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CLINICAL SCIENCE

Very low prevalence of ultrasound-detected tenosynovial abnormalities in healthy subjects throughout the age range: OMERACT ultrasound minimal disease study

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Handling editor Josef S Smolen

► Additional supplemental material is published online only. To view, please visit the journal online (http://dx.doi.org/10.1136/annrheumdis-2021-219931).

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Received 22 March 2021
Accepted 2 July 2021

To cite: Trickey J, Sahbudin I, Ammitzbøll-Danielsen M, *et al*. *Ann Rheum Dis* Epub ahead of print: [*please include* Day Month Year]. doi:10.1136/annrheumdis-2021-219931

ABSTRACT

Objectives This study aimed to determine the prevalence of ultrasound-detected tendon abnormalities in healthy subjects (HS) across the age range.

Methods Adult HS (age 18–80 years) were recruited in 23 international Outcome Measures in Rheumatology ultrasound centres and were clinically assessed to exclude inflammatory diseases or overt osteoarthritis before undergoing a bilateral ultrasound examination of digit flexors (DFs) 1–5 and extensor carpi ulnaris (ECU) tendons to detect the presence of tenosynovial hypertrophy (TSH), tenosynovial power Doppler (TPD) and tenosynovial effusion (TEF), usually considered ultrasound signs of inflammatory diseases. A comparison cohort of patients with rheumatoid arthritis (RA) was taken from the Birmingham Early Arthritis early arthritis inception cohort.

Results 939 HS and 144 patients with RA were included. The majority of HS (85%) had grade 0 for TSH, TPD and TEF in all DF and ECU tendons examined. There was a statistically significant difference in the proportion of TSH and TPD involvement between HS and subjects with RA (HS vs RA p<0.001). In HS, there was no difference in the presence of ultrasound abnormalities between age groups.

Conclusions Ultrasound-detected TSH and TPD abnormalities are rare in HS and can be regarded as markers of active inflammatory disease, especially in newly presenting RA.

Key messages

What is already known about this subject?
- Little is known about the prevalence of sonographic tenosynovial abnormalities in healthy subjects (HS) across the age range.

What does this study add?
- This is the largest cohort of healthy subjects with tendons scanned by ultrasound.
- There is very low prevalence of tendon synovial hypertrophy or power Doppler abnormalities in tendons of HS even in old age.
- Ultrasound-detected inflammation in digit flexor and extensor carpi ulnaris tendons in patients suspected to be in the early stages of rheumatoid arthritis (RA) should not be discounted as physiological, even in older age.

How might this impact on clinical practice or future developments?
- Ultrasound-detected tenosynovial abnormalities can be regarded as robust findings in the clinical management of early RA.

INTRODUCTION

Tenosynovitis (TS) of hand and wrist tendons is common in early untreated inflammatory polyarthritis.[1] However, clinical examination alone may not detect this pathology,[2] especially as conventional rheumatoid arthritis (RA) disease activity scoring systems focus on joints, not tendons. The use of MRI and ultrasound examination is more sensitive and has shown that the prevalence of detecting TS in patients with early RA is higher than by physical examination alone.[3]

There has been extensive focus on the sensitivity and role of ultrasound in detecting subclinical synovial inflammation.[4 5] Ultrasound has been shown to be highly sensitive in the detection of tenosynovial inflammation, with recent studies demonstrating that ultrasound-detected hand and wrist TS has a role in predicting outcome in early RA and flare in clinical remission.[6 7]

Although recent studies using MRI have focused on the prevalence of tendon abnormalities in healthy subjects (HS),[8] there are limited data on the prevalence of ultrasound-detected 'TS' abnormalities in HS, with data arising from small comparison cohorts (ie, case–control studies focused on patients with rheumatic diseases). Furthermore, current studies were not focused on the prevalence of sonographic tendon abnormalities in HS within the age range of 40–70 years when RA commonly presents.[9] The prevalence of such abnormalities therefore remains unknown in this group.

The objective of this Outcome Measures in Rheumatology (OMERACT) ultrasound study was therefore to determine the prevalence of ultrasound-detected tendon abnormalities characterising the presence of TS in HS according to the age range.

METHODS

Adult HS (18–80 years) were recruited between August 2017 and December 2018 in 23 ultrasound centres in 14 countries with experience of participating in OMERACT ultrasound studies. To ensure a wide range of age coverage, recruitment was obtained from a large range of populations: university or hospital research staff, health service workers, students, volunteers from local advertising or national cohorts such as the Birmingham 1000 Elders group[10] in the UK. Exclusion criteria were current or previous history of any form of inflammatory arthritis, joint trauma of hands or wrist in the previous month; hand or wrist pain ≥10/100 on the Visual Analogue Scale; hand osteoarthritis according to American College of Rheumatology (ACR) criteria[11]; history of infection; and recent or current use of medications that may affect ultrasound assessment (see online supplemental table 1). An additional 12 HS were excluded after data collection but before ultrasound analysis due to autoimmune, infectious or musculoskeletal conditions identified from medical history that could confound the results. Demographic data including body mass index (BMI) were collected. Metacarpophalangeal, proximal interphalangeal, metatarsophalangeal and wrist joints were clinically examined by an independent assessor in each centre, and subjects were excluded if synovitis was found.

Ultrasound assessment of bilateral digit flexors (DFs) 1–5 and extensor carpi ulnaris (ECU) tendons was performed using a multiplanar approach. The presence of hypoechoic tenosynovial hypertrophy (TSH) and power Doppler signal within tenosynovial power Doppler (TPD) was defined and graded using the OMERACT ultrasound scoring system for TS in RA.[12] The ungraded presence of tenosynovial effusion (TEF) was recorded. Adequate gel was used to avoid compression. Views were recorded according to European League Against Rheumatism (EULAR) standard reference scan guidelines.[13] Musculoskeletal specific preset parameters were used to optimise imaging for greyscale and power Doppler and reduce variability. Details of probes, machines and experience of sonographers in all centres can be found in online supplemental table 2. Quality and grading of recorded images were confirmed by a review of all images for the first HS recruited in each centre by an experienced blinded independent assessor (IS) in the hub centre. Any disagreement was then fed back to the centre and consensus was achieved to ensure reliability in subsequent scans.

Data for a comparison cohort of DMARD-naive patients presenting as patients with new early arthritis with RA fulfilling ACR-EULAR 2010[14] and/or 1987 criteria[15] at presentation were extracted from the Birmingham Early Arthritis (BEACON) inception cohort.[6] The following data were collected: 68 tender and 66 swollen clinical counts, age, sex, symptom duration, early morning stiffness duration, medication, erythrocyte sedimentation rate (ESR), C reactive protein (CRP), rheumatoid factor and anti-citrullinated protein antibody status. This cohort underwent identical baseline tendon ultrasound assessment except for the presence of TEF.

