.7) kg/m^2, mean CDAI 19.9 (12.8), mean DAS28-CRP 3.5 (1.3) and median disease duration 36.0 (16.5-114.0) months, 88.6% being seropositive, and 34.3% with a painful forefoot. A total of 140 intermetatarsal and 175 submetatarsal spaces were evaluated.

Ultrasound and MRI agreement in identifying forefoot bursae

IMB was observed in 13 (37.1%) patients via MRI (7 in one intermetatarsal space, 4 in two spaces, and 2 in three spaces) and in 11 (31.4%) patients via US (7 patients in one intermetatarsal space, 3 in two spaces, and 1 in three spaces). SMB was found in 6 (17.1%) patients using MRI (5 patients beneath one metatarsal region, and 1 beneath three regions) and in 3 (8.6%) patients using

US (2 patient beneath one metatarsal region, and 1 patient beneath two regions).

The interobserver agreement for the US examination of forefoot bursae demonstrated excellent reliability (overall FFB: PA=98.73%, k=0.888, p<0.001; IMB: PA=97.86%, k=0.891, p<0.001; SMB: PA=99.43%, k=0.854, p<0.001). The interobserver agreement for MRI examination also exhibited high reliability (overall FFB: PA=98.41%, k=0.900, p<0.001; IMB: PA=97.86%, k=0.914, p<0.001; SMB: PA=98.86%, k=0.851, p<0.001). The agreement between US and MRI, along with the Se and Sp of US, are detailed in Table I.

Forefoot bursitis characterization (patient level)

Overall, FFB was identified in 17 (48.6%) RA patients. IMB were identified in the first and third intermetatarsal spaces (8/21 bursitis each), and the second space (5/21 bursitis). SMB was found in the first submetatarsal region (4/8 bursitis), followed by the third submetatarsal (2/8 bursitis), and the second and forth submetatarsal regions (1/8 bursitis each).

Association of FFB with demographical and clinical data of the RA patients are detailed in Table II. There was no significant correlation between the calculated scores of IMB and SMB and age, BMI, disease duration, disease activity or level of forefoot pain (VAS) (all p>0.05).

Intermetatarsal bursitis (intermetatarsal space and joint level)

IMB demonstrated a significant negative association with disease duration (p=0.44), with a median duration of 24.0 months (11.0-48.0) in the presence of IMB compared to 41.0 months (21.5-156.0) in its absence. No significant associations were found with BMI, seropositivity, disease stage, disease activity or the presence of forefoot pain (all p>0.05). Additionally, there was no significant association between the presence of IMB and SMB at the joint level (p=0.992).

The presence of IMB was significantly associated with the opening toes sign (52.4% intermetatarsal spaces with bursitis vs 10.1% without bursitis, p<0.001) and the presence of hammer toe deformity (20.5% intermetatarsal spaces with bursitis vs 4.6% without bursitis, p=0.003). No associations were found between IMB and other toe deformities (all p>0.05). Pain during palpation of intermetatarsal spaces was noted in 23.8% of spaces with bursitis and 24.4% without bursitis (p=0.956). Similar results were observed for pain during palpation of adjacent joints (22.7% vs 21.4%, respectively, p=0.835). No significant associations were identified between IMB and the presence of flat foot or calcaneus valgus (p=0.185 and p=0.143, respectively).

Among all the IMB found, 23.8% exhibited accompanying synovitis in one adjacent joint, 42.9% in both adjacent joints. However, no significant associations were found between IMB and adjacent joint synovitis (p=0.709, p=0.116, and p=0.273, respectively). Considering only joint synovitis with grade ≥2, 28.6% of the IMB exhibited synovitis in one adjacent joint and 33.3% in both adjacent joints (p=0.682, and p=0.135, respec-

Table I. Agreement between US and MRI in identifying the forefoot bursitis in RA patients

Bursitis	MRI	US	MRI only	US only	PA	k	p-value	Se*	Sp*
IMB (n=140)	21	16	5	0	96.43	0.845	<0.001	76.2	100.0
SMB (n=175)	8	4	4	0	97.71	0.656	<0.001	50.0	100.0
FFB (n=315)	29	20	9	0	97.14	0.801	<0.001	69.0	100.0

Data are presented as absolute number (n); *Calculated for US considering MRI as "gold standard"; MRI: Magnetic Resonance Imaging; US: ultrasonography; PA: Percent of Agreement; k: Cohen's coefficient of agreement; Se: sensitivity; Sp: specificity; IMB: intermetatarsal bursitis; SMB: submetatarsal bursitis; FFB: forefoot bursitis.

