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Do ankle, hindfoot, and heel ultrasound findings predict the symptomatology and quality of life in rheumatoid arthritis patients?

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ankle, rheumatoid arthritis, quality of life, ultrasound, baropodometry

Abstract

Objectives: To evaluate the ankle, hindfoot, and heel changes (determined by physical examination, ultrasound and baropodometry) in patients with rheumatoid arthritis, to compare the findings with healthy subjects, and to analyze if these findings are associated with ankle pain and could affect the quality of life. **Methods:** We enrolled 35 rheumatoid arthritis patients and 35 healthy controls, and evaluated their ankles (tibiotalar joints, tendons), hindfeet (talonavicular, subtalar joints) and heels using clinical examination, DAS28-CRP, RAPID3 for the evaluation of functional status, quality of life in rheumatoid arthritis questionnaire, ultrasound, and baropodometry. **Results:** The ultrasound inter-observer agreement was good for the subtalar joint, and very good for the other structures. Flat foot was identified in 50% of feet in rheumatoid arthritis patients, with 83.8% having concomitant hindfoot valgus and less subtalar joint synovitis visible from the lateral approach (32.4% *vs* 55.6%, $p = 0.041$). The body mass index, RAPID3 and subtalar synovitis were independent predictors for the symptomatic ankle (all $p < 0.05$). Midfoot and heel plantar pressures were higher in rheumatoid arthritis patients compared to healthy controls, but when subtalar synovitis was present, the pressures decreased (avoidance of heel support). Poor quality of life in rheumatoid arthritis patients was independently predicted by DAS28-CRP, RAPID3, disease stage, hindfoot valgus, tibiotalar and subtalar synovitis, tendon pathology, Achilles tendon enthesophytes, calcaneal erosions, plantar fasciitis, and perifasciitis (all $p < 0.05$). **Conclusion:** The quality of life of rheumatoid arthritis patients is significantly affected by ankle and hindfoot pathology (inflammatory modifications, but also degenerative findings and deformities). Ultrasound scanning is an important tool in the evaluation of inflammatory and degenerative lesions in these regions, and their early detection might contribute to a better therapeutic management in these patients.

Introduction

Rheumatoid arthritis (RA) is a chronic and progressive systemic disease that leads progressively to joint damage and disability[1,2]. Approximately half of patients with RA report foot or ankle joints symptoms as the first manifestation of the disease[3,4], and in time 71% of these patients develop walking disability[5].

The quality of life (QoL) in RA patients is poorer compared to the general population, and even lower in those with foot involvement, especially regarding mobility, functionality, daily activities, and mental health[3,6]. The involvement of the hindfoot (talonavicular [TN] and subtalar [ST] joints) is associated with functional disability and walking difficulties[7]. However, feet are seldom examined in RA patients, the main reason being the omission of these joints in the most commonly used disease activity score with 28 joint count (DAS-28), and patients not being routinely referred to a podiatrist[8].

Baropodometry is a method that analyses foot dysfunctions by measuring and mapping the plantar surface pressures during standing and walking[9]. RA patients suffer several gait adaptations consisting of reduced walking speed, cadence, stride length and ankle power, double limb support time during walking, and increase of the peak forefoot plantar pressure[10]. In order to compensate for their foot dysfunction, they alter the patterns of foot loading by decreasing the duration and velocity of the center of pressure[11]. The increase in midfoot plantar pressure is an independent predictor for falls in RA patients[12]. There are only a few studies that reported or evaluated plantar pressures in RA patients[13,14].

Ultrasonography (US) is considered to be superior to clinical examination in the detection of synovitis, and its contribution to detecting damage from the early stages, evaluating the therapeutic response, monitoring disease activity or assessing persistent inflammation has been underlined in the European League Against Rheumatism (EULAR) recommendations[15]. However, as we previously noted in our systematic review[16], only few studies have been published on US findings for ankle and hindfoot in RA patients. Only one study has explored links between US-detected synovitis (subclinical) of the foot and ankle, and poor QoL and functional status[17].

The aim of the study was to evaluate the ankle, hindfoot, and heel in RA patients using clinical examination, US, and baropodometry, in order to determine the prevalence of lesions, compare the findings with healthy control subjects, and establish which factors have a significant impact on the presence of symptomatic ankle or poor QoL scores. Also, we assessed the role of US in identifying factors that can be influenced to prevent further damage, deformities and foot dysfunction in RA patients.

Material and methods

Patients and healthy controls

Consecutive RA patients presenting to the day-hospital department were enrolled between April and December 2018 in this observational, cross-sectional study. The inclusion criteria were: diagnosis of RA according to the 2010 American College of Rheumatology (ACR)/EULAR classification criteria[1], stable treatment in the past 3 months, and age over 18 years. The exclusion criteria included: unstable treatment in the past 3 months before enrollment [need for nonsteroidal anti-inflammatory or antalgic drugs, increase or decrease in oral steroid therapy, synthetic or biological disease-modifying anti-rheumatic drugs (DMARD) initiation, switch or combination, or topical administration of steroid drugs], history of foot and ankle surgery, trauma, tendinosis, other causes of architectural changes within the feet and ankles (e.g. diabetes, osteoarthritis), other inflammatory rheumatoid diseases (e.g. crystal arthropathies, spondylarthritis, etc.), and history of cancer with bone metastasis, including suspect pulmonary nodules where further evaluation was indicated.

The group of patients was compared to healthy control (HC) subjects matched for age, sex, and body mass index (BMI). The HC status was defined as asymptomatic subjects with no history of surgery, trauma, inflammatory and non-inflammatory diseases (including osteoarthritis) on the foot and ankle levels, and no architectural changes of the feet and ankles.

All the patients and subjects provided written informed consent before study enrollment. Also, the approval of the University Ethics Committee, number 51, of 22 January 2018, was obtained.

Clinical examination

The RA patients were examined by a rheumatologist with 4 years' experience in rheumatology (IP) following a pre-established protocol. Demographic data and the presence of pain at the level of each ankle, quantified by the Visual Analog Scale (VAS), were recorded. The status of symptomatic ankle was established by the presence of pain at the level of the ankle (patient's personal assessment) at the time of enrollment in the study. The swollen and tender joints were counted. The postural deformities of the arches of the feet (flat feet, high arched feet), postural changes of the hindfeet (hindfoot valgus or varus), pain caused by palpation of the anterior, medial, lateral and posterior ankles and hindfeet were assessed. The level of motion, and pain caused by passive or active movements of the ankle (dorsal flexion, plantar flexion, inversion, eversion) and hindfoot joints (inversion, eversion), were also recorded.

