Clinical and Experimental Rheumatology 2013; 31: 281-284.

Ultrasound examination of symptomatic ankles in shorter-duration rheumatoid arthritis patients often reveals tenosynovitis

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Received on February 13, 2012; accepted in revised form on September 3, 2012.

Key words: rheumatoid arthritis, ankle, Doppler, ultrasound, tenosynovitis

Competing interests: none declared.

ABSTRACT

Objectives. *This study investigated the frequency and characteristics of various pathologies in symptomatic ankles in RA patients, especially early RA patients, using power Doppler ultrasound (PDUS).*

Methods. *We analysed consecutive records of 100 ankles in 74 RA patients who had PDUS scans of symptomatic ankles in our department. The association between US findings and disease duration was analysed.*

Results. *Joint synovitis of ankles including in talocrural, subtalar and talonavicular joints was detected in 56 ankles. Ankle tenosynovitis was detected at the medial recess in 46 ankles, at the lateral recess in 29 ankles, and at anterior aspects in 10 ankles (in 61 ankles overall). Achilles tendon involvement including retrocalcaneal bursitis, Achilles tendon enthesitis, tendonitis, and paratendonitis was detected in 39 ankles. Disease duration was significantly shorter in the ankles with tenosynovitis than in those without tenosynovitis (11.4±21.6 vs. 32.0±58.3 months, p=0.039). Disease duration was even more significantly shorter in ankles with isolated tenosynovitis (i.e., ankles with tenosynovitis but without joint synovitis, n=30) than in all other ankles (5.9±8.7 vs. 25.2±47.8 months, p=0.0016). Tenosynovitis and isolated tenosynovitis, especially, were significantly more common in early RA ankles (disease duration <6 months) than in those with established RA (p=0.0357 and p=0.0236, respectively).*

Conclusions. *Tenosynovitis and especially isolated tenosynovitis are frequently detected by US in symptomatic ankles of early RA patients. US examination of ankles in early RA patients should include scans of the medial and lateral recess to enable early detection of ankle tenosynovitis.*

Introduction

Because recent advances in drug therapies for rheumatoid arthritis (RA) have increased the importance of early intervention, early diagnosis has never been more important. The application of ACR/EULAR 2010 Classification Criteria for RA (1) facilitates the use of sensitive tools for the detection of synovitis and musculoskeletal ultrasound (MSUS) is increasingly used in daily rheumatologic practice. The new criteria also encourage the evaluation of foot and ankle joints, which were historically neglected by the DAS28 scoring system. However, few studies have assessed US-detected pathologies of the ankle in early RA (2), although the pathologies of the forefoot were well investigated (3). We reported previously that power Doppler ultrasound (PDUS) sensitivity is superior to that of gray-scale ultrasound (GSUS) in detecting pathologic conditions in symptomatic ankles in RA patients (4). The current study investigates the frequency and characteristics of various pathologies in symptomatic ankles in RA patients, especially early RA patients, using PDUS.

Materials and methods

Patients

We analysed consecutive records of 100 ankles in 74 RA patients whose symptomatic ankles were scanned using PDUS in our department due to clinical need. All patients fulfilled ACR/EULAR2010 classification criteria (1). Symptomatic ankles were defined by the presence of spontaneous pain and/or local swelling and/or tenderness during ankle pressure and mobilisation. Clinical and serological data including gender, age, duration of RA, duration of RA treatment, current RA medication, rheumatoid factor (RF), anticyclic citrullinated peptide (anti-CCP) antibody, C-reactive protein (CRP), and matrix metalloproteinase 3 (MMP-3) were collected as described (4).

US assessment

US examinations were performed mainly using a GE LOGIQ 7 device (GE Medical Systems, Milwaukee, WI, USA). A 10–14 MHz linear transducer was used, mainly at a 12.0 MHz for gray-scale and 6.7 MHz for colour mode. PDUS was performed using standard methods with a pulse repetition frequency of 0.9–1.1 kHz. Ankles which were symptomatic on physical examination were scanned by an experienced-examiner (T.S.) according

to MSUS guidelines (5). Examinations aimed to determine the presence or absence of synovitis in talocrural, subtalar and talonavicular joints, and subtalar joints were examined from medial and lateral aspects. The following tendons were examined for presence of tenosynovitis: tibialis anterior (TA) and posterior (TP), peroneus longus (PL) and brevis (PB), flexor digitorum longus (FDL), flexor hallucis longus (FHL), extensor digitorum longus (EDL), and extensor hallucis longus (EHL). Ankle extensors including EDL, EHL, and TA were scanned from the anterior aspect. Ankle flexors including TP, FDL, and FHL were scanned from the medial aspect. Peroneal tendons were scanned from the lateral aspect. Posterior scans were performed to observe Achilles tendons (AT) and retrocalcaneal bursae. The definitions of pathological conditions were as described previously (6). Although there is much confusion in the terminology of AT inflammation, we mainly adhered to the classification described by Puddu *et al*. (7).