Table II. Association of forefoot bursitis with demographical and clinical data of the RA patients

	IMB			SMB		
	Absent (n=22)	Present (n=13)	p-value	Absent (n=29)	Present (n=6)	p-value
Age (years)	57.6 (10.8)	61.85 (11.9)	0.203	58.5 (11.8)	62.5 (8.3)	0.564
BMI (kg/m^2)	26.4 (5.8)	26.7 (5.7)	0.906	26.4 (5.6)	31.9 (4.7)	0.018
Disease duration	44.5 (22.0-192.0)	36.0 (11.0-60.0)	0.216	36.0 (12.0-132.0)	48.0 (22.0-60.0)	0.949
Seropositive	19 (86.4%)	12 (92.3%)	0.99	25 (86.2%)	6 (100%)	0.99
Symptomatic forefoot	9 (40.9%)	3 (23.1%)	0.463	11 (37.9%)	1 (16.7%)	0.640
CDAI	21.0 (11.7)	18.0 (14.7)	0.389	19.3 (13.0)	22.7 (12.5)	0.454
DAS28-CRP	3.6 (1.2)	3.3 (1.5)	0.511	3.5 (1.4)	3.6 (1.3)	0.881

Data are presented as number (%), mean (standard deviation, SD) or median (interquartile range, IQR); IMB: intermetatarsal bursitis; SMB: submetatarsal bursitis; BMI: body mass index; CDAI: Clinical Disease Activity Index; DAS28-CRP: Disease Activity Score 28 Joint Count with C-reactive protein.

tively). No significant associations were found between IMB and erosions or bone edema in one, both, or at least one adjacent MTP joint or metatarsal head (all p>0.05).

In the multivariable logistic regression analysis, including BMI, disease duration, seropositivity, disease stage, disease activity, concomitant synovitis, erosions, and bone edema in at least one adjacent joint, only disease duration emerged as an independent factor associated with IMB. However, the effect size was modest (OR=0.98, 95%CI 0.98-0.99, p=0.022).

Submetatarsal bursitis (joint level)

SMB exhibited a significant association with BMI (p=0.02), with median BMI of 32.25 kg/m^2 (26.83-34.29) in the presence of SMB, compared to 26.81 kg/m^2 (22.31-29.41) in its absence. However, no associations were observed between the presence of SMB and seropositivity, disease stage, disease duration, disease activity and the presence of forefoot pain (all p>0.05).

During physical examination, only two MTP joints where SMB was found exhibited pain upon palpation of the corresponding joint. A single toe with SMB also presented a clinical deformity (claw toe). However, no significant associations were identified between the presence of pain upon palpation of the corresponding MTP joint or toes deformities (mallet, hammer, or claw toe) and SMB (all p>0.05). Although 75% of the SMB were found in the presence of flat feet, all classified as at least stage III deformity, this association was not statistically significant (p=0.279).

Half (50%) of the SMB identified also associated synovitis in the corresponding MTF joint, yet no significant associations were found between SMB and corresponding MTF joint synovitis (p=0.729). In contrast, a significant association was observed between SMB and erosions of the corresponding metatarsal head (p=0.001), with all SMB accompanied by erosions. No significant association was found between SMB and bone edema of the corresponding metatarsal head (p=0.685).

In the multivariable logistic regression analysis, including the parameters BMI, flat foot, disease duration, seropositivity, disease stage, disease activity, concomitant synovitis, erosions, and bone edema in at least one adjacent joint, no independent factor associated with SMB was identified (all p>0.05).