Disease activity assessment and blood tests

The disease activity in RA patients was estimated by calculating the Clinical Disease Activity Index (CDAI)[18] and DAS 28 with CRP (DAS28-CRP)[19].

Questionnaires

The functionality and the effect of RA on daily life was assessed by applying the Routine Assessment of Patient Index Data 3 (RAPID3) questionnaire[20], measuring the physical function, the patient's assessment of pain (global, at any site), and overall health. The quality of life was evaluated for each patient using the validated Romanian language version of the RA Quality of Life (RAQoL) questionnaire[21,22] with a score range of 0 to 30 (the higher the score, the lower the QoL).

Baropodometric evaluation

The plantar pressure measurement was performed by a rheumatologist (CDB) with more than 15 years' experience, using the P-WALK baropodometric platform (BTS S.p.A., Milan, Italy), calibrated according to the manufacturer's recommendations. The plantar pressure distribution and the contact surface of the footprints were measured using static analysis, with the barefoot patient standing still in the middle of the platform for 10 seconds, with the feet slightly outlying, forming an angle of about 30°. The Pressure Color Scale for each measurement was preset at 100 kPa. The baropodometric evaluation provided an arch index that allowed the classification of each foot in high arch, normal foot or flat foot, a colored map of the foot contact area, and the maximum and average pressure for the 1st toe, 2nd to 5th toes, 1st to 5th metatarsal regions, midfoot (MF), medial heel (MH), and lateral heel (LH). For the purpose of the study, we only used the pressure results obtained at the MF, MH and LH levels.

Ultrasonography

The US evaluation was performed using GE Logiq S7 ultrasound machine (GE Healthcare, Chicago, USA) with ML6-15 linear transducer (at a frequency adapted to the examined region). In the Power Doppler (PD) mode, the frequency was 9 MHz, the gain was set at a minimal level to avoid noise artifacts, and the Pulse Repetition Frequency (PRF) was set at 0.8 kHz.

The US examination was performed by two examiners with 5 years' (OS) and 20 years' (DF) of experience in musculoskeletal US, respectively, in a blinded mode for the patient's complaints, or for other results. US images were stored for each structure following a pre-established protocol. In the case of disagreements between the two examiners, a third examiner (MCM), with more than 15 years' experience in musculoskeletal US, reviewed the images.

Following the Outcome Measures in Rheumatology (OMERACT)/EULAR definitions and recommendations[23-28], the tibiotalar (TT), anterior and posterior approaches, talonavicular (TN) and subtalar (ST), medial, lateral and posterior approaches were examined. The synovial hypertrophy (SH) in gray scale, PD signal, osteophytes and erosions were also identified and graded accordingly.

The tibialis tendons, long flexor and extensor tendons and peroneal tendons of the ankles were evaluated following the same guidelines[23]. The presence of tenosynovitis, PD signal and tendinosis were also recorded and graded[29].

In the heel region, the Achilles tendon (enthesophytes, retrocalcaneal bursitis and posterior calcaneal erosions) and plantar fascia (plantar fasciitis, perifasciitis, inferior calcaneal erosions) were evaluated according to the previous recommendations[27,30].

We included the TT joint and tendons in the ankle region, and the TN and ST joints in the hindfoot region. The Achilles tendon, plantar fascia and their adjacent structures were assigned to the heel region.

Statistical analysis

The sample size was calculated to be 35 for each group at a level of significance of 0.05 and a power of 0.80. For the estimation of sample size, the rearfoot peak plantar pressure was taken into account[31] with a difference between RA and HC groups of 18 kPa and a standard deviation of 30 kPa, the effect size of 0.6, and also the frequencies of ankle synovitis[32] of 18.3% in the RA group and 2.5% in the HC group, the effect size of 0.6.

The assessment for the normal distribution of continuous variables was performed using the Shapiro-Wilk test. Descriptive statistics were obtained, and the results were presented as numbers (percentages) for the frequencies of the categorical variables, mean ± standard deviation (SD) for normally distributed continuous variables, and median (interquartile range – IQR) for non-normally distributed continuous variables. Chi-square test or Fisher's exact test (as appropriate) were used to assess the association between categorical variables. The comparison of medians between the two groups was performed using Man-Whitney U test. The inter-observer agreement was assessed using the Cohen's kappa for dichotomous variables and weighted kappa for ordinal variables. The interpretation of the k coefficient values was as follows: 0–0.20 poor, 0.20–0.40 fair, 0.40–0.60 moderate, 0.60–0.80 good, and 0.80–1 very good.

Using the univariable and multivariable logistic regression analysis, the unadjusted and adjusted (for the other variables included) odds ratios for the prediction of hindfoot valgus and for the symptomatic ankle were calculated. The predictive variables of RAQoL were established using an ordinal logistic regression model. The variables to be included in the univariable logistic regression analysis were those having clinical relevance. The variables to be incorporated into the multivariable logistic regression models were selected from those that had statistical significance after the univariable