Statistical analysis

Statistical analysis was performed using Fisher's exact test and Welch's unpaired *t*-test. Statistical significance was assumed at a *p*-value of less than 0.05.

Results

Frequency of pathology upon US examination

We analysed consecutive records of 100 ankles in 74 patients consisting of 52 women and 22 men (median age 63.3 years, range 26–83 years) with median disease duration of 4.2 months (range 0.23 months to 19.4 years). Frequencies of US findings are summarised in Table I. Among the 100 ankles, synovitis of talocrural, subtalar and talonavicular joints were detected in 35, 33, and 27 ankles, respectively. Altogether, synovitis of the joints which the talus participates in was observed in 56 ankles. Ankle tenosynovitis was detected in 46 ankles at the medial recess (mainly tibialis posterior tendons), in 29 ankles at the lateral recess (peroneal tendons), and in 10 ankles at anterior aspects (extensors). Overall ankle tenosynovitis was observed in 61 ankles. Concerning Achilles tendon (AT) involvement, retrocalcaneal bursitis, AT enthesitis, AT tendonitis and AT paratendonitis was detected in 27, 22, 13, and 4 ankles, respectively. Overall AT involvement was observed in 39 ankles.

Table I.

	Early RA	Established RA	Overall
Number of ankles	62	38	100
Joint synovitis			
Talocrural joint synovitis (%)	32.2	39.5	35.0
Subtalar joint synovitis (%)	30.7	36.8	33.0
Talonavicular joint synovitis (%)	27.4	26.3	27.0
Overall (%)	48.4	68.4	56.0
Tenosynovitis			
Ankle flexors (TP, FDL, FHL) (%)	54.8	31.6	46.0
Peroneal tendons (PB, PL) (%)	33.9	21.1	29.0
Ankle extensors (TA, EDL, EHL) (%)	12.9	5.3	10.0
Overall (%)	69.4	47.4	61.0
Achilles tendon involvement			
Retrocalcaneal bursitis (%)	35.5	13.2	27.0
AT enthesitis (%)	19.4	26.3	22.0
AT tendonitis (%)	12.9	13.2	13.0
AT paratendonitis (%)	8.1	2.6	4.0
Overall (%)	38.7	39.5	39.0

TP: Tibialis posterior; FDL: flexor digitorum longus; FHL: flexor hallucis longus; PB: peroneus brevis; PL: peroneus longus; TA: tibialis anterior; EDL: extensor digitorum longus; EHL: extensor hallucis longus.

Association between US findings and disease duration

Disease duration was significantly shorter in ankles with tenosynovitis (mean ± SD: 11.4±21.6 months) than in ankles without tenosynovitis (32.0±58.3 months) (p=0.039) (Fig. 1). Disease duration was even more significantly shorter in ankles with isolated tenosynovitis (*i.e*. ankles with tenosynovitis but without joint synovitis) (5.9±8.7 months) than in all other ankles (25.2±47.8 months) (p=0.0016).

When classifying patients into those with early RA (duration <6 months) and those with established RA (duration >6 months), the 100 ankles in 74 patients were classified into 62 ankles in 47 early RA patients (median disease duration 2.8 months) and 38 ankles in 27 established RA patients (median disease duration 17.4 months). When the US evaluation was carried out, 81% of early RA patients were receiving no treatment, 2% were receiving methotrexate, 11% were receiving bucillamine, and 11% were receiving prednisolone (median dosage, 6 mg/day). Thirty percent of established RA patients were receiving no treatment, 37% were receiving methotrexate, 33% were receiving sulfasalazine, 11% were receiving taclorimus, 7% were receiving bucillamine, and 30% were receiving dual combination therapy. Eleven percent of established RA patients were receiving anti-TNF agents, and 41% were receiving prednisolone (median dosage, 5 mg/day). Ankle joint synovitis, ankle tenosynovitis, and AT involvement was observed in 48%, 69%, and 39% of ankles in early RA patients, respectively, and in 68%, 47%, and 40% of ankles in established RA patients, respectively (Table I). Tenosynovitis was significantly more common in ankles in early RA patients than in those with established RA (p=0.0357). Isolated tenosynovitis was significantly more common in ankles with early RA patients (39%) than in those with established RA (16%) (p=0.0236).