Baropodometry findings and associations with forefoot bursitis (joint level)

The medians of maximum and mean plantar pressures, as well as the contact surfaces recorded in the metatarsal regions, did not show significant differences between regions associated with IMB and those without: maximum plantar pressure 57.5 kPa (IQR: 20.5-96.0) vs 61.0 kPa (IQR: 29.0-121.5), p=0.255; mean plantar pressure 33.5 kPa (IQR: 12.0-57.0) vs 29.0 kPa (IQR: 15.0-59.0), p=0.561; and contact surface 6.25 cm^2 (IQR: 2.2-10.45) vs 5.9 cm^2 (IQR: 2.55-8.2), p=0.345.

Metatarsal plantar pressures were lower in the metatarsal region with associated SMB than in those without bursitis, but the differences were not statistically significant: maximum plantar pressure 40 kPa (IQR: 32.5-90.5) vs 61 kPa (IQR: 27-115), p=0.640; and mean plantar pressure 21 kPa (15.5-51.5) vs 31 kPa (15-59), p=0.615. On the other hand, the contact surface was significantly larger in metatarsal regions associated with SMB (p=0.015): 8.4 cm^2 (IQR: 6.95-13.75) vs 5.8 cm^2 (IQR: 2.3-9.1) cm^2. However, in the multiple linear regression analysis (including SMB, IMB and concomitant synovitis, erosions and bone edema of at least one adjacent joint) predicting contact surface, SMB exhibited a statistically significant positive association (B coefficient: 4.9, 95% CI: 1.8-7.9, SE=1.5, p=0.002), along with bone edema, which also exhibited a significant positive association (B coefficient: 2.5, 95% CI: 0.9-4.1, SE=0.8, p=0.003). The same multiple regression models used to predict maximum and mean plantar pressures did not reveal any associated factors (all p>0.05).

There were no significant differences observed in the medians of maximum and mean plantar pressure, as well as contact surface, between metatarsal regions associated with SMB and those associated with adjacent IMB (all p>0.05).

In figure 1 and figure 2 we exemplified 2 cases with FFB.

Discussions

FFB in RA patients is a subject barely found in the literature, although it could be one of the causes of metatarsalgia [43]. In our comprehensive evaluation of forefoot bursae in RA patients we found a significant prevalence of both IMB and SMB in this patient cohort. The interobserver agreement for both US and MRI examinations demonstrated excellent reliability, providing confidence in the accurate identification of FFB. Notably, our results contribute to the limited existing literature on this topic, emphasizing the need for a more in-depth understanding of the associations and clinical implications of FFB in RA patients.

The agreement between US and MRI in identifying forefoot bursae is a critical aspect of our study, shedding light on the reliability and concordance between these imaging modalities in the assessment of RA-related foot pathology. These results align with prior research reporting good interobserver agreement for US [11] and intraobserver agreement for MRI [5] in evaluating FFB in RA

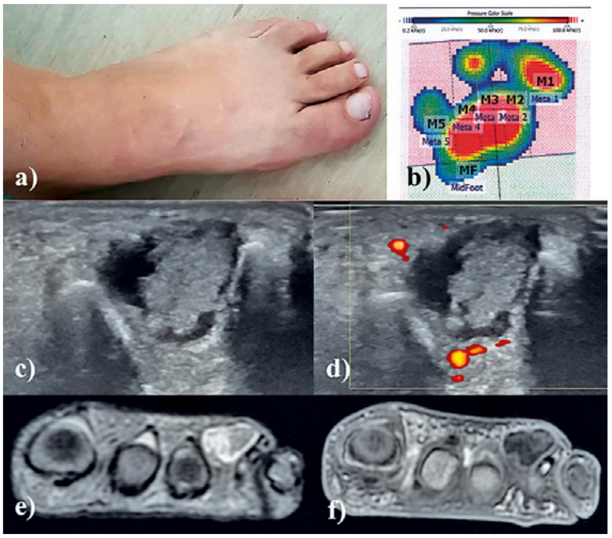

Fig 1. Female patient with IMB of the third intermetatarsal space having the following findings: a) clinical examination: opening toes sign of the third intermetatarsal space; b) baropodometry: increased plantar pressure at the same level; US: c) well-defined hypoechoic area within the intermetatarsal spaces, with anechoic areas inside, compressible and displaceable (fluid collection), d) without PD signal; MRI: e) well-defined mass in the intermetatarsal space with high signal intensity on coronal STIR sequences and f) peripheral enhancement on post-contrast coronal 3D T1 FSPGR.