Statistical analysis

Statistical analysis was performed using IBM SPSS Statistics V.26. Significance for the binary variable gender was assessed using Fisher's exact test. The continuous variables age and BMI (for all subjects) and early morning stiffness, CRP and joint counts (for patients with RA) were not normally distributed; significance was therefore assessed using the Kruskal-Wallis test. The tendon gradings were dichotomised into either present (grades 1–3) or absent (grade 0). Fisher's exact test was used to compare the proportions of grade 1–3 TSH, TPD or TEF between age groups in HS, and between HS and patients with RA.

RESULTS

One thousand and forty-nine HS were recruited and 939 HS were included after exclusions of subjects with protocol deviations (see flowchart in online supplemental figure 1). Baseline data for 144 patients with RA were randomly extracted from the BEACON database and matched with a cohort of 144 HS by age, sex and smoking status where possible. Table 1 shows the demographic and ultrasound characteristics of the two populations. Full ultrasound grading results are available in online supplemental table 2 and example of grading in online supplemental figure 2.

Healthy subjects

The median age of HS was 43 years (30–57). HS were grouped into three age groups: HS Y (young, 18–39 years) HS M (middle, 40–59 years) and HS O (old, 60–80 years) for analysis. The majority of volunteer HS were healthcare professionals (423, 45.0%). Other occupational groups included clerical staff (156, 16.6%), students (95, 10.1%), manual workers (68, 7.2%) and teachers (34, 3.6%).

A total of 11 237 tendons were scanned; 98% of these tendons were grade 0 for TSH, TPD and TEF (online supplemental table 3). The distribution of tendon abnormalities, when found, was symmetrical with no significant difference between right and left hands (online supplemental table 4). TEF was more frequently detected than TSH or TPD ($p<0.001$) (online supplemental table 5).

The majority (791/939, 84.2%) of HS presented grade 0 overall for all ultrasound lesions examined (TSH, TPD and TEF) in all DF 1–5 and ECU tendons. In particular 99% (931/939) of HS had grade 0 for TPD in all tendons scanned. There were no statistically significant differences between age groups (table 1 and figure 1).

Abnormalities were detected in 148 individuals across 939 HS and were of grade 1 severity, with the exception of one grade 2 for TSH in an ECU tendon. The ECU tendons had significantly

Table 1 Demographics and tendon changes (grade 1–3 TSH and power Doppler) for HS and patients with RA

	HS Y 18–39 year	HS M 40–59 year	HS O ≥60 years	HS Y/M/O P value	RA	RA versus age-matched and sex-matched HS* P value
n	405	350	184		144	
Age (years), median (IQR)	29 (25–33)	49 (44–54)	68 (62–72)	<0.001	54 (45–67)	1.000
Female, n (%)	268 (66.2)	285 (81.4)	117 (63.6)	<0.001	106 (73.6)	0.924
BMI, median (IQR)	23 (22–24)	25 (21–28)	26 (23–28)	<0.001	27 (24–32)	<0.001
Smoking						
Never (%)	316 (78)	241 (68)	115 (63)		68 (47)	0.021
Ever (%)	88 (22)	109 (31)	66 (36)		75 (52)	
Current (%)	47 (12)	56 (16)	12 (7)		28 (19)	
EMS (min), median (IQR)	n/a	n/a	n/a	n/a	60 (15–120)	n/a
Symptom duration (weeks), median (IQR)	n/a	n/a	n/a	n/a	26 (13–52)	n/a
CRP (mg/L), median (IQR)	n/a	n/a	n/a	n/a	7 (3–20)	n/a
DAS28 CRP, median (IQR)	n/a	n/a	n/a	n/a	5.1 (4.1–5.8)	n/a
Tender joint,† median (IQR)	0 (0–0)	0 (0–0)	0 (0–0)	n/a	17 (11–27)	<0.001
Swollen joint,† median (IQR)	0 (0–0)	0 (0–0)	0 (0–0)	n/a	6 (3–11)	<0.001
DF 1 TSH grade ≥1, n (%)	1 (0.1)	0 (0)	1 (0.3)	0.490	15 (5.2)	<0.001
DF 2 TSH grade ≥1, n (%)	1 (0.1)	2 (0.3)	0 (0)	0602	50 (17.3)	<0.001
DF 3 TSH grade ≥1, n (%)	2 (0.2)	1 (0.1)	2 (0.6)	0.432	50 (17.3)	<0.001
DF 4 TSH grade ≥1, n (%)	2 (0.2)	1 (0.1)	1 (0.3)	1.000	28 (9.8)	<0.001
DF 5 TSH grade ≥1, n (%)	1 (0.1)	4 (0.6)	0 (0)	0.220	36 (12.5)	<0.001
ECU TSH grade ≥1, n (%)	7 (0.9)	9 (1.3)	1 (0.3)	0.293	65 (22.6)	<0.001
DF 1 TPD grade ≥1, n (%)	1 (0.1)	0 (0)	1 (0.3)	0.490	10 (3.5)	0.002
DF 2 TPD grade ≥1, n (%)	0 (0)	1 (0.1)	0 (0)	0.568	36 (12.6)	<0.001
DF 3 TPD grade ≥1, n (%)	1 (0.1)	0 (0)	0 (0)	1.000	40 (13.9)	<0.001
DF 4 TPD grade ≥1, n (%)	0 (0)	0 (0)	1 (0.3)	0.194	20 (7)	<0.001
DF 5 TPD grade ≥1, n (%)	0 (0)	0 (0)	0 (0)	n/a	23 (8.1)	<0.001
ECU TPD grade≥1, n (%)	0 (0)	0 (0)	0 (0)	n/a	62 (21.7)	<0.001
Total grade tendon score,‡ mean (range)	0.04 (0-2)	0.05 (0-4)	0.04 (0-2)		3.02 (0-21)	
Total count of tendons grade ≥1,§ mean (range)	0.03 (0-2)	0.05 (0-4)	0.03 (0-2)		1.69 (0-11)	
Individuals with grade ≥1 TSH, n (%)	12 (3.0)	10 (2.8)	4 (2.1)		76 (52.8)	
Individuals with grade ≥1 TPD, n (%)	2 (0.5)	1 (0.3)	2 (1.1)		63 (43.7)	
Individuals with grade ≥1 TEF, n (%)	50 (12.2)	46 (13.2)	29 (15.8)		n/a	

*RA and HS age matched and sex matched to compare ultrasound graded tendon findings.
†Patients with RA had 66/68 joint counts; HS had joint counts of MCPs, PIPs, wrists and MTPs.
‡Total grade tendon score is the per patient sum of all grades of TSH and TPD tendon abnormalities.
§ Total count of tendons grade ≥1 includes TSH and TPD.
BMI, body mass index; CRP, C reactive protein; DAS28, Disease Activity Score in 28 joints; DF, digit flexor; ECU, extensor carpi ulnaris; EMS, early morning stiffness; HS, healthy subjects; M, middle; MCP, metacarpophalangeal; MTP, metatarsophalangeal; O, old; PIP, proximal interphalangeal; RA, rheumatoid arthritis; TEF, tenosynovial effusion; TPD, tendon power Doppler; TSH, tenosynovial hypertrophy; Y, young.

more grade ≥1 for TSH than the DF 1–5 tendons ($p<0.05$) (online supplemental table 6).