Tab. 1. *Demographic data of rheumatoid arthritis (RA) patients*

	RA (*n* = 35 patients)	Asymptomatic ankle (*n* = 42 ankles)	Symptomatic ankle (*n* = 28 ankles)	*p*-value*
Sex (female)	30 (85.7)	38 (90.5)	22 (78.6)	0.183
Age	59.2 ± 11.25	59.5 ± 11.48	58.75 ± 10.88	0.737
BMI	26.49 ± 5.64	24.63 ± 5.18	27.74 ± 5.59	**0.027**
Flat foot	37 (52.9)	20 (47.6)	17 (60.7)	0.282
Calcaneus valgus	34 (48.6)	19 (45.2)	15 (53.6)	0.494
Disease duration (mo)	36 (12–132)	42 (18.75–105)	36 (12–192)	0.981
Seropositive	31 (88.6)	38 (90.5)	24 (85.7)	0.705
Disease stage				
I	5 (14.3)	6 (14.3)	4 (14.3)	0.975
II	11 (31.4)	14 (33.3)	8 (28.6)	
III	14 (40)	16 (38.1)	12 (42.9)	
IV	5 (14.3)	6 (14.3)	4 (14.3)	
Disease duration				
<6 months	5 (14.3)	4 (9.5)	6 (21.4)	0.183
6–12 months	2 (5.7)	4 (9.5)	0	0.144
1–2 years	4 (11.4)	5 (11.9)	3 (10.7)	0.878
≥2 years	24 (68.6)	29 (69.0)	19 (67.9)	0.916
Smokers	6 (17.1)	6 (14.3)	6 (21.4)	0.524
Treatment				
sDMARD	33 (94.3)	40 (95.2)	26 (92.9)	>0.99
Cortison	14 (40)	12 (28.6)	16 (57.1)	**0.017**
bDMARD	7 (20)	10 (23.8)	4 (14.3)	0.329
CDAI	19.87 ± 12.7	17.05 ± 11.32	24.11 ± 13.63	0.059
DAS28-CRP	3.5 ± 1.34	3.15 ± 1.27	4.01 ± 1.28	**0.013**
RAPID3	11.43 ± 6.6	9.54 ± 6.4	14.27 ± 5.89	**0.002**
RAQoL	13 (4.5–19.5)	9.5 (1–17)	15 (7–22.75)	**0.037**

Data presented as numbers (%, percentages); mean ± standard deviation or median (IQR, interquartile range) as appropriate; BMI – body mass index; mo – months; sDMARD – synthetic disease modifying drugs; bDMARD – biological disease modifying drugs; VAS – visual analogue scale (0–10); CDAI – Clinical Disease Activity Index; DAS28-CRP – Disease Activity Score 28 with C-reactive protein; RAPID3 – Routine Assessment of Patient Index Data 3; RAQoL – Rheumatoid Arthritis Quality of Life; * Comparison between asymptomatic and symptomatic patients.

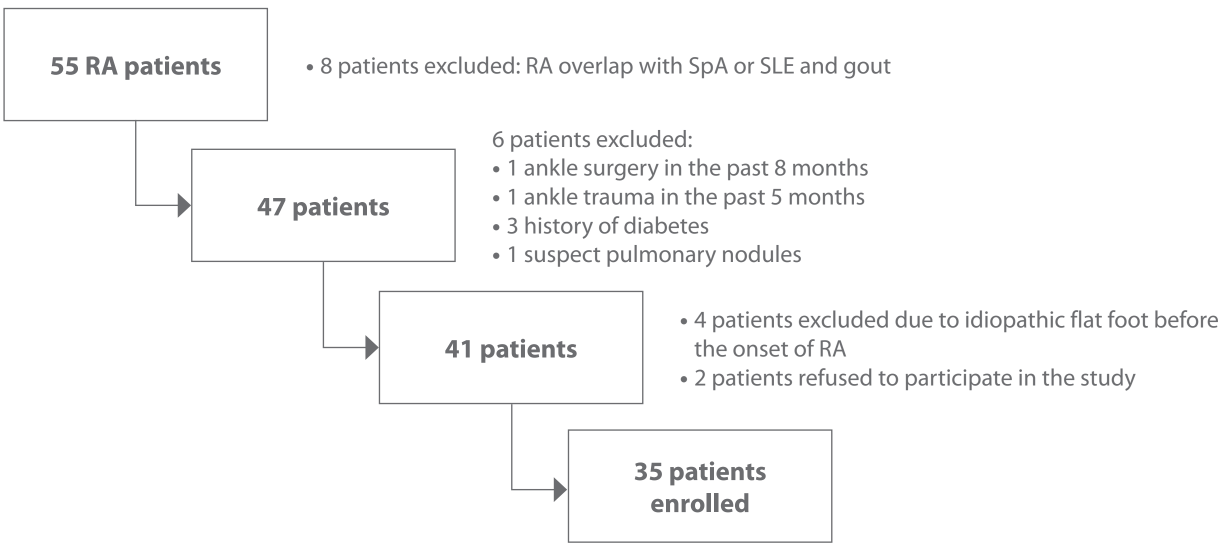

Fig. 1. *Patient selection diagram. RA – rheumatoid arthritis; SpA – spondyloarthritis; SLE – systemic lupus erythematosus*

Tab. 2. *Comparison of ultrasound findings for the ankle joint, tendon and heel structures between healthy controls (HC) and rheumatoid arthritis (RA) patients*

