Usefulness of US to show subclinical joint abnormalities in asymptomatic feet of RA patients compared to healthy controls

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Abstract

Objective

The aim of the present study was to demonstrate the utility of ultrasound to show subclinical feet disease in RA.

Methods

The foot joints (talocrural, talocalcaneal, talonavicular, naviculocuneiform, calcaneocuboid, 5th tarsometatarsal and 1st to 5th metatarsophalangeal [MTP] joints) of 50 healthy subjects and 50 RA patients, with asymptomatic feet, were compared bilaterally. Statistical significance was set at 5%.

Results

Twenty-two joints were examined per individual (2200 in the entire sample). Significantly higher values were found in the RA group regarding quantitative synovitis in all joints recesses ($p<0.003$), the presence of synovitis ($p<0.035$) (except the 5thtarsometatarsal and 3rdMTP joint), power Doppler (PD) signals ($p<0.029$) (talocalcaneal, talonavicular, 1st, 2nd, 3rd and 4thMTP joints) and bone erosion ($p<0.003$) (except for the talocrural and talocalcaneal joints). Synovitis, PD signals and erosion were observed in 18.3% and 3.05% ($p<0.001$), 5.77% and 0.22% ($p<0.001$) and 34.45% and 2.85% ($p<0.001$) of the RA group and control group, respectively. Greater DAS-28, HAQ and FFI values were associated with ultrasound findings in only some joints ($p<0.046$). Interobserver agreement was ≤0.686 for semi-quantitative synovitis, ≤0.641 for quantitative synovitis, ≤0.474 for PD signals and ≤1.000 for erosion. Low Cohen Kappa values were found in the correlation between radiography and ultrasound (0.084-0.400).

Conclusions

Ultrasound on RA asymptomatic feet demonstrated a significantly greater number of inflammatory changes in current activity (synovitis, PD signals) and sequelae (erosion) in comparison to control subjects. In the midfoot, the talonavicular joint has the greatest number of ultrasound findings.

Key words

rheumatoid arthritis, ultrasonography, synovitis, foot joints

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Introduction

Rheumatoid arthritis (RA) affects the feet in about 90% of patients throughout the course of the disease, with prevalence values of 91% in women and 85% in men (1). Chronic inflammation of the foot joints and tendons results in irreversible structural changes, such as valgus deformity of the calcaneus, flattening of the medial longitudinal arch and tibialis posterior dysfunction, which can impair gait (2). In clinical practice, however, the evaluation of the hands takes preference over the feet in such patients.

Clinical evaluation of rheumatoid feet may be hindered by factors such as deformity, obesity and peripheral swelling. Thus, the clinical manifestations of RA are often underestimated. Radiography is limited regarding the determination of changes in soft tissues and does not allow the early detection of bone erosions (2). Computed tomography and magnetic resonance imaging (MRI) are useful for the early detection of abnormalities in rheumatoid feet, but these exams are expensive and complex (3).

Ultrasound does not detect subcortical bone lesions, but offers satisfactory accuracy, safety and low cost for the assessment of the feet and ankles of patients with rheumatic disease, assisting in the differential diagnosis between joint, tendon or enthesis clinical and subclinical involvement (4). In bowel disease and psoriatic arthritis, ultrasound is able to show subclinical entheseal involvement independently of clinical features and disease severity (5, 6).

Despite knowledge on early and often asymptomatic changes in the feet of patients with RA, the few ultrasound studies conducted generally involve patients with symptomatic feet and fail to determine intraobserver agreement (7).

The detection of synovitis in asymptomatic feet of patients with RA using ultrasound may help explain the progression of bone destruction in patients considered "stable" and assist in the evaluation of subclinical disease activity and therapeutic decision making.

The first aim of the present study was to demonstrate the utility of ultrasound to show subclinical feet disease in RA. The secondary aims were the following:

1. to compare joint ultrasound exams on asymptomatic feet of RA patients and healthy controls to assess the presence of subclinical articular findings;
2. to analyse the association between foot joint ultrasound and global disease activity, function and goniometry;
3. to determine intraobserver and interobserver agreement regarding foot joint ultrasound;
4. to analyse the correlation between ultrasound and radiography in the detection of bone erosion in patients with RA.

Methods

A cross-sectional study was conducted involving out-patients of the *Universidade Federal de São Paulo* (UNIFESP), Brazil and received approval from the UNIFESP ethics committee.

The sample size was calculated as n=42 (α=5%, β=20% and standard deviation for quantitative synovitis=0.8). However, eight individuals were added to each group to enhance the statistical power, totalling 50 patients with RA and 50 controls.

