

Pattern of forefoot bursae in patients with rheumatoid arthritis and its effect on foot functions

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Aim of this work

The aim of this study was to investigate the pattern and prevalence of forefoot bursae (FFB) and their effect on foot functions in Egyptian patients with rheumatoid arthritis (RA).

Patients and methods

The study included 100 patients with RA diagnosed according to the 2010 American College of Rheumatology/European League Against Rheumatism (ACR/EULAR) classification criteria. The patients were recruited from the outpatient clinic of Physical Medicine, Rheumatology and Rehabilitation Department in Alexandria Faculty of Medicine. Musculoskeletal ultrasound (US) of the forefeet under the standardized EULAR guidance was done for all patients, and accordingly, the studied patients were further classified as those with US-detectable FFB (group I) and those without US-detectable FFB (group II). For group I patients, foot impact scale (FIS), foot anatomical changes assessment, and gait analysis were done.

Results

US-detectable FFB was found in 92% of the 100 patients with RA. The most frequent intermetatarsal bursa was the fourth one, and the most frequent submetatarsal bursa was the first one. There was a statistically significant relation between the total number of FFB on one side and its two subscales, meta-tarsophalangeal synovial hypertrophy, serum C-reactive protein level, visual analogue scale of foot pain, and step length on the other side. No statistically significant correlation was found between the total number of FFB and BMI, clinical disease activity index, or the foot deformities. Moreover, no statistical significant correlation was found between FIS and clinical disease activity index.

Conclusion

US-detectable FFB are highly prevalent in patients with RA and considered a significant contributory factor to foot disability among these patients. Foot disability may occur regardless of the RA activity state.

Keywords:

foot impact scale, forefoot bursae, rheumatoid arthritis, ultrasound

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Introduction

Rheumatoid arthritis (RA) is an inflammatory disease with articular, per articular, and extra-articular manifestations [1]. It is a known cause of disability that has an effect on all aspects of life [2,3]. Foot-related complications in patients with RA are poorly investigated in comparison with the problems of the hand or systemic disease [4]. The most frequent foot complications are metatarsal head erosion, meta-tarsophalangeal (MTP) joint deformity, and midfoot collapse [5–7]. It is largely postulated that the pathological processes of RA disease applied to the hand are similar to the foot [8,9]. The forefoot is a complex anatomical region having a number of extra-articular structures that could be affected by the RA process. Structures that incorporate a synovial membrane, such as joint linings, tendon sheaths, or intermetatarsal (IM) bursae, are the most frequently

affected by the systemic inflammation in RA [10–12]. Forefoot bursae (FFB) are of specific importance in patients with RA, as they are potentially responsive to both disease inflammatory cascade and adverse mechanical function [13,14]. Musculoskeletal ultrasound (US) is an important clinical instrument that is comparable with and more easy to use than MRI in the assessment of soft tissues in RA [15–17]. Using US, a higher incidence of bursae in the forefoot has been found than in control [18]. In various studies, it was agreed that bursae in RA forefoot may cause clinical symptoms when they became either enlarged or inflamed [18–20]. To optimize appropriate

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medical interventions, it would be of value to investigate the prevalence and distribution of US-detectable FFB in patients with RA. The current study was conducted to investigate the pattern and prevalence of FFB and their effect on foot functions in Egyptian patients with RA.

Patients and methods

The study included 100 patients with RA diagnosed according to the 2010 American College of Rheumatology/European League Against Rheumatism (ACR/EULAR) classification criteria [21], and they were recruited from the outpatient clinic of Physical Medicine, Rheumatology and Rehabilitation Department in the Main University Hospital in Alexandria Faculty of Medicine. Patients with RA with diabetes mellitus, sensory neuropathy, associated rheumatologic diseases, or local foot disease were excluded.

Demographic and clinical data including disease duration, drug intake, visual analogue scale of foot pain (VAS_F) [22], and disease activity using clinical disease activity index (CDAI) were done for all patients. Laboratory investigations included erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), and rheumatoid factor (RF). US of the forefeet under the standardized EULAR guidance using a Toshiba Xario 200 US system (Toshiba Medical System corporation, Japan) was done for all patients. According to the forefoot US findings, the studied patients were classified into group I – those with US-detectable FFB – and group II – those without US-detectable FFB. Group I patients were further subjected to foot impact scale (FIS), foot anatomical changes assessment, and gait analysis.