When classifying patients into those treated for less than 6 months and those treated for more than 6 months, the 100 ankles in 74 patients were classified into 78 ankles in 59 patients with short treatment (median treatment duration 0 months) and 22 ankles in 15 patients

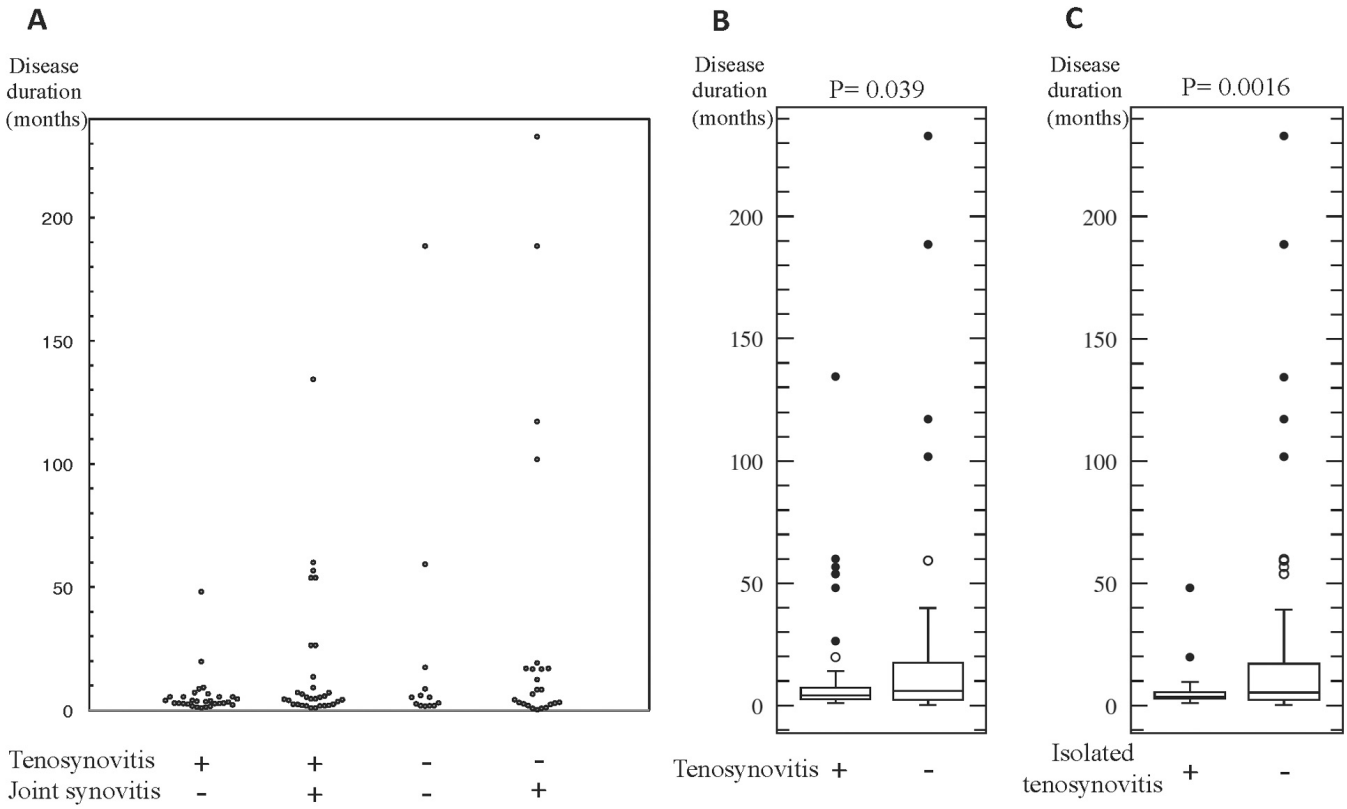

Fig. 1. Association between tenosynovitis and/or joint synovitis detected by US in symptomatic ankles, and disease duration in RA patients. **A.** Ankles were divided into four categories according to whether they were tenosynovitis positive or negative and whether they were joint synovitis positive or negative. **B.** Ankles were divided based on the presence or absence of tenosynovitis. **C.** Ankles were divided based on the presence or absence of isolated tenosynovitis (*i.e.* ankles with tenosynovitis but without joint synovitis).