The control group was composed of healthy subjects (individuals accompanying the patients) with no history of rheumatic disease and were matched with the study group patients for age and gender.

Inclusion criteria to the Study group were the following: RA following the 1987 classification criteria of The American Rheumatism Association (8) with more them one year since diagnosis, age between 18 and 65 years, and asymptomatic feet. Patients with two clinical diagnoses and with "early" RA were not included.

Exclusion criteria were the following: peripheral venous insufficiency with retrograde venous flow and/or ochre dermatitis (9); "early" RA; previous surgical intervention and/or fracture in feet/ankles; intra-articular corticosteroid injection in previous three months in any of the joints evaluated; foot neuro-pathy; pain and swelling in feet or ankles.

Clinical evaluation

A blinded rheumatologist performed the clinical evaluation of the patients with RA. The evaluation involved the Disease Activity Score (DAS-28) (10), the Stanford Health Assessment Questionnaire (HAQ) (11), Foot Function Index (FFI) (12, 13) and goniometry of the foot and metatarsophalangeal (MTP) joints.

Ultrasound evaluation

The Mylab 30 CV (Esaote, Biomédica - Genoa, Italy) with a linear transducer with a frequency of 6 to 18MHz was used.The ultrasound exams were performed by blinded rheumatologist with six year experience in muscleskeletical ultrasonography.

Standardised quantitative and semi-quantitative ultrasound evaluations were performed in both groups on the following joints: talocrural, talocalcaneal (medial, lateral and posterior windows); dorsal face of calcaneocuboid, talonavicular, medial naviculocuneiform, 5th tarsometatarsal and metatarsophalangeal (MTP) (dorsal and volar faces of 1st to 5th MTP joints and lateral face of 1st and 5th MTP joints). During the examination, the upper limbs were covered with a sheet so that they could not be seen.

The following variables were measured on each evaluation:

1. *Synovitis*: A modified score was used for the semi-quantitative measurement, ranging from 0 to 3 (14): 0-no synovial thickening; 1-minimal synovial thickening in joint recess; 2-synovial thickening in entire joint recess causing bulging of joint capsule; and 3-synovial thickening in joint recess with bulging of joint capsule and extending to at least one bone diaphysis. "Presence of synovitis" was defined as synovial hypertrophy of at least Grade 1 in the semi-quantitative analysis (grey scale – ultrasound) (15).
2. *Synovial blood flow*: A semi-quantitative score (0-3) was employed (16): 0-no signal; 1-minimal signal, presence of simple vessels; 2-moderate signal, presence of confluent vessels with signal in less than 50% of the area evaluated; 3-intense signal (more than 50% of area evaluated). "Active synovitis" or "presence of PD signal" was defined as the presence of intra-articular synovitis with a positive PD signal (at least Grade 1).
3. *Bone erosion*: A previously established semi-quantitative score (0-3) was employed (14): 0-uniform bone surface; 1-irregular bone surface; 2-bone surface defect on two planes; 3-bone defect causing extensive bone destruction. The "presence of erosion" was defined as the presence of at least Grade 2 erosion.

Radiographic evaluation

A blinded radiologist analysed the presence of erosion in each joint studied (17). For such, ankle (AP and profile) and foot (AP and profile with load) radiographs were taken.

Intra- and interobserver agreement

The patients with RA were submitted to clinical and ultrasound evaluations of the feet and ankles on the same day. The ultrasound measurements intra-observer/interobserver agreement was performed on the talocrural, talonavicular and 5th MTP joints, using 20% of the sample. For this, the ultrasound exams were performed by another rheumatologist.

Statistical analysis

Either the Student's *t*-test or the Mann-Whitney test was used for the comparison of the continuous variables, depending on the normality of the data. The categorical variables were compared between groups using either Pearson's chi-squared test or Fisher's exact test. Cohen's Kappa index and Spearman's correlation coefficient were used in the evaluation of intraobserver and interobserver agreement. Statistical significance was set at 5%.

Results

Twenty-two joints per individual were examined (2200 in the entire sample). As more than one joint recess was evaluated in some joints (3 in the talocalcaneal joint [posterior, medial and lateral] for synovitis, PD signal and erosion; 2 in the 1st to 5th MTP joints [dorsal and volar] for synovitis, PD signal and ero-

Table I. Characteristics of sample.

