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Editorial

High Frequency of Foot Insufficiency Fractures in Patients With Rheumatic Diseases Referred for Magnetic Resonance Imaging: What Is the Clinical Relevance?



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We greatly appreciated the manuscript by Björn Buehring et al[1] about the high prevalence of foot insufficiency fractures (IFs) in patients with inflammatory rheumatic and musculoskeletal diseases (RMDs) who were referred for magnetic resonance imaging (MRI) because of foot pain, for several reasons. First, in using MRI, IFs were frequently diagnosed (7.5%) in referred patients with RMDs who had foot pain, and even more frequently in patients with inflammatory RMDs than in patients with noninflammatory RMDs (9.1% vs 4.1%, respectively). Second, to diagnose IFs, MRI was superior to conventional radiographs. In 74.4% of patients with an IF detected on MRI, a conventional radiograph was performed earlier, whereas IFs were also detected on conventional radiograph in only 25%.

Here, we discuss the key issues arising from the study by Buehring et al,[1] which are the strength and weakness of the data, the clinical relevance for daily practice, and the research agenda.

Among the strengths of the study are the large numbers of MRIs (n = 1752) that were performed, demonstrating fractures in 7.5% of referred patients with RMDs and foot pain. Availability of data about inflammatory and noninflammatory RMDs made it possible to demonstrate that the risk factors for developing a foot IF was double in referred patients for MRI with inflammatory RMDs vs patients with noninflammatory RMDs, emphasizing the elevated fracture risk in patients with inflammatory rheumatic diseases.[2,3] The relatively high fracture rate of 7.5% is relevant against the background that foot problems occur in 80% to 90% of patients with rheumatoid arthritis (RA)[4,5]; however, rheumatologists often pay less attention to feet problems in daily practice, partly because the use of commonly used disease activity scores, such as the Disease Activity Score in 28 joints, do not incorporate the feet. In general, the differential diagnoses in an elderly patient with RMD and foot pain are arthritis, degenerative disease, and fracture. Because the physical examination often is not very helpful in the differential diagnosis, imaging techniques are very welcome. Unfortunately, conventional radiographs are not sensitive for early erosions induced by arthritis, nor for early osteoarthritis or for discrete fractures—all of which support the need for more sensitive imaging techniques in patients with RMDs and foot pain. MRI shows this superiority and can discriminate between RA-related characteristics and other diagnoses, including fractures.[6] Obviously, treatment options differ widely between these diagnoses of foot complaints.

The main weaknesses are the retrospective design of the study, wherein the data were collected from patient records, which often deliver suboptimal information. For instance, no detailed data were available about whether there was an occurrence of an acute pain episode, which suggests a fracture, or not, which then points more to the direction of arthritis or degenerative disease. Additionally, it is unclear whether IFs occurred after a minor trauma, reflecting osteoporosis, or rather after an adequate trauma or repeated strain. Data on disease activity also show some weaknesses, as only yes or no responses for high disease activity could be retrieved from the patient records. This may have played a role in the unexpected and unlikely finding in the multivariate analysis that high disease activity was associated with a low

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risk of IFs. An explanation for that unexpected result could be that rheumatologists usually start with another antirheumatic drug treatment in patients with polyarticular RA (and do not perform an MRI of the foot), whereas in patients with only foot pain (and thus no high disease activity), an MRI is performed. Another point to consider is that the study was performed in a large, tertiary center. It is possible that the prevalence of IFs is lower in nonacademic hospitals wherein patients have less severe rheumatic disease.

What is the clinical relevance of the finding that IFs were detected in a higher percentage of referred patients with foot pain who had inflammatory RMDs than those with noninflammatory RMDs? In our opinion, this prevalence is substantial, not only in patients with inflammatory RMDs (9.1%) but also in patients with noninflammatory RMDs (4.1%), which is lower but still remarkable. However, this raises several new questions. Were all fractures true IFs, related to minor and inappropriate loads, or were they stress fractures, usually related to repetitive strain? What is the prevalence of IFs in healthy individuals of the same age and gender with complaints of foot pain? Were MRIs performed in both feet, and in what percentage of patients were IFs found in the nonpainful foot? Further, in how many patients with rheumatic disease and a painful foot were MRIs not performed? There is no doubt about the higher sensitivity for detecting fractures by MRI than by conventional radiography, but there remain questions about the specificity and thus the clinical relevance of the imaging abnormalities detected by MRI. Previous studies show that specific RMD-related features, such as arthritis, tenosynovitis, bone marrow edema, and erosions, can be detected reliably with MRI.[7,8]

Perhaps the most difficult point is in which patients with RMD and foot pain an MRI should be performed, and how frequently. The current study[1] focuses on patients with a painful foot, and the data do not support a 2-step strategy with an initial radiograph because IFs were detected on radiographs in only 25%, which is in line with an earlier but smaller study from Denmark.[6] Performing an MRI in all patients with foot pain is costly, and there is limited access to MRI in many regions and countries. Another issue is that RMDs are chronic. Should an MRI be repeated when the pain persists or exaggerates, to detect an IF on a subsequent MRI? Alternatively, should we limit performing MRI to those patients with an acute episode of pain after a minor trauma followed by persistent foot pain? Unraveling underlying osteoporotic risk factors for IF in patient groups may help in identifying which patients have the highest need for advanced imaging techniques like MRI.

What is the clinical consequence of the finding of an IF on an MRI in a patient with RMD with a painful foot, apart from symptomatic treatment for pain relief? Many guidelines exclude forefoot fractures from secondary fracture prevention programs,[9,10] and there are no studies in which patients are enrolled based on fractures detected with MRI in which a treatment effect of an osteoporotic drug has been shown. However, the data from Buehring et al[1] show that these patients had common risk factors for fractures, such as smoking, low bone mineral density, a history of fractures, drug treatment for osteoporosis and fracture prevention, and use of methotrexate, which is known to be associated with stress fractures[11]; all of these support the presence of underlying osteoporosis and increased fracture risk. Osteoporosis, defined as *t*-score < -2.5 was found in 43% of patients with IFs (vs 16% in those without IFs), and osteoporosis and/or osteopenia was found in 67% vs 35%. Thus, evaluation of underlying osteoporosis and fracture risk with a medical history, dual-energy x-ray absorptiometry, and vertebral fracture assessment seems to be indicated after an IF in RMDs, because effective, relatively safe, and cheap antiosteoporotic drugs, such as oral bisphosphonates, are available.

In conclusion, we acknowledge the exciting new MRI data on IFs in referred patients with RMDs and foot pain. MRI can be very helpful in the differential diagnosis of arthritis, degenerative disease, and IF in patients with RMDs and foot pain, all of which have different therapeutic consequences for symptomatic pain relief. Diagnosing an IF may open up an effective option for secondary fracture prevention in patients with RMDs and foot pain, in which an elevated underlying risk for osteoporosis and fractures can frequently be diagnosed. Identification of underlying osteoporotic risk factors plays a crucial role in detection of high-risk patients and this may help in deciding which patients need advanced imaging techniques like MRI.

However, the current study is not an endpoint, but rather a starting point, for a research agenda in both patients with and without inflammatory RMD. This research agenda should include new issues such as the prevalence of IFs in patients with and without a recent trauma in their medical history, the prevalence of IFs in the nonpainful foot, and the prevalence of IFs in healthy individuals of the same age and gender with foot pain.

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