with long treatment (median treatment duration 26 months). Joint synovitis was significantly more common in ankles in long-treated patients (82%) than in those in short-treated patients (49%) (p=0.0071). Isolated tenosynovitis was significantly more common in ankles in short-treated patients (37%) than in those in long-treated patients (5%) (p=0.0030).

Discussion

Although it is generally thought that hindfoot involvement exhibiting deformity or radiological erosions develops in later stages in RA, it is not uncommon for early RA patients to present swelling or tenderness in the ankle area (9). It seems that assessing ankle pathologies has become increasingly important for the early diagnosis of RA. For example, Harrison and Symmons showed in the NOAR cohort that persistent synovitis was predicted by the presence of RF, a tender joint count greater than six, and ankle synovitis (10).

Nevertheless, the number of reports that address the nature, distribution, and frequency of ankle pathologies in early RA is small (11). This may be partly because physical examination of synovial pathologies in RA ankles is often difficult, for several reasons. Anatomical structures in the ankle lie close together or may be overlying, making differentiation between adjacent structures problematic. Inflamed synovia are relatively small in size and located relatively deeply beneath the skin. Obesity, peripheral oedema, and predisposing degenerative conditions such as osteophytes, especially in elderly patients, also impede the detection of synovitis.

Recently, however, magnetic resonance imaging (MRI) and US, highly sensitive methods for detecting musculoskeletal pathologies, have made it easier to assess ankle lesions in early RA patients. Although MRI is currently accepted as the gold standard, accessibility issues, including cost, prevent it from being widely used for examination of symptomatic ankles in RA. In contrast, US is extremely versatile; it allows the examiner to image many joints during one examination, at low cost, and therefore is easy to use for checking symptomatic ankles. Wakefield *et al*. compared GSUS scans with physical examinations and contrast-enhanced high-field MRI in terms of the tests' ability to detect synovitis and tenosynovitis in symptomatic ankles of established RA patients with mean disease duration of 6.8 years, and concluded that GSUS was as specific as MRI, although GSUS was less sensitive than MRI and offered poorer interobserver reliability; the authors suggested that the nonuse of PDUS in their study might have decreased the apparent sensitivity of US (12).

Indeed, we have reported previously that PDUS is more sensitive than GSUS in detecting pathologic conditions in symptomatic ankles in RA patients (4). Recently, Filer *et al*. also demonstrated that PDUS has high sensitivity for detecting ankle synovitis (2). In addition,

Micu *et al*. reported that inter-observer reliability was good for ankle tenosynovitis when using PDUS (13). Thus, US appears to be the most useful and practical means for examining ankle pathologies in clinical rheumatologic practice.

To the best of our knowledge, this is the first study demonstrating a statistically significant relationship between the prevalence of ankle tenosynovitis and RA disease duration. Disease duration was significantly shorter in the ankles with tenosynovitis, and was even more significantly shorter in the ankles with isolated tenosynovitis. We also confirmed that tenosynovitis, especially isolated tenosynovitis, was significantly more common in symptomatic ankles in early RA patients than in those with established RA. In addition, our data suggest that ankle tenosynovitis is more frequently detected in medial and lateral recesses of the ankle.

Our observations can be partly explained by the fact that patients with established RA had received more aggressive drug treatment and/or had received longer treatment than patients with early RA. A recent report by Hammer *et al*. suggested that ankle tenosynovitis could be quickly improved by treatment with biologics (14). It is possible that joint synovitis is more refractory to treatment and more persistent than tenosynovitis in ankles with established RA. Nevertheless, an essential feature of ankle involvement in early RA is that tenosynovitis is more frequently observed than is joint synovitis.