There was no statistically significant difference in the proportion of TSH or TPD ≥1 in HS with manual professions, or in those who practice sports or hobbies which may have high impact on the upper limbs (online supplemental tables 7 and 8).

Patients with RA

Patients with RA were matched with 144 HS by age (within 2 years) and sex, and with smoking status in 116/144 HS. TS as defined by TSH and power Doppler grade ≥1 in DF and ECU tendons was more prevalent in patients with RA (52.8%) compared with HS (0.9%). There were significantly more TSH and TPD grade ≥1 detected in patients with RA compared with age-matched and sex-matched HS ($p=0.002$ to <0.001) (online supplemental table 9).

DISCUSSION

Our study is the first to assess tendon involvement in large numbers of HS, encompassing the age incidence of RA with 367 HS over 50 years, and showing a very low prevalence of abnormal findings. The few abnormalities observed were almost exclusively grade 1 in severity. Due to the large population assessed, we provide conclusive data validating and expanding on the findings of existing studies with few HS.[16–18]

TEF was more prevalent than TSH or TPD in HS. Although MRI studies have suggested TEF to be almost ubiquitous in DF tendons in HS,[19] we have shown that ultrasound detects smaller numbers: less than 2% of DF tendons even in the older age group. Visualisation of tendons in two dimensions is the most likely cause of this difference. Tenosynovial abnormalities on ultrasound were significantly more prevalent in early RA compared with matched HS.

By explicitly selecting only subjects with minimal joint pain and without overt osteoarthritis, and by using a non-random

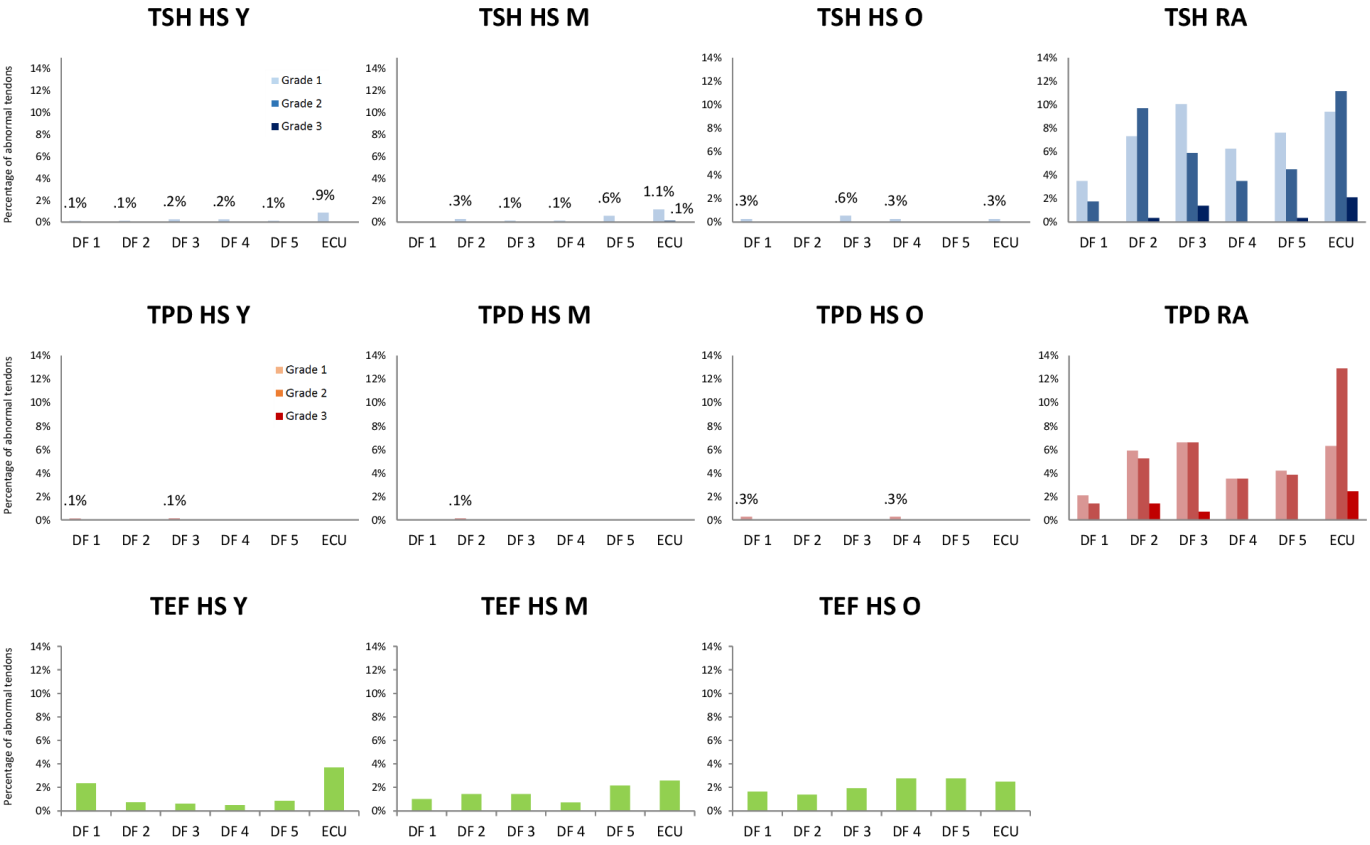

Figure 1 Percentage of tendons with grade 1–3 TSH and TPD, and presence of TEF in DF tendons 1–5 and ECU for HS according to age groups, compared with patients with RA. TEF measured only in HS. HS Y, 18–39 years; HS M, 40–59 years; HS O, 60–80 years. DF, digit flexor; ECU, extensor carpi ulnaris tendon; HS, healthy subjects; M, middle; O, old; RA, rheumatoid arthritis; TEF, tenosynovial effusion; TPD, tenosynovial power Doppler; TSH, tenosynovial hypertrophy; Y, young.