	Study group (n=50)	Control group (n=50)	*p*-value
Age (years); mean (± SD)	49.4 (10.8)	49.2 (11.4)	0.928*
Gender (F:M)	43:07	43:07	1.000**
Weight (kg); mean (± SD)	65.59 (10.50)	69.60 (12.73)	0.089*
Height (m); mean (± SD)	1.56 (0.70)	1.59 (0.10)	0.112*
BMI (kg/m^2); mean (± SD)	26.86 (3.79)	27.55 (4.26)	0.398*
Positive RF	31 (62%)	–	–
Presence of morning stiffness	12 (24%)	–	–
Years of disease; mean (± SD)	9.81 (6.12)	–	–
Functional type I:II:III	39:10:1	–	–
NSAID use	5	–	–
Use of corticoid	24	–	–
Use of DMARDs	47	–	–
Use of methotrexate	36	–	–
Use of leflunomide	21	–	–
Uso of CDP	4	–	–
Use of SSA	1	–	–
Use of immunobiological	5	–	–
ESR (mm/1sth); mean (± SD)	21.30 (15.70)	–	–
HAQ (0-3); mean (± SD)	0.575 (0.551)	–	–
DAS-28; mean (± SD)	3.52 (1.12)	–	–
FFI (0-100); mean (± SD)	12.40 (12.30)	–	–

n: number of patients; F: female; M: male; SD: standard deviation; BMI: body mass index; RF: rheumatoid factor; NSAID: non-steroidal anti-inflammatory drug; DMARDs: disease-modifying anti-rheumatic drugs; CDP: chloroquinediphosphate; SSA: sulfasalazine; ESR: erythrocyte sedimentation rate; HAQ: Stanford Health Assessment Questionnaire; DAS-28: Disease Activity Score - 28 joint assessment; FFI: Foot Functional Index; Statistical tests: *Student's *t*-test; **Pearson's chi-squared test; (-): data evaluated only in study group (calculation of *p*-value not possible).

Table II. Comparison between groups regarding quantitative evaluation of synovitis using ultrasound.

Joint (n=100 for each joint)		Study group Mean mm (± SD)	Control group Mean mm (± SD)	*p*-value
Talocrural		1.46 (0.80)	0.78 (0.30)	<0.001
Talocalcaneal (Posterior)		1.13 (0.94)	0.70 (0.22)	0.002
Talonavicular		1.45 (0.78)	0.95 (0.57)	<0.001
Naviculocuneiform		0.67 (0.58)	0.44 (0.20)	< 0.001
Calcaneocuboid		0.50 (0.40)	0.32 (0.11)	<0.001
5th tarsometatarsal		0.40 (0.35)	0.26 (0.13)	<0.001
1st MTP	dorsal	1.77 (0.93)	1.42 (0.9)	0.002
	volar	0.76 (0.59)	0.42 (0.23)	<0.001
2nd MTP	dorsal	1.30 (0.91)	0.76 (0.46)	<0.001
	volar	0.57 (0.39)	0.35 (0.11)	<0.001
3rd MTP	dorsal	1.04 (0.76)	0.58 (0.24)	<0.001
	volar	0.48 (0.20)	0.34 (0.10)	<0.001
4th MTP	dorsal	0.85 (0.60)	0.60 (0.54)	<0.001
	volar	0.55 (0.37)	0.34 (0.11)	<0.001
5th MTP	dorsal	0.77 (0.65)	0.46 (0.24)	<0.001
	volar	0.60 (0.43)	0.32 (0.14)	<0.001

n: number of each joint; SD: standard deviation; MTP: metatarsophalangeal; Statistical test: Mann-Whitney test.

sion; 1 extra recess in the 1st and 5th MTP joints [lateral] for erosion), a total of 1800 joint recesses were evaluated for synovitis and PD in each group (total: 3600 joint recesses) and 2000/group were evaluated for erosion (total: 4000 joint recesses). Table I displays the characteristics of the sample, demonstrating homogeneity between the groups.

Ultrasound evaluation

1. Quantitative evaluation of synovitis

The study group had significantly higher values than the control group for all measurements in all joints studied, with *p*-values ranging from <0.001 to 0.003 (Table II).

2. Semi-quantitative evaluation of synovitis, PD signals and erosion

The study group had a significantly higher occurrence of synovitis (at least Grade 1) in the following joints: talocrural, talocalcaneal (3 windows), talonavicular, naviculocuneiform, calcaneocuboid, 1st MTP (dorsal and volar faces), 2nd MTP (dorsal and volar faces), 3rd MTP (dorsal face), 4th MTP (dorsal and volar faces) and 5th MTP (dorsal and volar faces), with *p*-values ranging from <0.001 to 0.035. Among the total of 1800 joint recesses evaluated in each group, synovitis was found in 333 (18.3%) in the study group and 55 (3.05%) in the control group ($p<0.001$). The study group had a significantly higher frequency of PD signals (at least Grade 1) in the following joints: talocalcaneal (lateral window), talonavicular, 1stMTP (dorsal face), 2nd MTP (dorsal face), 3rd MTP (dorsal face) and 4th MTP (dorsal face). Among the 1800 joint

Table III. Comparison between groups regarding synovitis, Power Doppler signals and bone erosion using ultrasound.