Results

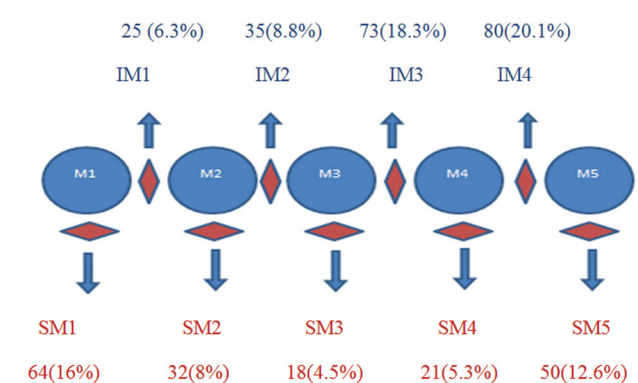
Most studied patients were females (91 females and nine males), aged from 23 to 67 years, with disease duration ranged from 1 to 33 years. The mean BMI in the studied patients was $29.53 \pm 5.01 \text{ kg/m}^2$. At the time of examination, only nine patients were in remission, 23 patients were in low disease activity and equal number were in moderate disease activity, whereas a larger number of patients (45) were in high disease activity according to the CDAI values. The mean CRP level was $13.77 \pm 16.83 \text{ mg/dl}$ and that of the ESR was $45.46 \pm 25.69 \text{ mm}$. A total of 69 patients were RF positive, among them 36 patients were having high positive titer. The VAS_F ranged from 0 to 82. Most studied patients (66%) were having low pain level (5 to <44), 23% of them were having moderate foot pain level (44 to <74), whereas the remaining 16% were

having severe pain level of 74 or more on a scale of 100 mm. Clinical foot anatomical changes were found in 79% of group I patients (73 patients). The most frequent one was limited ankle and subtalar joint mobility that was detected in 50 patients, followed by pes planus in 21 patients. Hallux valgus was present in 15 patients, fifth MTP exostosis in four patients, and lesser toe deformity in one patient. The FIS which was done for group I patients ranged from 7 to 40, with a mean value of 19.13 ± 7.29 . The FIS activity limitation/participation restriction (FIS_{AP}) subscale ranged from 2 to 24, with a mean value of 9.71 ± 4.29 , whereas the FIS impairment/footwear (FIS_{IF}) subscale ranged from 3 to 16, with a mean value of 9.32 ± 3.25 . US-detectable synovial hypertrophy of the MTP joints was present in 60% of the studied patient. US-detectable FFB was found in 92% of the patients, with the most frequent IM bursa was the fourth one and the most frequent submetatarsal (SM) bursa was the first (Figs. 1 and 2). There was a statistically significant relation between FFB on one side and FIS and its two subscales (Figs. 3–5), MTP synovial hypertrophy, serum CRP level, VAS_F (Fig. 6), and step length on the other side. No statistical significant correlation was found between FFB on one side and BMI, CDAI, or the foot anatomical changes on the other side. Moreover, no statistical significant correlation was found between FIS and CDAI.

Discussion

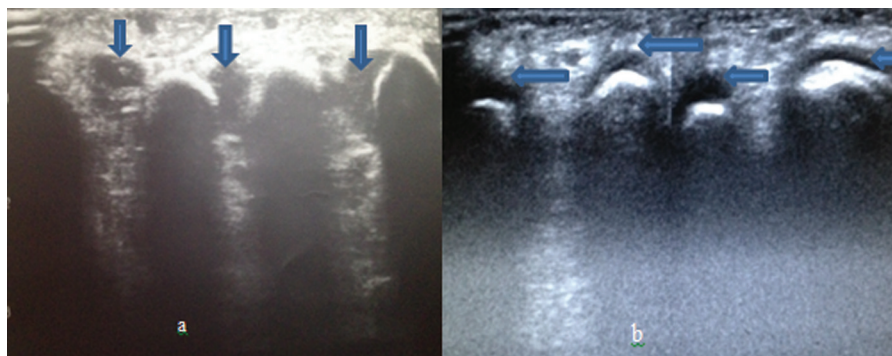
Foot pain and its secondary limitations on the activities of daily living are common complaints of patients with RA, but unfortunately clinical examination of the foot may not be routinely done. This lack of examination may be because of the use of common measurement tools of disease activity (DAS28 and CDAI) that omit the feet and ankle joints. Foot examination is agreed to

Figure 1



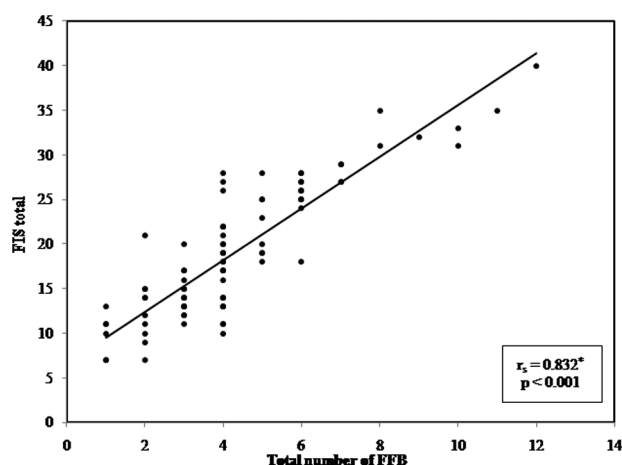
Percent distribution of the ultrasound-detectable forefoot bursae in the studied patients. IM, intermetatarsal bursa; M, metatarsal head; SM, submetatarsal bursa.