recruitment strategy to ensure inclusion of an older cohort, HS in this study may have fewer tendon changes than an unselected general population of 60–80 year olds. However, it was not our purpose to document the presence of tendon abnormalities in unselected primary or secondary care early arthritis clinics or in osteoarthritis, but to assess if HS with no symptoms may have ultrasound inflammatory abnormalities. The lack of a formal reliability study which would have been logistically difficult in such a large study, and the consecutive, not blinded recruitment may be seen as potential limitations. We mitigated these by designing a blinded central regrading strategy of the first HS scan performed by each centre.[20]

The very low prevalence of TSH and TPD across a large age range in HS suggests that these findings can be seen as potentially pathological, and not simply the consequence of ageing, by health professionals performing ultrasound in early arthritis or disease management clinics. The interpretation of such findings should depend on the clinical context. In addition, DF and ECU tendons can be easily examined during routine ultrasound examination and so could be included in abbreviated scanning protocols.

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Funding The authors acknowledge the support of the National Institute for Health Research (NIHR) National Office for Clinical Research Infrastructure Translational Research Collaboration for Joint and Related Inflammatory Diseases and the support of their affiliated NIHR Biomedical Research Centres. We also acknowledge funding from the Versus Arthritis UK RACE collaboration between Glasgow, Birmingham and Newcastle Universities received by AF, and the Arthritis Therapy Acceleration Programme funded by the Kennedy Institute of Rheumatology.

Competing interests There are no declared competing interests from authors except the following: CC declared grants from NIHR Versus Arthritis, Lilly sponsored EULAR conference travel, Modern Biosciences payment as DSM committee member, Roche consultancy fee and Novartis sponsored writing of one medical paper. KI declared a Mitsubishi-Tanabe research grant for RA; Abbvie, Eli Lilly, Mitsubishi-Tanabe, Bristol-Myers-Squib and Novartis speaker's fees; and participation on a DSM board for Abbvie, Eli Lilly and Mitsubishi-Tanabe. RK declared support from Abbvie, Roche, Novartis and UCB with payments for travel to meetings/lectures, presentations, speakers' bureaus, manuscript writing/educational events.

Patient consent for publication Not required.

Ethics approval Ethical approval was obtained as appropriate in all participating centres according to each country's regulations, and written informed participant consent was obtained where necessary.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement All data relevant to the study are included in the article or uploaded as supplemental information. Anonymised data are available on request from the authors.

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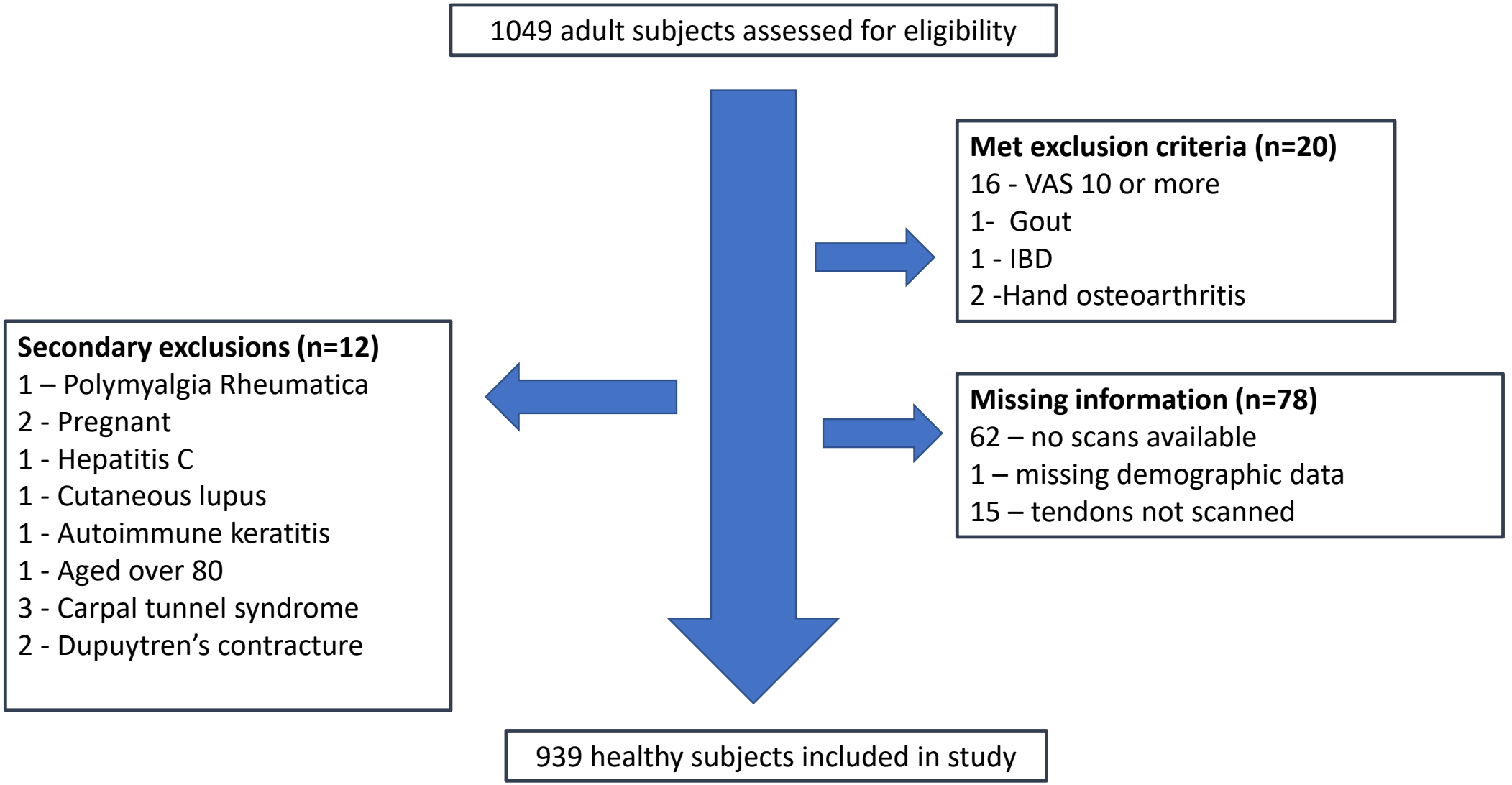
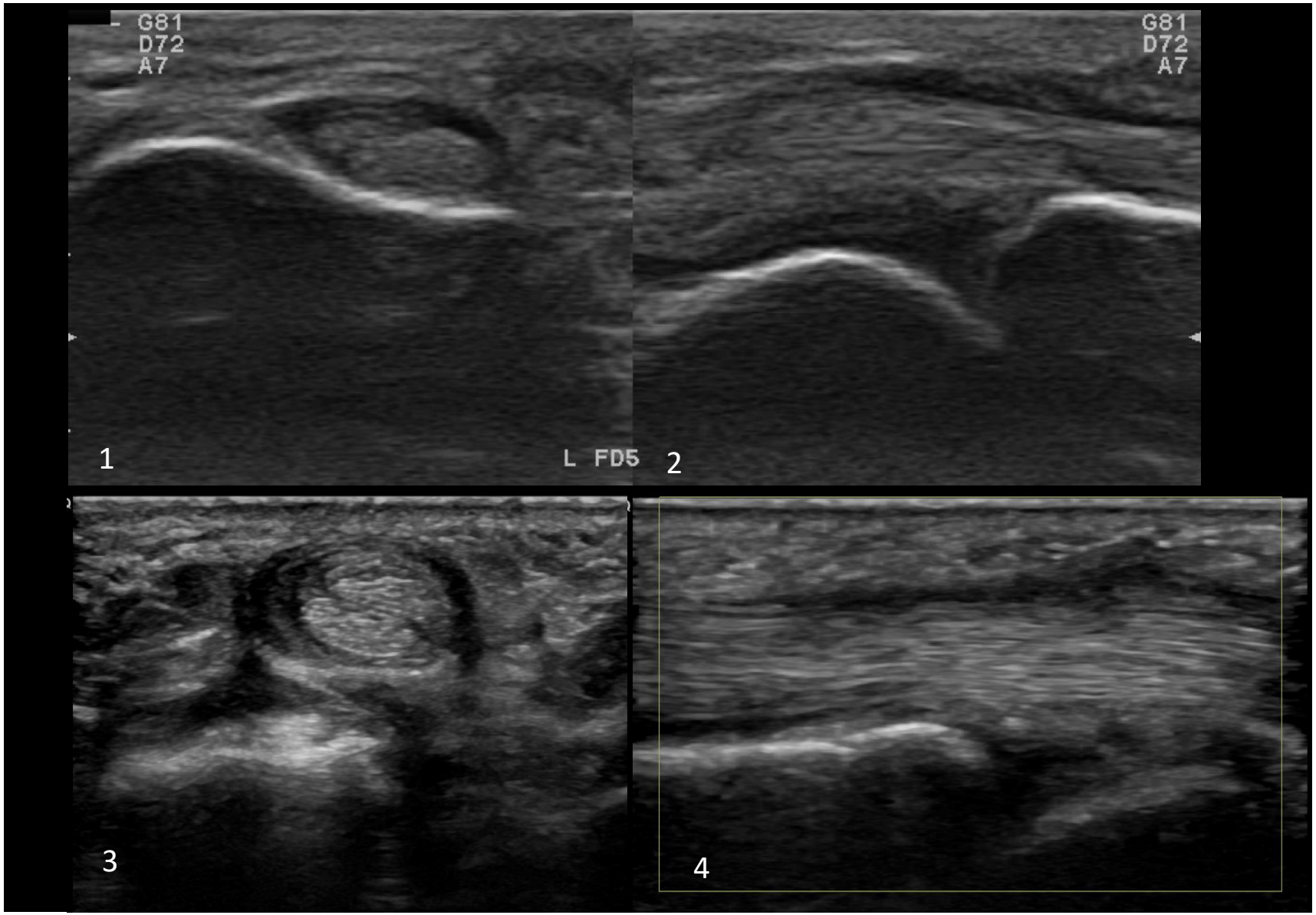