Interestingly, tenosynovitis rather than joint synovitis has been reported to be the first structural change that occurs in TNF-mediated arthritis cases in human tumour necrosis factor (TNF)-transgenic mice (15). In that study, initial pathological change observed was tenosynovitis of the peroneal tendon in the hind paw, and this inflammation in the vicinity of the tendons subsequently spread onto adjacent joints, leading to the resorption of mineralised cartilage and bone. The authors of that study suggested that new cases of tenosynovitis should be taken seriously, since they might prefigure the development of RA. It may also be that tenosynovitis precedes the development of joint arthritis in some cases in the very early phase of human RA.

The most significant limitation of this study is that it is a retrospective study reviewing the US records of symptomatic ankles with RA. The examinations were performed due to clinical need, and the frequencies of the revealed pathologies were only relative. To explore the real prevalence of ankle tendon and joint involvement during the course of RA, a prospective study examining both symptomatic and asymptomatic ankles using US data should be performed.

In conclusion, the use of US for the early diagnosis of RA should be encouraged, and scanning symptomatic ankles using PDUS from both medial and lateral aspects, as well as the anterior aspect, is likely to be of benefit.

References

1. ALETAHA D, NEOGI T, SILMAN AJ *et al*.: Rheumatoid arthritis classification criteria: an American College of Rheumatology/European League Against Rheumatism collaborative initiative. *Arthritis Rheum* 2010; 62: 2569-81.
2. FILER A, DE PABLO P, ALLEN G *et al*.: Utility of ultrasound joint counts in the prediction of rheumatoid arthritis in patients with very early synovitis. *Ann Rheum Dis* 2011; 70: 500-7.
3. SCIRE CA, IAGNOCCO A, MEENAGH G *et al*.: Ultrasound imaging for the rheumatologist XXXIII. Sonographic assessment of the foot in early arthritis patients. *Clin Exp Rheumatol* 2011; 29: 465-9.
4. SUZUKI T, TOHDA E, ISHIHARA K: Power Doppler ultrasonography of symptomatic rheumatoid arthritis ankles revealed a positive association between tenosynovitis and rheumatoid factor. *Mod Rheumatol* 2009; 19: 235-44.
5. BACKHAUS M, BURMESTER GR, GERBER T *et al*.: Guidelines for musculoskeletal ultrasound in rheumatology. *Ann Rheum Dis* 2001; 60: 641-9.
6. WAKEFIELD RJ, BALINT PV, SZKUDLAREK M *et al*.: Musculoskeletal ultrasound including definitions for ultrasonographic pathology. *J Rheumatol* 2005; 32: 2485-7.
7. PUDDU G, IPPOLITO E, POSTACCHINI F: A classification of Achilles tendon disease. *Am J Sports Med* 1976; 4: 145-50.
8. LESIC A, BUMBASIREVIC M: Disorders of the Achilles tendon. *Current Orthopaedics* 2004; 18: 63-75.
9. BROOK A, CORBETT M: Radiographic changes in early rheumatoid disease. *Ann Rheum Dis* 1977; 36: 71-3.
10. HARRISON B, SYMMONS D: Early inflammatory polyarthritis: results from the Norfolk Arthritis Register with a review of the literature. II. Outcome at three years. *Rheumatology* (Oxford) 2000; 39: 939-49.
11. JAAKKOLA JI, MANN RA: A review of rheumatoid arthritis affecting the foot and ankle. *Foot Ankle Int* 2004; 25: 866-74.
12. WAKEFIELD RJ, FREESTON JE, O'CONNOR P *et al*.: The optimal assessment of the rheumatoid arthritis hindfoot: a comparative study of clinical examination, ultrasound and high field MRI. *Ann Rheum Dis* 2008; 67: 1678-82.
13. MICU MC, SERRA S, FODOR D, CRESPO M, NAREDO E: Inter-observer reliability of ultrasound detection of tendon abnormalities at the wrist and ankle in patients with rheumatoid arthritis. *Rheumatology* (Oxford) 2011; 50: 1120-4.
14. HAMMER HB, KVIEN TK: Ultrasonography shows significant improvement in wrist and ankle tenosynovitis in rheumatoid arthritis patients treated with adalimumab. *Scand J Rheumatol* 2011; 40: 178-82.
15. HAYER S, REDLICH K, KORB A, HERMANN S, SMOLEN J, SCHETT G: Tenosynovitis and osteoclast formation as the initial preclinical changes in a murine model of inflammatory arthritis. *Arthritis Rheum* 2007; 56: 79-88.