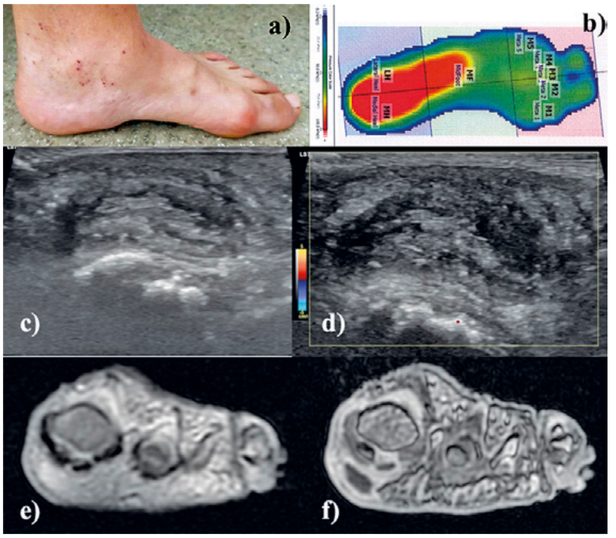

Fig 2. Female patient with SMB in the first submetatarsal region with the following findings: a) clinical examination: flat foot; b) baropodometry: flat foot and increased contact surface of the first submetatarsal region (17.9 cm^2); c) US: ill-defined heterogenous area within the fat pad under the first metatarsal head, d) without PD signal; MRI: e) ill-defined heterogenous mass within the first submetatarsal fat pad with high signal intensity on coronal STIR sequences and f) peripheral enhancement on post-contrast coronal 3D T1 FSPGR., with central non-enhancing area.

patients. Bowen et al [11] initially reported moderate US interobserver agreement (83.3%, k=0.522), between a radiologist and a less experienced podiatrist, which significantly improved to good (k=0.702) after a consensus and training session. Our results showed excellent agreement (k=0.888) between sonographers, probably related to the training sessions prior to the beginning of the study. Comparing the diagnostic performance of US and MRI, our study contributes valuable insights into the strengths and limitations of each imaging modality, extending our previous research focused on foot and ankle assessments [44].

The agreement between US and MRI for FFB visualization was excellent (overall agreement 97.14%, k=0.801), suggesting a great reliability of US in their detection. Given its higher availability, even bedside, shorter examination duration and lower costs compared to MRI, US could become the method of choice for many practitioners evaluating RA patients, including forefoot bursae. While our study demonstrated overall concordance between US and MRI, a direct comparison of sensitivity and specificity was not conducted, leaving potential for future research.

Various US and MRI definitions for the IMB and SMB and US examination techniques were found in literature. Some authors examined the intermetatarsal spaces using US "longitudinally and transversely from the plantar view" [11], others by "dorsal longitudinal scan (and transverse when indicated)" [27] or in "sagittal and transverse plane using a dorsal approach while the examiner push with her/his non examining thumb on the plantar aspect of the space" [31], and others from "both a plantar and dorsal approach in longitudinal and transverse scanning planes" [10]. Thereby, there is a need for standardization of the intermetatarsal spaces examination technique.

In our investigation, IMB was common finding (37.1% of our RA cohort – mean disease duration of 36 months), predominantly in the first and third intermetatarsal spaces. This aligns with previous studies of Iagnocco et al [43] (23.1%) and Hammer et al [27] (20.6% - mean disease duration of 10 years), but is lower than Bowen et al's [9] findings (90.8% - mean disease duration of 13 years), all representing US studies on established RA patients. Dakkark et al [5], in a MRI study on early RA patients (mean symptom duration 10 weeks), reported IMB in 69% of their cases. The variation in prevalence may be attributed to differences in disease duration, suggesting our cohort possibly captures an earlier stage of RA progression. Interestingly, we observed a significant correlation between IMB and clinical signs, such as the opening toes sign and the presence of hammer toe deformity, emphasizing the clinical relevance of FFB in RA-related foot deformities.