1049 adult subjects assessed for eligibility
Met exclusion criteria (n=20)
16 - VAS 10 or more
1- Gout
1 - IBD
2 -Hand osteoarthritis
Missing information (n=78)
62 – no scans available
1 – missing demographic data
15 – tendons not scanned
Secondary exclusions (n=12)
1 – Polymyalgia Rheumatica
2 - Pregnant
1 - Hepatitis C
1 - Cutaneous lupus
1 - Autoimmune keratitis
1 - Aged over 80
3 - Carpal tunnel syndrome
2 - Dupuytren's contracture
939 healthy subjects included in study


G81
D72
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1
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G81
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2
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4

Supplementary table 1: inclusion and exclusion criteria for healthy subjects

Inclusion criteria
Age 18-80 years
Exclusion criteria
Previous/current inflammatory joint disease (including crystal arthropathy)
Visual analogue score (VAS) for joint pain > 10/100.
Any history of joint trauma in the last month.
Fulfilling hand osteoarthritis ACR criteria
Any clinical joint inflammation as identified by a physician.
Previous or current inflammatory bowel disease.
History of culture-proven enteric and/or genitourinary infection in the last month
Current or previous corticosteroids use in the last 4 weeks.
Current non-steroidal anti-inflammatory use.

Supplementary table 2: Ultrasound machines and transducers used by centres

Centre	**Contributors**	**Years of ultrasound experience**	**Ultrasound qualifications**	**Machine**	**Linear Transducer**
Institute of Inflammation and Ageing, University of Birmingham, UK	Andrew Filer	15	EULAR teach the teacher EULAR level 2 (max)	GE Logiq E9	8-18MHz; 6-15MHz
	Ilfita Sahbudin	9	MSc in Musculoskeletal Ultrasound, University of Bournemouth		
	Jeanette Trickey	6	BSR Basic Ultrasound Course		
University College London, UK	Coziana Ciurtin	10	EULAR level 2 (max)	GE Logiq E8	8-15MHz
Hôpital Ambroise Paré, Paris, France	Maria-Antonietta D'agostino	25	EFSUMB level 3 (max), EULAR level 2 (max)	ESAOTE MyLab70 XVG	6-18MHz PD 11 MHz, PRF 750Hz
	Hélène Gouze	6	French Musculoskeletal Ultrasound Course, EULAR Ultrasound intermediate Course		
Department of Rheumatology Cliniques Universitaires Saint-Luc, Brussels Belgium	Maria Stoenoiu	15	EFSUMB level 3 (max), EULAR level 2 (max)	GE Logic E9	M L6-15; L8-18i
	Mihaela Maruseac	5	EULAR intermediate, EFSUMB level 2		