	US finding	HC (*n* = 70)	RA (*n* = 70)	*p*-value	Asymptomatic RA ankle (*n* = 42 ankles)	Symptomatic RA ankle (*n* = 28 ankles)	*p*-value
Joints							
TT	SH	8 (11.4)	49 (70.0)	**<0.001**	28 (66.7)	21 (75.0)	0.456
	PD+	0	8 (11.4)	**0.006**	2 (4.8)	6 (21.4)	**0.032**
	Osteophytes	4 (5.7)	7 (10.0)	0.346	5 (11.9)	2 (7.2)	0.694
	Erosions	0	4 (5.7)	0.120	3 (7.1)	1 (3.6)	0.645
ST	SH	3 (4.3)	47 (67.1)	**<0.001**	31 (73.8)	16 (57.1)	0.146
	PD+	0	11 (15.7)	**0.001**	7 (16.7)	4 (14.3)	0.789
	Osteophytes	8 (11.4)	1 (1.4)	**0.033**	0	1 (3.6)	0.400
	Erosions	0	5 (7.1)	0.058	2 (4.8)	3 (10.7)	0.383
TN	SH	9 (12.9)	44 (62.9)	**<0.001**	26 (61.9)	18 (64.3)	0.840
	PD+	0	11 (15.7)	**0.001**	6 (14.3)	5 (17.9)	0.745
	Osteophytes	26 (37.2)	16 (22.9)	0.065	10 (23.8)	6 (21.4)	0.816
	Erosions	0	7 (10.0)	**0.013**	4 (9.5)	3 (10.7)	0.871
Tendons							
TA	TS	0	5 (7.1)	**0.048**	4 (9.5)	1 (3.6)	0.641
	PD+	0	1 (1.4)	0.316	0	1 (3.6)	0.400
	Tendinosis	2 (2.9)	1 (1.4)	0.559	1 (2.4)	0	0.411
EHL	TS	0	3 (4.3)	0.245	2 (4.8)	1 (3.6)	0.810
	PD+	0	2 (2.9)	0.496	1 (2.4)	1 (3.6)	0.770
	Tendinosis	0	0	n/a	0	0	n/a
EDL	TS	0	2 (2.9)	0.496	2 (4.8)	0	0.513
	PD+	0	0	n/a	0	0	n/a
	Tendinosis	0	0	n/a	0	0	n/a
TP	TS	3 (4.3)	13 (18.6)	**0.008**	9 (21.4)	4 (14.3)	0.452
	PD+	0	3 (4.2)	0.245	2 (4.8)	1 (3.6)	0.810
	Tendinosis	9 (12.9)	4 (5.7)	0.145	2 (4.8)	2 (7.1)	0.674
FHL	TS	0	3 (4.3)	0.245	2 (4.8)	1 (3.6)	0.810
	PD+	0	0	n/a	0	0	n/a
	Tendinosis	0	0	n/a	0	0	n/a
FDL	TS	0	2 (2.9)	0.496	1 (2.4)	1 (3.6)	0.770
	PD+	0	0	n/a	0	0	n/a
	Tendinosis	0	0	n/a	0	0	n/a
Peroneal	TS	0	7 (10.0)	**0.013**	5 (11.9)	2 (7.1)	0.694
	PD+	0	1 (1.4)	0.316	1 (2.4)	0	0.411
	Tendinosis	0	7 (10.0)	**0.013**	4 (9.5)	3 (10.7)	0.871
Heel							
Achilles tendon	Enthesophytes	42 (60.0)	55 (78.6)	**0.017**	33 (78.6)	22 (78.6)	0.99
	Retrocalcaneal bursitis	0	22 (31.4)	**<0.001**	9 (21.4)	13 (46.4)	**0.027**
	Posterior calcaneal erosions	4 (5.7)	11 (15.7)	**0.046**	5 (11.9)	6 (21.4)	0.328
Plantar fascia	Plantar fasciitis	14 (20.0)	45 (64.3)	**<0.001**	24 (57.1)	21 (75)	0.127
	Perifasciitis	0	12 (17.1)	**<0.001**	4 (9.5)	8 (28.6)	**0.038**
	Inferior calcaneal erosions	0	11 (15.7)	**0.001**	7 (16.7)	4 (14.3)	0.789

Data presented as numbers (%, percentages); n/a – non-applicable; TT – tibiotalar joint; TN – talonavicular joint; ST – subtalar joint; TA – tibialis anterior; EHL – extensor hallucis longus; EDL – extensor digitorum longus; TP – tibialis posterior; FHL – flexor hallucis longus; FDL – flexor digitorum longus; SH – synovial hypertrophy; PD+ – Power Doppler positive; TS – tenosynovitis.

Tab. 3. *Comparison of ultrasound findings for the ankle joint between healthy controls (HC) and rheumatoid arthritis (RA) patients*

Joint	US finding	Grading	HC (*n* = 70)	RA (*n* = 70)	*p*-value	Asymptomatic RA ankle (*n* = 42 ankles)	Symptomatic RA ankle (*n* = 28 ankles)	*p*-value
TT	SH	Overall	8 (11.4)	49 (70.0)	**<0.001**	28 (66.7)	21 (75.0)	0.456
		Grade 1	8 (11.4)	41 (58.6)	**<0.001**	26 (61.9)	15 (53.6)	0.097
		Grade 2	0	8 (11.4)		2 (4.8)	6 (21.4)	
		Grade 3	0	0		0	0	
	PD+	Overall	0	8 (11.4)	**0.006**	2 (4.8)	6 (21.4)	**0.032**
	Osteophytes	Overall	4 (5.7)	7 (10.0)[a]	0.346	5 (11.9)	2 (7.2)	0.694
	Erosions	Overall	0	4 (5.7)	0.120	3 (7.1)	1 (3.6)	0.645
		Grade 1	0	3 (4.3)	0.128	2 (4.8)	1 (3.6)	0.689
		Grade 2	0	1 (1.4)		1 (2.4)	0	
		Grade 3	0	0		0	0	
ST	SH	Overall	3 (4.3)	47 (67.1)	**<0.001**	31 (73.8)	16 (57.1)	0.146
		Grade 1	3 (4.3)	36 (51.4)	**<0.001**	24 (57.1)	12 (42.9)	0.261
		Grade 2	0	10 (14.3)		7 (16.7)	3 (10.7)	
		Grade 3	0	1 (1.4)		0	1 (3.6)	
	PD+	Overall	0	11 (15.7)	**0.001**	7 (16.7)	4 (14.3)	0.789
	Osteophytes	Overall	8 (11.4)	1 (1.4)[a]	**0.033**	0	1 (3.6)	0.400
	Erosions	Overall	0	5 (7.1)	0.058	2 (4.8)	3 (10.7)	0.383
		Grade 1	0	2 (2.9)	0.075	1 (2.4)	1 (3.6)	0.596
		Grade 2	0	3 (4.3)		1 (2.4)	2 (7.2)	
		Grade 3	0	0		0	0	
TN	SH	Overall	19 (12.9)	44 (62.9)	**<0.001**	26 (61.9)	18 (64.3)	0.840
		Grade 1	9 (12.9)	33 (47.1)	**<0.001**	20 (47.6)	13 (46.4)	0.920
		Grade 2	0	11 (15.7)		6 (14.3)	5 (17.9)	
		Grade 3	0	0		0	0	
	PD+	Overall	0	11 (15.7)	**0.001**	6 (14.3)	5 (17.9)	0.745
	Osteophytes	Overall	26 (37.2)	16 (22.9)	0.065	10 (23.8)	6 (21.4)	0.816
		Grade 1	24 (34.3)	15 (21.4)	0.180	9 (21.4)	6 (21.4)	0.712
		Grade 2	2 (2.9)	1 (1.4)		1 (2.4)	0	
		Grade 3	0	0		0	0	
	Erosions	Overall	0	7 (10.0)a	**0.013**	4 (9.5)	3 (10.7)	0.871

Data presented as numbers (%, percentages); [a]All Grade 1; TT – tibiotalar joint; TN – talonavicular joint; ST – subtalar joint; SH – synovial hypertrophy; PD+ – Power Doppler positive.

logistic regression and using the forward method. *P*-values under 0.05 were considered statistically significant. The analysis was performed using Microsoft Excel in Office 365 (Microsoft, Redmond, Washington, SUA), and SPSS Statistics v.23 (IBM, Armonk, New York, USA).