Joint (n=100 for each joint)		SG SYN (1800 JR)	CG SYN (1800 JR)	*p*-value	SG PD (1800 JR)	CG PD (1800 JR)	*p*-value	SG BE (2000 JR)	CG BE (2000 JR)	*p*-value
Talocrural		36	1	<0.001*	5	0	0.059*	4	0	0.121*
Talocalcaneal	*Posterior*	*27*	*0*	*<0.001**	*4*	*0*	*0.121**	*13*	*1*	*0.001**
	Medial	12	0	<0.001*	4	0	0.121*	5	0	0.059*
	Lateral	15	0	<0.001*	6	0	0.029*	4	0	0.121*
Talonavicular		42	15	<0.001*	17	1	<0.001*	38	2	<0.001*
Naviculocuneiform		12	0	< 0.001**	4	0	0.121*	32	3	<0.001*
Calcaneocuboid		7	0	0.014*	3	0	0.246*	9	0	0.003*
5th tarsometatarsal		6	1	0.118*	2	1	1.000	12	0	<0.001*
1st MTP	dorsal	44	28	0.018**	19	1	<0.001*	48	3	<0.001*
	Volar	19	5	0.004*	4	0	0.121	32	3	<0.001*
	lateral	-	-	-	-	-	-	81	14	<0.001*
2nd MTP	dorsal	32	3	<0.001*	14	0	<0.001*	62	2	<0.001*
	Volar	13	0	<0.001*	0	0	1.000*	17	0	<0.001*
3rd MTP	dorsal	21	1	<0.001*	11	0	0.001*	51	3	<0.001*
	Volar	5	0	0.059*	0	0	1.000*	12	0	<0.001*
4th MTP	dorsal	16	0	<0.001*	6	0	0.029*	41	4	<0.001*
	Volar	8	0	0.007*	1	1	1.000*	16	0	<0.001*
5th MTP	dorsal	8	1	0.035*	4	0	0.121*	82	7	<0.001*
	Volar	10	0	0.010*	0	0	1.000*	41	3	<0.001*
	lateral	–	–	–	–	–	–	89	12	<0.001*
Total of affected JR		333(18.3%)	55(3.05%)	<0.001**	104(5.77%)	4(0.22%)	<0.001**	689(34.45%)	57(2.85%)	<0.001**

n: number of each joint; SG: study group; CG: control group; MTP: metatarsophalangeal; JR: joint recesses; Statistical tests: *Fisher's exact test; **Pearson's chi-squared test; At least grade 1 synovitis (SYN) and Power Doppler (PD) and at least grade 2 bone erosion (BE) on semi-quantitative scores; (–): Lateral face of 1st and 5th MTP joints not evaluated for synovitis or PD.

Table IV. Association between DAS-28, HAQ and FFI and presence of synovitis, PD signals and bone erosion in study group.

Joint (n=100 for each joint)	DAS-28 *vs*. SYN (*p*)	DAS-28 *vs*. PD (*p*)	DAS-28 *vs*. BE (*p*)	HAQ *vs*. SYN (*p*)	HAQ *vs*. PD (*p*)	HAQ *vs*. BE (*p*)	FFI *vs*. SYN (*p*)	FFI *vs*. PD (*p*)	FFI *vs*. BE (*p*)
Talocrural	0.137	0.045	0.229	0.653	0.160	0.593	0.725	0.125	0.438
Talocalcaneal	*0.142*	*0.400*	*0.085*	*0.067*	*0.833*	*0.024*	*0.265*	*0.860*	*0.178*
Talonavicular	0.465	0.346	0.023	0.961	0.704	0.355	0.116	0.424	0.352
Naviculocuneiform	0.149	0.025	0.153	0.027	0.022	0.028	0.104	0.157	0.001
Calcaneocuboid	0.032	0.157	0.608	0.913	0.702	0.041	0.850	0.414	0.353
5th tarsometatarsal	0.119	0.062	0.420	0.446	–	0.001	0.113	–	0.007
1st MTP	0.147	0.493	0.449	0.473	0.573	0.849	0.464	0.861	0.770
2nd MTP	0.067	0.508	0.726	0.054	0.588	0.833	0.227	0.450	0.709
3rd MTP	0.763	0.668	0.998	0.263	0.973	0.316	0.986	0.757	0.772
4th MTP	0.202	0.352	0.123	0.743	1.000	0.094	0.778	0.675	0.797
5th MTP	0.090	0.618	0.072	0.020	0.098	0.469	0.099	0.168	0.292