Ghent University, Belgium	Ruth Wittoek	15	EULAR level 2	ESAOTE MyLab 60	
	Philippe Carron	13	EULAR level 3		
University of Ferrara, Italy	Alessandra Bortoluzzi	12	Basic EULAR ultrasound course; advanced MSUS course endorsed by the Italian Society for Rheumatology	ESAOTE MyLab 70XVG	14–18 MHz
University of Ferrara, Italy	Georgios Filippou	20	EULAR level 2 (max)	Samsung RS80A	4-18 MHz; 3-12MHz
Università degli Studi di Torino, Turin, Italy	Annamaria Iagnocco	37	EFSUMB level 3 (max), EULAR level 2 (max)	ESAOTE MyLab8	L4-15 (4-15 MHz); LA 435 (6-18MHz)
	Teodora Șerban	11	EFSUMB level 1, EULAR level 2 (max), Romanian Ministry of Health Certified Sonographer		
	Irene Azzolin	5	Musculoskeletal Ultrasound in Rheumatology -EULAR Basic Course		
University of Pavia, Italy	Garifallia Sakellariou	11	none	ESAOTE Mylab 70 XVG	ESAOTE LA435 (6-18 MHz) PRF 0.75;
Sacro Cuore Hospital, Negrar, Verona, Italy	Ilaria Tinazzi	16	EULAR intermediate ultrasound course in 2007	ESAOTE MyLabClassC	10-18 MHz PRF 750 Hz
Copenhagen University Hospital, Denmark	Lene Terslev	22	EFSUMB level 3 (max), EULAR level 2 (max) Danish Rheumatology Association level 5 (max)	GE Logiq E9	ML 6-15 Colour Doppler (CD) 7.5 MHz, PRF 0.4
	Mads Ammitzball Danielsen	10	EFSUMB level 2, EULAR level 1, Danish Rheumatology Association level 4		
Aarhus University Hospital, Denmark	Ellen-Margrethe Hauge	16	Danish Rheumatology Association level 3 (max)	Hitachi Noblus	18-5 L64 Colour Doppler (CD) 6.5 MHz
	Mads Nyhuus Bendix Rasch	10	Danish Rheumatology Association level 4		
Diakonhjemmet	Hilde Berner Hammer	20	EFSUMB level 3 (max),	GE Logiq E9	6-15 MHz

Hospital, Oslo, Norway			EULAR level 2 (max) EULAR faculty US courses		
Leiden University Medical Center, The Netherlands.	Marion Kortekaas	16	EULAR level 2 (max), US level of the Dutch Rheumatology Association (max)	GE logic E9	5-18 MHz
	Sarah Ohrndorf	14	EULAR level 2 (max)		
Pomeranian Medical University, Szczecin, Poland	Marcin Milchert	13	Large Vessel Vasculitis Ultrasound courses attendances and tutorship (Hospital of Southern Norway Trust, Kristiansand, Norway) Tutorship of Large Vessel Vasculitis Ultrasound courses Southend Hospital, UK and others. Certificates in Vascular Doppler Sonography and MS Sonography of Polish Ultrasonography Society and Polish Rheumatology Society	Phillips Epiq 5	18 MHz
	Jacek Fliciński	12	Level 1 of EULAR Competency Assessment in MSUS Teach the Teachers course Certificate of Proficiency Musculoskeletal Sonography Polish Rheumatological Society		
Medical University of Vienna, Vienna, Austria	Peter Mandl	16	EFSUMB level 3 (max), EULAR level 2 (max)	GE Logiq E9	6-15MHz, 8-18MHz
	Carina Borst	3	none		
Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania	Daniela Fodor	25	EFSUMB level 3, EULAR level 2	GE S7	L8-18I
University of Medicine and Pharmacy, Craiova,	Florentin Vreju	15	EULAR intermediate course, EULAR advanced course, EULAR teach-the-	ESAOTE Mylab 25 Gold	18MHz

Romania			teachers course, EFSUMB		
Medical University of Plovdiv, Bulgaria.	Rositsa Karalilova	13	EULAR level 2 (maximum), EULAR Certificate for Ultrasound Trainers in Rheumatology	ESAOTE MyLab 7	3-18 MHz
Hospital Universitario Fundación Jiménez Díaz, Madrid, Spain.	Esperanza Naredo	25	EFSUMB level 3 (max, EULAR level 2 (max)	GE Logiq E9	ML6-15 (6-15MHz)
	Cesar Sifuentes-Cantu	5	Certifications by the Mexican College of Rheumatology		
	Giuliana M.C. La Paglia	6	EULAR intermediate ultrasound course, EFSUMB level 1		
Instituto Nacional de Rehabilitacion, Mexico City, Mexico	Carlos Pineda	23	PANLAR Level 3, ECOMER Level 3 (max)	GE Logiq e	8-18 MHz
	Marwin Gutierrez	17	EFSUMB Level 3; EULAR Level 2; PANLAR Level 3		
	Gustavo Leon				
	Cristina Reategui-Sokolova	6	Fellowships in Peruvian and Mexican hospitals.		
Zagazig University, Egypt	Mohamed Mortada	17	EULAR advanced course of musculoskeletal ultrasonography	Hitachi Aloka F37	18 MHz
Japanese Red Cross Medical Center, Tokyo, Japan	Takeshi Suzuki	17	EULAR intermediate course, EULAR teach-the-teachers course, JCR-certified sonographer	HI VISION Avius	5-18 MHz PD frequency 7.5MHz, PRF 800Hz
Chiba University Hospital, Japan	Kei Ikeda	18	EULAR intermediate course, EULAR advanced course, EULAR teach-the-teachers course, JCR-certified sonographer	HI VISION Avius; HI VISION Ascendus	EUP-L75 (5-18MHz)

Supplementary table 3: complete ultrasound grade results for tenosynovial hypertrophy, tenosynovial Power Doppler and tendon sheath effusion in Heathy Subjects and patients with Rheumatoid Arthritis

Healthy Subjects

	HS Y (18-39 years)			HS M (40-59 years)			HS O (60-80 years)			p value* HS Y vs M vs O
	G 1 n (%)	G 2 n (%)	G 3 n (%)	G 1 n (%)	G 2 n (%)	G 3 n (%)	G 1 n (%)	G 2 n (%)	G 3 n (%)	
TSH										
DF 1	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)	0.490
DF 2	1 (0.1)	0 (0.0)	0 (0.0)	2 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0602
DF 3	2 (0.2)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	2 (0.6)	0 (0.0)	0 (0.0)	0.432
DF 4	2 (0.2)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)	1.000
DF 5	1 (0.1)	0 (0.0)	0 (0.0)	4 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.220
ECU	7 (0.9)	0 (0.0)	0 (0.0)	8 (1.1)	1 (0.1)	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)	0.293
TPD										
DF 1	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)	0.490
DF 2	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.568
DF 3	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1.000
DF 4	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)	0.194
DF 5	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	n/a
ECU	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	n/a