Results

Demographics of RA patients and HC subjects

Fifty-five RA patients were examined clinically, but only 35 RA patients were enrolled (Fig. 1). After matching for sex (85.7% females), age and BMI, a total of 35 HC individuals were recruited (HC vs RA: 58.91 ± 11.59 vs 59.2 ± 11.25 years old, $p = 0.743$, and 25.72 ± 3.40 vs 26.49 ± 5.64 kg/m^2, $p = 0.244$). The RA patients were split into 2 subgroups depending on the presence/absence of symptoms in the ankle region (Tab. 1).

US inter-observer agreement

The inter-observer agreement for all the US findings in the joint, tendon and heel structures was very good (kappa: 0.82–0.88), except for the subtalar joint, where the level of agreement was good (kappa: 0.71–0.75).

RA vs HC US findings

The US findings for the ankle/hindfoot joint, tendon and heel structures are summarized in Tab. 2, Tab. 3, Tab. 4, and Tab. 5.

US vs Clinical Examination in RA patients

The presence of flat foot (37 ankles) was significantly associated with calcaneus valgus (34 ankles) ($p < 0.001$), 31 ankles (83.8%) having both modifications, and with tibialis posterior (TP) tendinosis ($p = 0.029$).

Tab. 4. *Comparison of ultrasound findings for the ankle tendons between healthy controls (HC) and rheumatoid arthritis (RA) patients*

Tendon	US finding	Grading	HC (n = 70)	RA (n = 70)	p-value	Asymptomatic RA ankle (n = 42 ankles)	Symptomatic RA ankle (n = 28 ankles)	p-value
TA	TS	Overall	0	5 (7.1)	**0.048**	4 (9.5)	1 (3.6)	0.641
		Grade 1	0	4 (5.7)	0.075			
		Grade 2	0	0				
		Grade 3	0	1 (1.4)				
	PD+	Overall	0	1 (1.4)	0.316	0	1 (3.6)	0.400
	Tendinosis	Overall	2 (2.9)	1 (1.4)	0.559	1 (2.4)	0	0.411
EHL	TS	Overall	0	3 (4.3)	0.245	2 (4.8)	1 (3.6)	0.810
		Grade 1	0	1 (1.4)	0.225			
		Grade 2	0	2 (2.9)				
		Grade 3	0	0				
	PD+	Overall	0	2 (2.9)	0.496	1 (2.4)	1 (3.6)	0.770
	Tendinosis	Overall	0	0	n/a	0	0	n/a
EDL	TS	Overall	0	2 (2.9)[a]	0.496	2 (4.8)	0	0.513
	PD+	Overall	0	0	n/a	0	0	n/a
	Tendinosis	Overall	0	0	n/a	0	0	n/a
TP	TS	Overall	3 (4.3)	13 (18.6)	**0.008**	9 (21.4)	4 (14.3)	0.452
		Grade 1	3 (4.3)	11 (15.7)	0.061			
		Grade 2	0	1 (1.4)				
		Grade 3	0	1 (1.4)				
	PD+	Overall	0	3 (4.2)	0.245	2 (4.8)	1 (3.6)	0.810
	Tendinosis	Overall	9 (12.9)	4 (5.7)	0.145	2 (4.8)	2 (7.1)	0.674
FHL	TS	Overall	0	3 (4.3)[a]	0.245	2 (4.8)	1 (3.6)	0.810
	PD+	Overall	0	0	n/a	0	0	n/a
	Tendinosis	Overall	0	0	n/a	0	0	n/a
FDL	TS	Overall	0	2 (2.9)[a]	0.496	1 (2.4)	1 (3.6)	0.770
	PD+	Overall	0	0	n/a	0	0	n/a
	Tendinosis	Overall	0	0	n/a	0	0	n/a
Peroneal	TS	Overall	0	7 (10.0)	**0.013**	5 (11.9)	2 (7.1)	0.694
		Grade 1	0	6 (8.6)	**0.025**			
		Grade 2	0	1 (1.4)				
		Grade 3	0	0				
	PD+	Overall	0	1 (1.4)	0.316	1 (2.4)	0	0.411
	Tendinosis	Overall	0	7 (10.0)	**0.013**	4 (9.5)	3 (10.7)	0.871

Data presented as n(%); [a]All Grade 1; n/a – non-applicable; TA – tibialis anterior; EHL – extensor hallucis longus; EDL – extensor digitorum longus; TP – tibialis posterior; FHL – flexor hallucis longus; FDL – flexor digitorum longus; TS – tenosynovitis; PD+ – Power Doppler positive.

Considering only the ankles with calcaneus valgus, ST joint synovitis was detected in 20 (58.8%) ankles: 8 (40%) from the medial scan, 3 (15%) from the lateral scan, 6 (30%) from both medial and lateral scans, 1 (5%) from medial and posterior scans, 1 (5%) from lateral and posterior scans, and 1 (5%) from all three scans. Lateral ST synovitis was detected significantly less frequently in patients with hindfoot valgus (32.4% vs 55.6%, p = 0.041) (Fig. 2).

Including the relevant parameters in a logistic regression model for the prediction of hindfoot valgus, we found that age (OR = 1.1, p = 0.006), disease duration (OR = 1.02, p = 0.001), and DAS28-CRP (OR = 1.46, p = 0.035) were independent predictors of hindfoot valgus.

The rest of the clinical examination was poorly associated with the US findings. The exceptions included pain in the anterior ankle and TT joint synovitis (p = 0.013), pain in the Achillean region and enthesophytes (p = 0.018), and pain in the inferior heel and plantar fasciitis (p = 0.008) or perifasciitis (p <0.001).