n: number of each joint; MTP: metatarsophalangeal; PD: Power Doppler; DAS-28: Disease Activity Score - 28 joint assessment; HAQ: Stanford Health Assessment Questionnaire; FFI: Foot Functional Index; Statistical tests: Pearson's chi-squared test for DAS-28 and Mann-Whitney test for HAQ and FFI; * DAS-28 categorised as remission *vs*. activity; At least grade 1 synovitis (SYN) and Power Doppler (PD) and at least grade 2 bone erosion (BE) on semi-quantitative scores; (-): not possible to perform statistical analysis because only one patient had PD signals in both right and left joints (insufficient positive data for calculation).

recesses evaluated in each group, PD signals were detected in 104 (5.77%) in the study group and four (0.22%) in the control group ($p<0.001$).

The study group had a significantly higher occurrence of erosion (at least Grade 2) in the following joints: talocalcaneal (posterior window), talonavicular, naviculocuneiform, calcaneocuboid, 5th tarsometatarsal, 1st MTP (dorsal, volar and lateral faces), 2nd MTP (dorsal and volar faces), 3rd MTP (dorsal and volar faces), 4th MTP (dorsal and volar faces) and 5th MTP (dorsal, volar and lateral faces). Bone erosion was the most common ultrasound finding in the study group. Among the 2000 joint recesses evaluated in each group, erosion was found in 689 (34.45%) in the study group and 57 (2.85%) in the control group ($p<0.001$). Table III displays the comparison of ultrasound findings in both groups regarding synovitis, PD signals and erosion.

3. Associations between foot ultrasound exams, global disease activity (DAS-28), and function (HAQ and FFI)

In the analysis of associations between ultrasound findings and the DAS-28 (categorised based on the degree of activity – remission [≤2.6], low activity [2.7-3.2], moderate activity [3.3-5.2], high activity [>5.2]), this index proved positively associated with synovitis in the calcaneocuboid joint ($p=0.032$), PD signals in the talocrural ($p=0.045$) and naviculocuneiform ($p=0.025$) joints and erosion in the talonavicular joint ($p=0.023$). The "presence of erosion" had a statistical association with "moderate activity" (DAS-28) in comparison to the "absence of erosion" in the talonavicular joint ($p=0.023$) (Table IV).

Higher HAQ values were associated with synovitis in the naviculocuneiform ($p=0.027$) and 5th MTP ($p=0.020$) joints, PD signals in the naviculocuneiform joint ($p=0.022$) and erosion in the talocalcaneal ($p=0.024$), naviculocuneiform ($p=0.028$), calcaneocuboid ($p=0.041$) and 5thtarsometatarsal ($p=0.001$) joints. Higher FFI values were only associated with erosion in the naviculocuneiform and 5th tarsometatarsal joints, with *p*-values of 0.001 and 0.007, respectively (Table IV).

4. Association between foot ultrasound and goniometry in patients with RA

With regard to synovitis (at least Grade 1 in semi-quantitative analysis), a significant association was found only for a reduction in the extension of the 3rd MTP joint ($p=0.042$). PD (at least Grade 1) was only significantly correlated with lower extension values for the 1st MTP ($p=0.034$) and 4thMTP ($p=0.010$) joints. Erosion (at least Grade 2) was only significantly correlated with lower flexion and extension values for the 4th MTP joint ($p=003$ and $p=0.021$, respectively).

5. Intra- and interobserver agreement for foot ultrasound

Regarding the quantitative measurement of synovitis, good intraobserver agreement was found for all joints studied, with higher r values on the talonavicular (0.734) (measurement 1), talocrural (0.719) (measurement 2) and 5thMTP (0.725) (volar measurement) joints. For all measurements in this analysis, *p*-values were <0.001. Regarding interobserver agreement, the best r values were found for the dorsal and volar faces of the 5th MTP joint (0.641 and 0.465, respectively), both with <0.001 (Table V).

Regarding the presence of synovitis, a good intraobserver agreement was found for the joints studied, with percentage of exact agreement (PEA) values ranging from 92.5% (dorsal face of 5th MTP joint) to 100% (volar face of 5th MTP joint). Kappa values were 0.828 for the talocrural joint ($p<0.001$), 0.886 for the talonavicular joint ($p<0.001$), 0.375 for the dorsal face of the 5thMTP joint ($p=0.002$) and 1.000 for the volar face of the 5th MTP joint ($p<0.001$). Good interobserver agreement was also found, with PEA values ranging from 82.5% (talonavicular joint) to 90% (talocrural jointand volarface of the 5thMTP joint) (Table V).