Figure 2



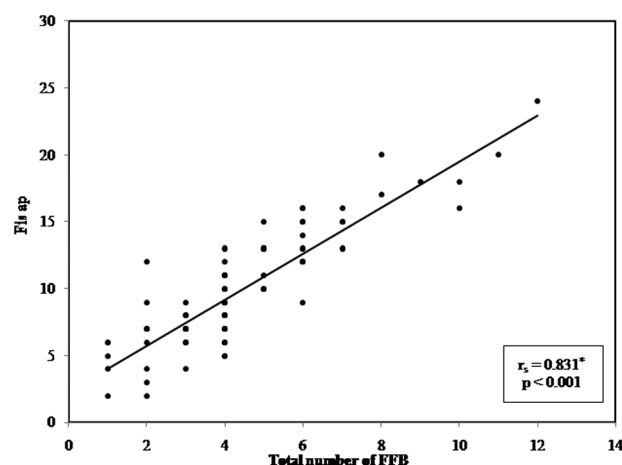
(a) Right multiple IM FFB in a 37-year-old female patient with RA with disease duration of 12 years. (b) Left multiple SM FFB in a 42-year-old female patient with RA, the disease duration of 20 years. FFB, forefoot bursae; IM, intermetatarsal bursa; RA, rheumatoid arthritis; SM, submetatarsal bursa.

Figure 3



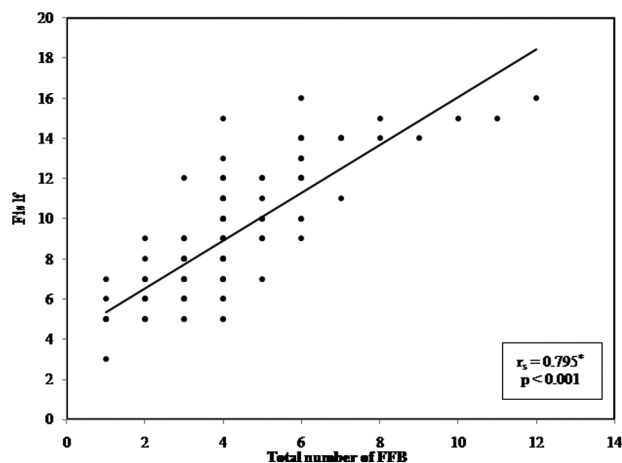
A scatter blot showing the positive statistical correlation between the total number of FFB and total FIS. FFB, forefoot bursae; FIS, foot impact scale.

Figure 4



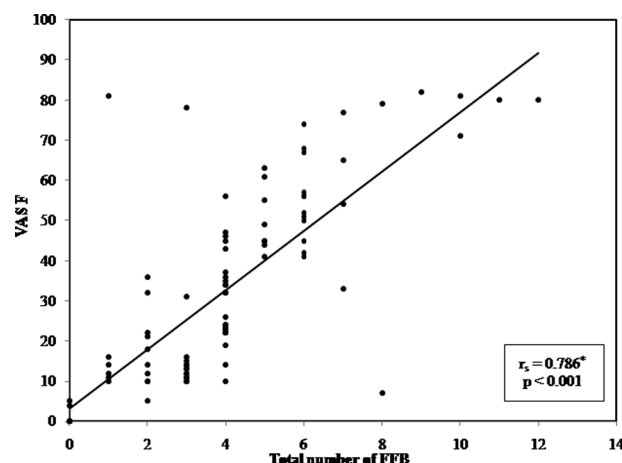
A scatter blot showing the positive statistical correlation between the total number of FFB and FIS_{AP}. FFB, forefoot bursae; FIS_{AP}, foot impact scale activity/participation subscale.

Figure 5



A scatter blot showing the positive statistical correlation between the total number of FFB and FIS_{IF}. FFB, forefoot bursae; FIS_{IF}, foot impact scale impairment/footwear.