Subtalar joint synovitis

In 47 hindfeet of the RA patients, ST synovitis was identified from the medial approach in 34 (72.3%) hindfeet, from the lateral approach in 31 (66%), and from the posterior approach in 5 (10.6%). In 15 (31.91%) hindfeet, ST

Tab. 5. *Comparison of ultrasound findings for heel structures between healthy controls (HC) and rheumatoid arthritis (RA) patients*

Heel	US finding	Grading	HC (*n* = 70)	RA (*n* = 70)	*p*-value	Asymptomatic ankle (*n* = 42 ankles)	Symptomatic ankle (*n* = 28 ankles)	*p*-value
Achilles tendon	Enthesophytes	Overall	42 (60.0)	55 (78.6)	**0.017**	33 (78.6)	22 (78.6)	0.99
		Grade 1	40 (57.1)	30 (42.9)	**<0.001**			
		Grade 2	2 (2.9)	24 (34.3)				
		Grade 3	0	1 (1.4)				
	Retrocalcaneal bursitis	Overall	0	22 (31.4)	**<0.001**	9 (21.4)	13 (46.4)	**0.027**
		Grade 1	0	20 (28.6)	**<0.001**			
		Grade 2	0	2 (2.9)				
		Grade 3	0	0				
	Posterior calcaneal erosions	Overall	4 (5.7)	11 (15.7)	**0.046**	5 (11.9)	6 (21.4)	0.328
		Grade 1	4 (5.7)	4 (5.7)	**0.025**			
		Grade 2	0	7 (10.0)				
		Grade 3	0	0				
Plantar fascia	Plantar fasciitis	Overall	14 (20.0)	45 (64.3)	**<0.001**	24 (57.1)	21 (75)	0.127
	Perifasciitis	Overall	0	12 (17.1)	**<0.001**	4 (9.5)	8 (28.6)	**0.038**
	Inferior calcaneal erosions	Overall	0	11 (15.7)	**0.001**	7 (16.7)	4 (14.3)	0.789
		Grade 1	0	8 (11.4)	**0.003**			
		Grade 2	0	3 (4.3)				
		Grade 3	0	0				
Data presented as numbers (%, percentages).								

synovitis was visualized both from the medial and lateral approaches, and in 3 (6.38%) hindfeet from all the three approaches.

Symptomatic vs asymptomatic RA patients

Out of the 35 RA patients, 14 (40%) were symptomatic, with median (IQR – interquartile range) VAS of 5 (3–7). The distribution of US findings in the asymptomatic and symptomatic ankle groups is detailed in Tab. 2 Tab. 3, Tab. 4 and Tab. 5.

The results of the unadjusted univariable and adjusted multivariable logistic regression for the prediction of the symptomatic ankle are listed in Tab. 6.

Baropodometry in RA patients and HC subjects

The maximum and mean plantar pressures and contact surfaces in the HC subjects and RA patients (with or without ST synovitis) are shown in supplementary Tab. 7. Significant differences were found in the medial and lateral plantar pressures in the RA patients (with or without ST joint synovitis) (Tab. 8), but in no relation to the US changes in other joints, tendons or heels.

The maximum and mean midfoot pressures were higher in the symptomatic ankle [72 (32.5–96.5) vs 49 (16–129) kPa, $p = 0.043$ and 25 (18.5–39.5) vs 18 (9–59), $p = 0.040$, respectively], and in hindfoot valgus patients [94.5 (29–162) vs 25 (15–95.5), $p = 0.046$]. In flat feet, medians of MF maximum and mean pressures [72 (32.5–96.5) vs 49 (16–129) kPa, $p = 0.043$, and 40 (16–60.5) vs 10 (7–25) kPa, $p = 0.002$, respectively], MF contact surface [24.15 (9.9–31.55) vs 6.4 (2.7–22.4) cm^2, $p = 0.022$], MH maximum and mean plantar pressures [140 (65.5–216) vs 50 (34–144) kPa, $p = 0.008$, and 76 (31–85.5) vs 24 (16–75) kPa, $p = 0.005$, respectively], LH maximum and mean pressures [136 (64–210.5) vs 52 (33–136) kPa, $p = 0.0010$, and 71 (30–82.5) vs 25 (15–73) kPa, $p = 0.010$, respectively] and total maximum pressures [162.4 (106.7–267.1) vs 52.6 (35.4–197.3), $p = 0.006$] were higher comparing with no-flat foot RA patients.

Quality of life of RA patients

The RAQoL score of RA patients with symptomatic ankle was significantly higher compared to the asymptomatic ankle group ($p = 0.037$). Including all the relevant variables (clinical, US and baropodometric findings) in the multivariable ordinal logistic regression model for the prediction of the RAQoL score, the DAS28-CRP ($p < 0.001$), RAPID3 score ($p < 0.001$), disease stages ($p = 0.016$), hindfoot valgus ($p = 0.010$), ankle joint synovitis [TT synovitis ($p < 0.001$), ST synovitis ($p < 0.001$)], ankle tendon pathology [TP PD positive tenosynovitis ($p = 0.029$), TP tendinosis ($p = 0.005$), peroneal tendinosis ($p < 0.001$)], Achilles tendon enthesophytes ($p < 0.001$), posterior calcaneal erosions ($p = 0.011$), plantar fasciitis ($p = 0.04$), and perifasciitis ($p = 0.007$) were found to be independent predictors.