Table V. Intraobserver and interobserver agreement for synovitis, PD signals and bone erosion.

Intraobserver agreement								
Joint		SYN Quantitative	SYN Semiquantitative		PD Semiquantitative		BE Semiquantitative	
		Spearman (*p*)	PEA	Kappa (*p*)	PEA	Kappa (*p*)	PEA	Kappa (*p*)
Talocrural		0.719 (<0.001)	95%	0.828 (<0.001)	100%	1.000 (<0.001)	95%	-0.026 (0.871)
Talonavicular		0.734 (<0.001)	95%	0.886 (<0.001)	87.5%	–	87.5%	0.541 (0.001)
5th MTP	Dorsal	0.622 (<0.001)	92.5%	0.375 (0.002)	100%	-1.000 (<0.001)	90%	0.798 (<0.001)
	Volar	0.725 (<0.001)	100%	1.000 (<0.001)	100%	1.000 (<0.001)	85%	0.643 (<0.001)
	Lateral	–	–	–	–	–	90%	0.798 (<0.001)
Interobserver agreement								
Joint		SYN Quantitative	SYN Semiquantitative		PD Semiquantitative		BE Semiquantitative	
		Spearman (*p*)	PEA	Kappa (*p*)	PEA	Kappa (*p*)	PEA	Kappa (*p*)
Talocrural		0.404 (0.010)	90%	0.713 (<0.001)	100%	1.000 (<0.001)	100%	1.000 (<0.001)
Talonavicular		0.379 (0.016)	82.5%	0.557 (<0.001)	100%	1.000 (<0.001)	90%	0.304 (0.007)
5th MTP	Dorsal	0.641 (<0.001)	85%	0.318 (0.039)	97.5%	0.474 (0.003)	80%	0.600 (<0.001)
	Volar	0.465 (0.002)	90%	0.286 (0.053)	100%	1.000 (<0.001)	82.5%	0.557 (<0.001)
	Lateral	–	–	–	–	–	80%	0.614 (<0.001)

SYN: synovitis; PD: Power Doppler; BE: bone erosion; MTP: metatarsophalangeal; PEA: percentage of exact agreement; (–): lateral face of 5th MTP joint not evaluated for synovitis or PD; (– –): Statistical correlation analysis not possible for PD in talonavicular joint.

Good intraobserver agreement was found for PD signals in the joints studied, with PEA values ranging from 87.5% (talonavicular joint) to 100% (talocrural joint anddorsal and volar faces of the 5th MTP joint). When it was possible to calculate this index, Kappa values were 1.000 for the talocrural joint ($p<0.001$), 1.000 for the dorsal face of the 5th MTP joint ($p<0.001$) and 1.000 for the volar face of the 5th MTP joint ($p<0.001$). Inter-observer agreement was considered good, with PEA values ranging from 97.5% (dorsal face of the 5th MTP joint) to 100% (talocrural and talonavicular joints and volar face of the 5th MTP joint) (Table V).

Good intraobserver agreement was also found for erosion, with PEA values ranging from 85% (volar face of the 5th MTP joint) to 95% (talocrural joint). Kappa values were -0.026 for the talocrural joint ($p=0.871$), 0.541 for the talonavicular joint ($p<0.001$), 0.798 for the dorsal face of the 5th MTP joint ($p<0.001$), 0.643 for the volar face of the 5th MTP joint ($p<0.001$) and 0.798 for the lateral face of the 5thMTP joint ($p<0.001$). Good interobserver agreement was observed, with PEA values ranging from 80% (dorsal and lateralfaces of the 5th MTP joint) to 100% (talocrural joint) (Table V).

Correlation between radiography and ultrasound for detection of bone erosion in patients with RA

This analysis was performed by a blinded radiologist with a 30-year-experience in musculoskeletal radiology and the ultrasonography expert.

Good correlations between radiography and ultrasound were found only for the talocalcaneal, talonavicular, naviculocuneiform and calcaneocuboid joints ($p=0.009$, $p<0.001$, $p=0.002$ and $p=0.009$, respectively). The radiologist detected erosion in 34 joints, whereas the ultrasound examiner detected erosion in 66 joints. Similar data were found regarding the other MTP joints, but with a smaller degree of difference (Table VI).

Discussion

RA affects the feet in a large number of cases. If not diagnosed and treated early enough, this condition can lead to irreversible structural alterations that can go on to compromise gait and quality of life (18).

The majority of studies involving the analysis of RA using ultrasound address the hands and wrists. The few studies addressing the feet and ankles of patients with RA generally assess symptomatic feet (2, 19). Thus, the finding of subclinical synovitis in these joints is likely underestimated in daily practice. According to Riente and collaborators (2011), an ultrasound exam of rheumatoid feet is more sensitive than a clinical exam for the detection of joint inflammation and allows a better understanding of the characteristics and progression of the disease, as suggested in a study published in 1999 (20, 21).