Figure 6



A scatter blot showing the positive statistical correlation between the total number of FFB and VAS_F. FFB, forefoot bursae; VAS_F, visual analogue scale for foot pain.

be an important tool for predicting disability, and a poor prognosis in patients with RA [19]. A high FIS score found in the current work could be explained by the high prevalence of FFB, foot anatomical changes, or MTP synovial changes among the studied patients. The same results were found in previous studies [18–20]. In the current work, the FFB were detected clinically in 36% of the patients ($n=100$). That low prevalence of clinical FFB if compared with that of US-detectable FFB (92%) might be because of small-sized asymptomatic bursae not detected clinically. This runs in accordance with the findings of Koski *et al.* [23] who found clinical FFB in 32% of their patients with RA. A comparable result was also found in a study done by Bowen *et al.* [18] who reported a prevalence of clinical FFB of 23.5%. The prevalence of US-detectable FFB in the current study was 92%, which is much higher than the detected number by clinical examination. This further supports the importance of incorporating US examination in patients with RA, especially when pain is present with no clinical signs to explain its cause. This high prevalence of US-detectable FFB was found in various previous studies [18,20,24]. In the current study, the most frequent FFB was the fourth IM bursa (IM 4/5) (20.1%) whereas the most frequent SM bursa was the first (16.1%), with the least frequent one of all being the third SM bursa. The same finding was reported by Bowen *et al.* [18] and Hooper *et al.* [24]. The SM bursae are considered pathological or symptomatic, so pain and/or activity limitation may occur with their hypertrophy [18]. US-detectable synovial hypertrophy of the MTP joints was present in 60% of the studied patients. Similar results were detected by Bowen *et al.* [25] where the US-detectable MTP synovial changes were present in 67.5% of their patients. There was no statistically significant correlation between the total number of FFB and CDAI. Similar results were found by Bowen *et al.* [18] and Hooper *et al.* [24]. On the contrary, Hooper *et al.* [20] previously described an association between reductions in FFB and reduced DAS28–CRP. An association between elevated BMI and mechanical impairment was postulated in terms of both kinematic and kinetic joint loading. Indeed, the extra loading and torsional stress applied on the soft tissues of the forefoot because of elevated BMI are unclear [26–29]. In the current study, no correlation was found between total number of FFB and BMI, which suggests these bursae are mostly of inflammatory origin and not related to the mechanical loading. Similar results regarding the correlation between BMI and FFB number were found by Hooper *et al.* [24]. The positive statistically significant correlation

found between total number of FFB and CRP could be explained by the inflammatory cause of the bursal hypertrophy or the MTP synovial changes. There was statistically significant relation between the total number of FFB and MTP synovial changes in group I patients, and this might be explained also by the inflammatory nature of both synovial and bursal hypertrophy. The same observation regarding the relation between the FFB and the synovial hypertrophy was found by Awerbuch *et al.* [11], Boutry *et al.* [30], and Jaganathan *et al.* [12]. Moreover, the inflammatory nature of the disease is also the postulated explanation for the lack of relation between the total number of FFB and the different foot anatomical changes found in the current study. There was a positive statistically significant correlation between the total number of FFB and FIS and its two subscales. This may support that FFB participate to patient-related foot disability and so increased clinical attention is mandatory. The same results were found by Bowen *et al.* [18] who found a significant association between the number of US-detectable FFB and both FIS subscales which was independent of BMI, age, and RA duration even after the adjustment for disease activity ESR, CRP, and DAS28. The same researchers confirmed similar finding in another published research later in 2010 [19]. No statistically significant correlation between FIS or its two subscales and CDAI could be found in the current study, raising the importance of incorporating foot examination and disease activity assessment in the foot of all patients with RA. Moreover, it emphasizes that foot has a major effect on the patient's ability to return to work and perform daily living activities. Otter *et al.* [31] reported in a survey that foot problems in many patients with RA occur regardless of disease duration or the received medications, and may even be detected in patients with RA receiving biologic therapy. The positive statistically significant correlation between the total number of FFB and VAS_F could be explained by the pain caused by the FFB among the studied patients. The negative statistically significant correlation between the total number of FFB and the step length could be explained by the affected gait patterns in a trial to decrease loading on the forefoot by shortening the preswing phase of gait. Turner *et al.* [32] and Khazzam *et al.* [33] mentioned a reduced motion at the forefoot of the patients with RA owing to foot pain that affected the gait kinematics. This study has several strengths and some limitations. It was a large clinical study representative of secondary care in Egypt using patient-reported clinical outcome measures, including disease activity and foot-specific measures. This was a

double-blind study where US assessment was done by an expert ultrasonographer. The disease activity and foot-specific measures were done by a rheumatologist not involved in sonographic examination, thus avoiding data collection bias. Unfortunately, an access to MRI to verify the presence of FFB detected by musculoskeletal US was not available. Dynamic plantar pressure measurements and instrumental gait assessment were not available in our institute.

Conclusion

US-detectable FFB are highly prevalent in patients with RA and considered a significant contributory factor to foot disability among these patients. Foot disability may occur regardless of the RA activity state.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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