	Present n (%)	Present n (%)	Present n (%)	
TEF				
DF 1	19 (2.3)	7 (1.0)	6 (1.7)	<0.001
DF 2	6 (0.7)	10 (1.4)	5 (1.4)	0.001
DF 3	5 (0.6)	10 (1.4)	7 (1.9)	<0.001
DF 4	4 (0.5)	5 (0.7)	10 (2.8)	<0.001
DF 5	7 (0.8)	15 (2.1)	10 (2.8)	<0.001
ECU	30 (3.7)	18 (2.6)	9 (2.5)	0.001

HS, healthy subject; G, grade; THS, tenosynovial hypertrophy; TPD, power Doppler within the tendon sheath; TEF, tenosynovial effusion; DF, digit flexor tendon; ECU, extensor carpi ulnaris tendon. * Fisher's exact test

Patients with Rheumatoid Arthritis

	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)		Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)
TSH				**TPD**			
DF 1	10 (3.5)	5 (1.8)	0 (0.0)	DF 1	6 (2.1)	4 (1.4)	0 (0.0)
DF 2	21 (7.3)	28 (9.7)	1 (0.4)	DF 2	17 (5.9)	15 (5.3)	4 (1.4)
DF 3	29 (10.1)	17 (5.9)	4 (1.4)	DF 3	19 (6.6)	19 (6.6)	2 (0.7)
DF 4	18 (6.3)	10 (3.5)	(0.0)	DF 4	10 (3.5)	10 (3.5)	0 (0.0)
DF 5	22 (7.6)	13 (4.5)	1 (0.4)	DF 5	12 (4.2)	11 (3.9)	0 (0.0)
ECU	27 (9.4)	32 (11.2)	6 (2.1)	ECU	18 (6.3)	37 (12.9)	7 (2.5)

TSH, tenosynovial hypertrophy; TPD, power Doppler within tendon sheath; TEF, tenosynovial effusion

Supplementary Table 4: Healthy subjects and RA patients with grade 0 for ultrasound findings

	TSH all grade 0 n (%)	TPD all grade 0 n (%)	TEF all grade 0 n (%)	TSH, TPD and TEF all grade 0 n (%)
Healthy subjects n= 939	907 (96.6)	931 (99.1)	808 (86.0)	791 (84.3)
RA patients n= 144	68 (47.2)	81 (56.3)	n/a	n/a

HS, healthy subjects; RA, patients with Rheumatoid Arthritis; TSH, tenosynovial hypertrophy; TPD, power Doppler within tendon sheath; TEF, tenosynovial effusion

Supplementary table 5: Distribution ultrasound findings of grade ≥ 1 in left and right tendons in healthy subjects

	HS Y (18-39 yrs)		HS M (40-59 yrs)		HS O (60-80 yrs)		All age groups		
	Left n (%)	Right n (%)	Left n (%)	Right n (%)	Left n (%)	Right n (%)	Left n (%)	Right n (%)	p value* L vs R
TSH									
DF1	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)	1 (0.1)	1 (0.1)	1.000
DF2	1 (0.2)	0 (0.0)	0 (0.0)	2 (0.6)	0 (0.0)	0 (0.0)	1 (0.1)	2 (0.2)	1.000
DF3	1 (0.2)	1 (0.2)	1 (0.3)	0 (0.0)	1 (0.5)	1 (0.6)	3 (0.3)	2 (0.2)	1.000
DF4	1 (0.2)	1 (0.2)	1 (0.3)	0 (0.0)	0 (0.0)	1 (0.6)	2 (0.2)	2 (0.2)	1.000
DF5	1 (0.2)	0 (0.0)	2 (0.6)	2 (0.6)	0 (0.0)	0 (0.0)	3 (0.3)	2 (0.2)	1.000
ECU	3 (0.7)	4 (1.0)	5 (1.4)	4 (1.1)	1 (0.6)	0 (0.0)	9 (1.0)	8 (0.9)	1.000
TPD									
DF1	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)	1 (0.1)	1 (0.1)	1.000
DF2	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	-
DF3	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	-
DF4	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	1 (0.1)	-
DF5	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-
ECU	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-
TEF									
DF1	7 (1.7)	12 (3.0)	4 (1.1)	3 (0.8)	3 (1.6)	3 (1.6)	14 (1.5)	18 (1.9)	0.481
DF2	2 (0.5)	4 (1.0)	6 (1.7)	4 (1.1)	3 (1.6)	2 (1.1)	11 (1.2)	10 (1.1)	1.000
DF3	3 (0.7)	2 (0.5)	6 (1.7)	4 (1.1)	2 (1.1)	5 (2.7)	11 (1.2)	11 (1.2)	1.000
DF4	2 (0.5)	2 (0.5)	3 (0.8)	2 (0.6)	4 (2.2)	6 (3.2)	9 (1.0)	10 (1.1)	1.000
DF5	5 (1.2)	2 (0.5)	8 (2.2)	7 (1.9)	4 (2.2)	6 (3.2)	17 (1.8)	15 (1.6)	0.845
ECU	14 (3.5)	16 (4.)	9 (2.6)	9 (2.6)	3 (1.7)	6 (3.3)	26 (2.8)	31 (3.3)	0.442

HS, healthy subject; TSH, tenosynovial hypertrophy; TPD, power Doppler within tendon sheath; TEF, tenosynovial effusion; L, left; R, right. *Fisher's exact test

Supplementary table 6: Difference in proportion of TEF grade ≥1 compared to TSH grade ≥1 and TPD grade ≥1 in HS

	DF TSH grade ≥ 1 n (%)	DF TEF grade ≥ 1 n (%)	p value*
Total number of tendons at each level	1873	1873	
DF1 TSH vs DF1 TEF	2 (0.1)	32 (1.7)	0.000
DF2 TSH vs DF2 TEF	3 (0.2)	21 (1.1)	0.000
DF3 TSH vs DF3 TEF	5 90.3)	22 (1.2)	0.000
DF4 TSH vs DF4 TEF	4 (0.2)	19 (1.0)	0.001
DF5 TSH vs DF5 TEF	5 (0.3)	32 (1.7)	0.000
ECU TSH vs ECU TEF	17 (0.9)	57 (3.0)	0.000
DF1 PD vs DF1 EF	2 (0.1)	32 (1.7)	0.000
DF2 PD vs DF2 EF	1 (0.1)	21 (1.1)	0.000
DF3 PD vs DF3 EF	1 (0.1)	22 (1.2)	0.000
DF4 PD vs DF4 EF	1 (0.1)	19 (1.0)	0.000
DF5 PD vs DF5 EF	0 (0)	32 (1.7)	n/a
ECU PD vs ECU EF	0 (0)	57 (3.0)	n/a