Ultrasound of MCP and MTP joints have been considered superior to x-ray to detect erosive disease and comparably sensitive to MRI to detect synovitis in mild and moderate RA (22) and, in an early arthritis setting, high scores of joint effusion, synovial hypertrophy and power Doppler together of MTP joints, are suggestive of RA when compared to undifferentiated arthritis, spondyloarthritis and non-inflammatory diseases (23).

The main purpose of the present study was to compare ultrasound findings of the feet of healthy controls and asymptomatic feet of patients with RA to

Table VI. Correlation between radiography and ultrasound regarding detection of bone erosion.

Joint (n=100 for each joint)	Bone erosion radiography x US		
	PEA	Kappa (p)	*p*-value
Talocrural	80%	0.107 (0.126)	0.178*
Talocalcaneal	*83%*	*0.285 (0.002)*	*0.009**
Talonavicular	72%	0.400 (<0.001)	<0.001**
Naviculocuneiform	72%	0.299 (0.002)	0.002**
Calcaneocuboid	83%	0.285 (0.002)	0.009*
5th tarsometatarsal	68%	0.154 (0.058)	0.100*
1st MTP	34%	-0.084 (0.140)	0.140**
2nd MTP	47%	0.088 (0.190)	0.213*
3rd MTP	52%	0.048 (0.594)	0.594**
4th MTP	59%	0.136 (0.150)	0.150**
5th MTP	49%	0.033 (0.368)	0.620*

n: number of joints; US: ultrasound; MTP: metatarsophalangeal; PEA: percentage of exact agreement; Statistical tests: *Fisher's exact test; **Pearson's chi-squared test.

determine whether there is a greater frequency of subclinical synovitis, PD signals and erosion in the latter group, despite being asymptomatic. While not the gold standard (magnetic resonance), ultrasound was chosen as the imaging method due to its low cost, practicality, rapid execution and good level of acceptance on the part of patients. Ultrasound was compared to radiography for the detection of erosion to confirm the superiority of the former in different joints of the foot. This superiority has been demonstrated for joints of the hand (24), but few studies have demonstrated it in the feet (19).

In the present study, a greater number of ultrasound alterations were found in the study group, especially for the qualitative (semi-quantitative) variables of synovitisand erosion. Synovitis was found in 18.33% and 3.05% and PD signals were found in 5.77% and 0.22% of joint recesses in the study and control groups, respectively, among a total of 1800 joint recesses evaluated for these variables using ultrasound. Moreover, erosion was found 34.45% and 2.85% of joint recesses in the study and control groups, respectively, among the 2000 joint recesses evaluated for this variable.

Practically all the joints studied (with the exception of the 5th tarsometarsal) had a greater frequency of synovitis (OMERACT concept) in the study group. This finding demonstrates the importance of assessing rheumatoid feet, even when asymptomatic, as well as the pertinence of ultrasound as a complement to the physical exam in such patients.

The small degree of PD signal detection in the study group may partially be explained by the duration of the disease (mean: 9.81 years), as PD signals are correlated with early onset synovial hypertrophy in the MCP joints using magnetic resonance (25). However, with the exception of four joint recesses in the control group (0.22%), PD signals were only detected in the study group. This was therefore the least common ultrasound alteration in the control group, suggesting that PD signals are more specific to joint inflammation disease.

Although seen in 2.85% of joint recesses in the control group, bone erosion was the most common ultrasound alteration in the study group (34.45%), suggesting prior subclinical inflammation in the joints of the foot. Besides being asymptomatic, these joints had apparently suffered or are suffering continual joint damage.

The joints that exhibited the greatest number of ultrasound alterations (synovitis, PD signals and erosion) in the study group over the control group were the talonavicular, 1st MTP, 2nd MTP, 3rd MTP and 4th MTP joints. Subclinical synovitis in the MTP joints was expected, as these joints are known to be affected early in RA. However, the present results draw attention to the talonavicular joint, which is underrated in the routine evaluation of these patients.

No repeated association pattern was found between ultrasoundof the foot joints and the DAS-28, HAQ, FFI or goniometric measures. No studies were found in the literature on the ultrasound examination of rheumatoid feet assessing the association between this exam and global or specific function in patients with RA that could be used for purposes of comparison. The present study is the first to perform such an analysis.

Three previous studies have employed ultrasound to assess the feet of healthy individuals (with no known rheumatic disease). Koski (1990) reports that bone-joint capsule distances greater than 3mm in the MTP joints should be considered pathologic (280 joints evaluated) (26).