The negative association between IMB and disease duration suggests a higher prevalence in individuals with shorter RA duration, hinting at factors beyond the inflammatory process duration contributing to FFB development. This aligns with Dakkak et al's [5] observations, linking both FFB types to early RA, independent of RA-MRI score. Notably, our multivariable logistic regression identified disease duration as the sole independent factor associated with IMB, albeit with a small effect size. Furthermore, we observed synovitis in 23.8% and 42.9% of intermetatarsal spaces with bursitis, respectively, in one or both adjacent MTP joints. Considering only at least grade 2 synovitis, similar frequencies (28.6% and 33.3%, respectively) were obtained. This finding aligns with previous reports of synovitis in one (29%) and both adjacent joints (37.7%) of intermetatarsal spaces with bursitis [27]. Still, we did not identify any significant association between the IMB and adjacent joints synovitis.

In contrast, SMB was less frequent (17.1% of our RA cohort) and exhibited a distinct pattern (mostly under the first and third metatarsal heads), showing a significant association with BMI, suggesting the influence of mechanical factors. Notably, 75% of SMB cases occurred in the presence of flat feet, stage III, a deformity that we associated with increased plantar pressure of the metatarsal regions (data not shown). This underscores the interplay between structural deformities and specific submetatarsal bursal pathology. Moreover, half of the SMB had accompanying MTP joint synovitis (non-significant association), but all were accompanied by joint erosions (significant association), highlighting the potential impact of inflammation on joint structures in RA patients with forefoot involvement.

Our study did not explore the dynamic aspects of FFB, such as changes over time or responsiveness to treatment. Previous research [9,10], highlights significant association between FFB and foot impairment or activity restriction, suggesting that forefoot bursae should be targeted by RA therapy. Bowen et al [28] suggested that FFB varies over time, independent of the treatment (even antiTNF therapy). Our findings, except for BMI and SMB, showed no association between forefoot bursae and demographic and clinical data of RA patients. Hence, more studies are needed to determine if therapy should target FFB and its potential benefits. Presumably, one might find that architectural changes or foot deformities, possibly related to FFB, could better explain the symptomatology and foot impairment and their prevention or correction would be of greater benefit to the patients.

Baropodometry findings provided additional insights into the biomechanical aspects of FFB. The lack of significant differences in plantar pressures and contact surfaces between regions with and without IMB suggests that bursal inflammation may not be directly influenced by plantar loading patterns. However, the larger contact surface in metatarsal regions associated with SMB raises intriguing questions about the dynamic interactions between bursal pathology and forefoot weight distribution. Since we found lower plantar pressures and higher contact surface in metatarsal region with SMB, one might suggest that SMB may play a role in decreasing pressure in the corresponding metatarsal area by increasing surface contact, possibly linking architectural foot changes to the development of SMB as a compensation for forefoot pressure overload. This is also supported by our multiple linear regression indicating that a SMB was associated with a 4.9 cm^2 increase in the contact surface. Additionally, Bowen et al [32] reported negative correlations between US detectable forefoot pathology scores and peak plantar pressures of the lateral forefoot.

To the best of our knowledge, this study is the first to compare US and MRI performance in identifying FFB and correlate it with plantar pressure and surface measurements. Nonetheless, our study is not without limitations. Firstly, the small sample size, particularly in instances of FFB, attributed to the costs of MRI and financial constraints, may impact the generalizability of our findings. Secondly, the absence of a comparative analysis between RA patients and healthy subjects, limits our ability to contextualize observed variations. Moreover, the cross-sectional design of the study provides a snapshot at a specific point in time, and thus, causality or the temporal relationship between FFB and other factors cannot be established. The absence of long-term follow-up data hinders our understanding of the dynamic changes in FFB over time in RA patients. Nevertheless, RA is known for its heterogeneity in disease presentation, thus the inclusion of patients with varying disease stages, severity, and treatment regimens may introduce variability in the study population.

In **conclusion**, our study reveals a substantial prevalence of FFB in RA patients, endorsing the utility of both US and MRI in evaluating this condition, supported by the high interobserver agreement for both techniques and their good overall concordance. Baropodometric analysis indicates no significant differences in plantar pressures for IMB, while larger contact surfaces are observed in SMB regions. These imaging modalities provide complementary information, contributing to a comprehensive understanding of forefoot pathology in RA.

Conflict of interests: none

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