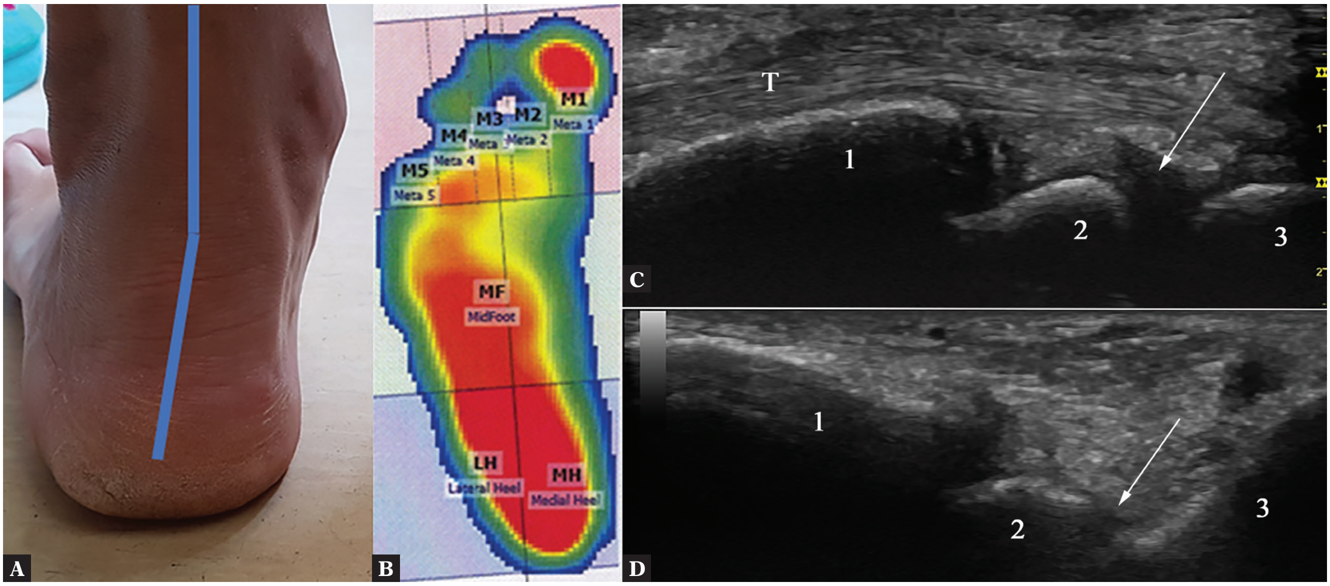

Fig. 2. *Example of RA patients with hindfoot valgus.* **A.** *Clinical aspect of the left rearfoot of the patient, the blue lines depict the malalignment of the mid-calcaneal axis and mid-tibial axis, with the outward deviation of the mid-calcaneal axis.* **B.** *Baropodometric aspect of the left foot showing flat foot pattern with increased surface and pressure of the midfoot (MF) and increased pressure of the lateral and medial heel (LH, MH) represente by the predominant red color.* **C.** *Grade 2 subtalar joint synovitis (arrow) visible from the medial approach; T – extensor hallucis longus tendon; 1 – tibia; 2 – talus; 3 – calcaneus.* **D.** *Subtalar joint (arrow) visible from the lateral approach without visible synovitis; 1 – fibula; 2 – talus; 3 – calcaneus*

Discussion

Our study confirmed that the QoL of RA patients is significantly affected by ankle and hindfoot pathology (not only inflammatory, but also degenerative findings and deformities), and that US is an important tool in detecting the majority of these changes. Apart from the DAS-28 calculation system and clinically hindfoot valgus visualization, all the other predictors for poor QoL can be detected/evaluated by US.

In our study, ST synovitis was a common element found by analyzing the predicting factors for symptomatic ankles, hindfoot deformity, and poor QoL. The data obtained from baropodometry, in relation with ST joints synovitis, offer interesting findings. In patients with ST synovitis, the maximum and mean pressure in the lateral or medial heel were similar to HC, but significantly lower compared to the RA patients without ST synovitis. This observation needs more in-depth exploration.

The mechanism underlying the development of hindfoot valgus in patients with RA is based on ST and TN joint modifications that are stress-related and result from ligament weakening caused by joint inflammation. The main displacements that occur in RA patients' ankles/hindfeet are the plantar flexion of the navicular bone and the lateral, upward shift and valgus rotation of the calcaneus bone[33]. Since hindfoot valgus results in a pronated ST joint, meaning

Tab. 6. *Logistic regression for the prediction of symptomatic ankle*

Predictor	Unadjusted OR	*p*-value	Adjusted OR*	*p*-value
BMI	1.1	**0.027**	1.34	**0.001**
Cortisone therapy	0.36	0.069		
DAS28-CRP	1.7	**0.01**		
RAPID3	1.13	**0.005**	1.2	**0.028**
Hindfoot valgus	3.45	**0.022**		
Flat foot	1.7	0.284		
TT SH PD+	5.45	**0.048**		
Lat ST SH	3.03	**0.033**	1.93	**0.007**
Post ST SH	11.18	**0.03**		
Retrocalcaneal bursitis	3.18	**0.03**		
Perifasciitis	3.8	**0.047**		

*Adjusted for other variables included in the regression model; BMI – body mass index; DAS28-CRP – Disease Activity Score 28 with C-reactive protein; RAPID3 – Routine Assessment of Patient Index Data 3; TT SH PD+ – Power Doppler positive tibiotalar joint synovitis; Lat ST SH – ST joint synovial hypertrophy from the lateral approach; Post ST SH – ST joint synovial hypertrophy from the posterior approach.

Tab. 7. *Differences in the midfoot and rearfoot plantar pressures in rheumatoid arthritis (RA) patients and healthy control (HC) subjects*

Plantar region	HC	RA	*p*-value
Midfoot			
Maximum pressure (kPa)	34.5 (26–48)	84 (22–160.5)	**0.022**
Mean pressure (kPa)	16 (10–21)	27 (10–61.5)	**0.011**
Surface (cm^2)	25.55 (20.1–33.4)	16.3 (5.8–28.9)	**<0.001**
Medial heel			
Maximum pressure (kPa)	71 (62–79)	121.5 (47–223)	0.115
Mean pressure (kPa)	37 (32–41)	61 (21–89)	0.333
Surface (cm^2)	20.85 (19–22.9)	14.75 (10.2–19.2)	**<0.001**
Lateral heel			
Maximum pressure (kPa)	64.5 (57–72)	125.5 (47–236)	0.052
Mean pressure (kPa)	34 (30–29)	61 (23–101)	0.213
Surface (cm^2)	21.75 (19.8–24.2)	16.35 (10.2–19.6)	**<0.001**
Data presented as median (IQR, interquartile range); kPa – kilopascals; cm^2 – centimeter square.			

that the lateral joint space is diminished, either the synovial growth is altered towards the lateral edge of the joint, or the visualization of the synovitis in the lateral scan is impaired by a reduction of the joint space. This might explain why we found less ST synovitis visible from the lateral approach in patients with hindfoot valgus. The presence of synovitis could be an important source of pain[34,35], and probably for this reason the patients had modified walking/standing heel pressure by avoiding heel support (we found that the pressure on the anterior foot in these patients was increased, data not shown). In a 20-year follow-up study, Belt *et al*.[36,37] radiographically monitored ankle and ST joint damage in patients with early-RA (≤6 months), and found that ST joint damage appeared in the first year of follow-up. Most of our patients had stable disease, the majority having over 2 years of disease duration. Probably, an earlier diagnosis of ST synovitis, before the development of permanent deformities, along with effective therapeutic modalities (topical corticosteroid injections, orthosis, rehabilitation therapy, etc.), could have influenced this unfavorable evolution. However, in order to verify this supposition, larger longitudinal studies are needed.