Schmidt *et al*. (2004) evaluated 102 healthy individuals (204 joints of each subtype) and described quantitative values for the measurement between the joint capsule and subchondral bone in different joints; the following measurements (±2 SD) were respectively found for the talocrural, talonavicular, 1st MTP and 2nd MTP joints: 1.1mm (1.0), 1.4mm (1.2), 1.7mm (1.8) and 1.6mm (1.5) (15). However, the study cited did not aggregate these quantitative values with semi-quantitative values of synovitis and/or PD signals, as suggested by OMERACT.

Luukkainen *et al*. (2009) evaluated the talocrural and MTP joints in 50 healthy individuals and found upper normal mean values of 2.7mm and 2.8mm, respectively (27). This finding resembles that reported in the study by Koski for the MTP joints (26).

The present study found smaller quantitative measurements of synovitis in comparison to these studies conducted with healthy individuals.

Wakefield *et al*. (1999) used ultrasound to detect synovitisin rheumatoid feet, assessing the MTP joints of 30 patients with onset RA (symptomatic and asymptomatic feet) and 20 healthy controls, and found synovitisin 131 of the 300 MTP joints (44%) in the RA group and only twoof the 100 MTP joints (2%) in the control group (19). The present study found a lower number of joints with synovitis in the RA

group (117 among 500 joints; 23.4%) as well as the control group (33 among 500 joints; 0.66%). This finding in the study group may be associated with the lack of symptoms (pain, increased sensitivity and/or joint swelling) in the feet of patients in the present study, whereas the finding in the control group may be related to the larger sample size in the present study.

Rienteand *et al*. (2011) evaluated 100 patients with RA with symptomatic (85%) or asymptomatic feet. The authors found that synovitis and erosion were respectively more present in 2nd and 5th MTP joints. These findings are very similar to those of the present study. The study cited also evaluated the talonavicular, calcaneocuboid and 4th and 5th tarsometatarsal joints and found that the talonavicular joint was the most affected (18%) (20). This joint was also the most affected (42%) in the midfoot of the patients with RA in the present study.

Only two previous studies have evaluated interobserver agreement in the ultrasound examination of rheumatoid feet (2, 14). Szudlarek *et al*. (2003) found good interobserver agreement in the evaluation of semi-quantitative scores of synovitisand erosion for the 1st and 2nd MTP joints (intraclass correlation coefficient [ICC]=0.81 and 0.89 for synovitis and ICC=0.79 and 0.85 for erosion, respectively) (12). The present study found a smaller ICC for synovitisin the 5th MTP joint (0.281 for the dorsal face and 0.403 for the volar face) as well as lower ICC values for the semiquantitative erosion score (0.680 for the dorsal face of the 5th MTP joint).

Wakefield *et al*. (2008) evaluated interobserver agreement regarding synovitis in five patients with RA (2). The present study found better interobserver agreement regarding the talocrural and talonavicular joints with a larger sample (20 individuals). The present results resemble those described by Schmidt *et al*. (2004) (15), who found better ICC values in the evaluation of interobserver agreement regarding synovitis in healthy individuals in measurements equivalent to the present measurement 2 of the talocrural joint, measurement 1 of the talonavicular joint and the measurement of the dorsal face of the MTP joints.

The present study has practical importance in the evaluation of feet in patients with RA, offering a better understanding of the role of ultrasound in the diagnosis of subclinical alterations, considering the difficulties encountered with a physical exam. This study also draws attention to the fact that inflammation and joint damage are found in asymptomatic feet of patients with RA. Thus, these joints should be actively investigated in such patients even in the absence of clinical complaints.

However, further studies are needed to determine what ultrasound joint parameters are prospectively correlated with joint foot damage and progression of the disease. The results of the present study confirm the authors' impression that greater importance should be given to rheumatoid feet, even when asymptomatic, and reinforce the importance of joint ultrasound in the detection of subclinical alterations in patients with RA.

In conclusion, rheumatoid feet, even when asymptomatic, exhibited a greater number of ultrasound alterations in comparison to the control group. Among the joints evaluated, the talonavicular had the greatest number of alterations, exhibited the best correlation between radiography and ultrasoundin the detection of erosion and achieved good inter- and intraobserver agreement regarding joint ultrasound.

Key messages

- Rheumatoid feet, even when asymptomatic, exhibited joint ultrasound alterations;
- Talonavicular joint showed more ultrasound alterations, best correlation radiography/ultrasound for erosion and good inter/intraobserver agreement;
- More studies are needed to determine what ultrasound parameters are prospectively correlated with joint damage and disease progression.

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