Given its complex anatomy and the lack of experience of the examiners, the US evaluation of the ST joint is quite difficult, and requires good training[28,38]. Magnetic resonance imaging (MRI) is a better ankle and hindfoot joint evaluation technique[39,40], but it is expensive, time-consuming and not easily or widely available.

In the clinical practice, the use of US for foot and ankle evaluation in RA is still in its early stages. Recently,

Tab. 8. *Medial heel and lateral heel plantar pressure related to the presence of subtalar joint synovitis*

Plantar region	RA ST-	RA ST+	*p*-value
Medial heel			
Maximum pressure (kPa)	165 (55.5–267.5)	70 (41.5–184.5)	**0.049**
Mean pressure (kPa)	83 (29–134.5)	34 (19–81)	**0.038**
Lateral heel			
Maximum pressure (kPa)	171 (52.5–290)	68 (43–180)	**0.046**
Mean pressure (kPa)	79 (27.5–121)	34 (18.5–79.5)	**0.048**
Total maximum pressure (kPa)	203.9 (58.85–267.15)	121.1 (45.45–193.05)	**0.026**
	RA lat ST-	**RA lat ST+**	
Medial heel			
Maximum pressure (kPa)	127 (49.5–237)	35 (31–101)	**0.034**
Mean pressure (kPa)	70 (25–96.5)	16 (15–53)	**0.048**
Lateral heel			
Maximum pressure (kPa)	131 (51–249)	38 (31.5–94)	**0.030**
Mean pressure (kPa)	67 (24.5–106.5)	19 (15.5–48.5)	**0.048**
Total maximum pressure (kPa)	149.5 (54.25–266.25)	36.3 (30.25–86.85)	**0.008**
Data presented as median (IQR, interquartile range); kPa – kilopascals; ST – subtalar joint; RA ST- – RA patients' feet without subtalar synovitis; RA ST+ – RA patients' feet with subtalar synovitis; RA lat ST- – RA patients' feet without subtalar synovitis in the lateral approach; RA lat ST+ – RA patients' feet with subtalar synovitis in the lateral approach.			

multidisciplinary recommendations have been published for the diagnosis and treatment of foot conditions in patients with RA[41] and, despite the lack of evidence (4b level of evidence, based on the "opinion of the expert group") radiological examination is preferred regardless of its known limitations[42]. US was considered useful only in cases with inconclusive clinical examination or for injection guiding[41], even though there are studies demonstrating the benefit of US in synovitis (even subclinical) and periarticular structures inflammation detection[39,41,43], and in monitoring the therapeutic response[44].

We often found changes in the heel and surrounding structures, even if the region was not directly damaged in RA. Being superficial, the Achilles tendon and plantar fascia can be easily assessed by US, with very good resolution and reliability[45]. Probably mechanical factors are the main cause underlying these changes, but we established that retrocalcaneal bursitis and perifasciitis had a significant effect on the patients' symptomatology and QoL. In the symptomatic patients, US can be used for guiding corticosteroid injection, with no need to change or escalate RA treatment.

It has been shown that pathological findings involving the ankle and hindfoot can be detected in healthy individuals. The hindfoot and ankle, being weight-bearing areas, undergo significant mechanical stress and, for this reason, structural damage might occur. Still, there are limited data regarding the frequency of US modifications in healthy subjects, and available results vary. Luukkainen *et al*.[46] found TT joint effusion in 4% of the examined ankles, but no PD signal. Micu *et al*.[47], in young healthy women, found inflammatory-like US findings in 1.33% of the examined ST joints and in one TP tendon, but none in the TT and TN joints. Sant'Ana Petterle *et al*.[43], besides TT and TN joints synovitis (in 1%, and 15% respectively), found TN joint erosions (in 2% of the examined joints). We found synovitis in healthy subjects more frequently (11.4% in TT, 4.3% in ST, and 12.9% in TN), which is probably related to the higher mean age of our healthy group in comparison to the other studies. However, these findings were more common in RA patients, similarly to other published studies[32,43,48].

Inamo *et al*.,[17] retrospectively assessed US-detected subclinical synovitis (overall in feet, ankles and hindfeet joints), and concluded that its presence impaired the functionality and QoL in RA patients. There are no other studies available in the literature regarding the correlation of US findings of the ankles/hindfeet with QoL in RA patients. We established that the ankle and hindfoot synovitis (TT and ST joints), TP tenosynovitis and plantar fasciitis predicted poorer QoL in RA patients. With all being sources for pain, the deformities and dysfunctionality of the feet directly influence the QoL, since the patients' daily activities are impaired.

To the best of our knowledge, our study is the first one to evaluate the relationship between the midfoot and hindfoot plantar pressures and the ankle and hindfoot US findings correlated with the clinical examination.

The study has some limitations. Firstly, the number of patients was small, and the proportion of symptomatic ankles was smaller compared to asymptomatic ankles. We did not use the DAS44 score for the evaluation of our patients (score including ankle and foot evaluation). We chose the DAS28 score following the EULAR/ACR recommendations for reporting disease activity in RA patients[49]. The lack of comparison of US findings to other imaging techniques, especially MRI, is another important limitation, but based on very good/good inter-observer agreement – and the involvement of a third experienced examiner for the resolution of disagreements – we may state that the US conclusions are reliable. Since our study was transverse, the relevance of the US findings for patients and the sensitivity to change could not be assessed. We also evaluated the overall functionality of the RA patients, but there are other measuring tools (questionnaires) targeted at the foot functional status. We did not have complete data regarding the health status of the ankles and hindfeet before the onset of RA, which might have biased our results. We did not assess the anterior part of the ST joint as Mandl *et al*.[28] recommended. We took into consideration the OMERACT recommendations in which the ST joint evaluation should exclude the anterior part of the joint (talocalcaneonavicular joint)[38].

Conclusions

In RA patients, pathological US findings are more common than in healthy subjects, and the plantar pressures are altered in comparison to healthy individuals, which is probably related to foot deformities or ST joint synovitis. Poor QoL in RA patients is significantly affected by ankle, hindfoot (mainly ST joint) and heel pathologies. US can be used for the detection of inflammatory and degenerative changes in these regions and, together with clinical examination and DAS28-CRP calculation, should be considered in all patients.

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Conflict of interest

Authors do not report any financial or personal connections with other persons or organizations, which might negatively affect the contents of this publication and/or claim authorship rights to this publication.

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