TSH, tenosynovial hypertrophy; TPD, power Doppler within tendon sheath; TEF, tenosynovial effusion; DF, digit flexor tendon; ECU, extensor carpi ulnaris tendon. *McNemar's test

Supplementary table 7: Comparison of ECU tenosynovial hypertrophy with DF tendons 1-5 in healthy subjects

	ECU TSH grade ≥ 1 n (%)	DF TSH grade ≥ 1 n (%)	p value*
Total number of tendons	1867	1867	
ECU TSH vs DF1 TSH	17 (0.9)	2 (0.1)	0.001
ECU TSH vs DF2 TSH	17 (0.9)	3 (0.2)	0.003
ECU TSH vs DF3 TSH	17(0.9)	5 (0.3)	0.017
ECU TSH vs DF4 TSH	17 (0.9)	4 (0.2)	0.007
ECU TSH vs DF5 TSH	17 (0.9)	5 (0.3)	0.017

TSH, tenosynovial hypertrophy; TPD, power Doppler within tendon sheath; TEF, tenosynovial effusion; DF, digit flexor tendon; ECU, extensor carpi ulnaris tendon. *McNemar's test

Supplementary table 8: HS with grade ≥ 1 TSH, TPD and TEF in manual workers vs non manual workers

	Manual worker Tendon number (%)	Non manual worker Tendon number (%)	p value*
Total number of tendons at each level	136	1735	
TSH			
DF 1 TSH G ≥ 1	1 (0.7)	1 (0.1)	0.140
DF 2 TSH G ≥ 1	0 (0.0)	3 (0.2)	1.000
DF 3 TSH G ≥ 1	0 (0.0)	5 (0.3)	1.000
DF 4 TSH G ≥ 1	0 (0.0)	4 (0.2)	1.000
DF 5 TSH G ≥ 1	0 (0.0)	5 (0.3)	1.000
ECU TSH G ≥ 1	1 (1.5)	16 (0.9)	1.000
TPD			
DF 1 TPD G ≥ 1	1 (0.7)	1 (0.1)	0.140
DF 2 TPD G ≥ 1	0 (0.0)	1 (0.1)	1.000
DF 3 TPD G ≥ 1	0 (0.0)	1 (0.1)	1.000
DF 4 TPD G ≥ 1	0 (0.0)	1 (0.1)	1.000
DF 5 TPD G ≥ 1	0 (0.0)	0 (0.0)	n/a
ECU TPD G ≥ 1	0 (0.0)	0 (0.0)	n/a
TEF			
DF 1 TEF G ≥ 1	5 (3.7)	27 (1.6)	0.175
DF 2 TEF G ≥ 1	2 (1.5)	19 (1.1)	0.768
DF 3 TEF G ≥ 1	0 (0.0)	22 (1.3)	0.588
DF 4 TEF G ≥ 1	0 (0.0)	19 (1.1)	0.583
DF 5 TEF G ≥ 1	3 (2.2)	29 (1.7)	0.658
ECU TEF G ≥ 1	4 (2.9)	52 (3.0)	1.000

HS, healthy subject; G, grade; THS, tenosynovial hypertrophy; TPD, power Doppler within the tendon sheath; TEF, tenosynovial effusion; DF, digit flexor tendon; ECU, extensor carpi ulnaris tendon. * Fisher's exact test

Supplementary table 9: Ultrasound tendon findings in healthy subjects with high impact vs low impact hobbies

	High impact upper limb hobbies Tendon Number (%)	Low impact upper limb hobbies Tendon Number (%)	p value*
Total number of tendons at each level	376	1502	
TSH			
DF 1 TSH G ≥ 1	1 (0.3)	1 (0.1)	0.361
DF 2 TSH G ≥ 1	0 (0.0)	3 (0.2)	1.000
DF 3 TSH G ≥ 1	0 (0.0)	5 (0.3)	0.590
DF 4 TSH G ≥ 1	0 (0.0)	4 (0.3)	0.590
DF 5 TSH G ≥ 1	0 (0.0)	5 (0.3)	0.590
ECU TSH G ≥ 1	0 (0.0)	17 (1.1)	0.033
TPD			
DF 1 TPD G ≥ 1	1 (0.3)	1 (0.1)	0.361
DF 2 TPD G ≥ 1	0 (0.0)	1 (0.1)	1.000
DF 3 TPD G ≥ 1	0 (0.0)	1 (0.1)	1.000
DF 4 TPD G ≥ 1	0 (0.0)	1 (0.1)	1.000
DF 5 TPD G ≥ 1	0 (0.0)	0 (0.0)	n/a
ECU TPD G ≥ 1	0 (0.0)	0 (0.0)	n/a
TEF			
DF 1 TEF G ≥ 1	3 (0.8)	29 (1.9)	0.199
DF 2 TEF G ≥ 1	1 (0.3)	20 (1.3)	0.145
DF 3 TEF G ≥ 1	1 (0.3)	21 (1.4)	0.123
DF 4 TEF G ≥ 1	1 (0.3)	18 (1.2)	0.189
DF 5 TEF G ≥ 1	3 (1.8)	29 (1.9)	0.199
ECU TEF G ≥ 1	18 (4.8)	39 (2.6)	0.049

HS, healthy subject; G, grade; THS, tenosynovial hypertrophy; TPD, power Doppler within the tendon sheath; TEF, tenosynovial effusion; DF, digit flexor tendon; ECU, extensor carpi ulnaris tendon. * Fisher's exact test

Supplementary table 10: Ultrasound tendon findings in age and sex matched healthy subjects and patients with RA

	HS tendons grade ≥1 Number (%)	RA tendons grade ≥1 Number (%)	p value* HS vs RA (age and sex matched)
Total number of tendons at each level	288	288	
DF 1 TSH grade ≥1 n (%)	0 (0)	15 (5.2)	< 0.001
DF 2 TSH grade ≥1 n (%)	0 (0)	50 (17.4)	< 0.001
DF 3 TSH grade ≥1 n (%)	1 (0.3)	50 (17.4)	< 0.001
DF 4 TSH grade ≥1 n (%)	1 (0.3)	28 (9.7)	< 0.001
DF 5 TSH grade ≥1 n (%)	5 (1,7)	36 (12.5)	< 0.001
ECU TSH grade ≥1 n (%)	6 (2.1)	60 (20.1)	< 0.001
DF 1 TPD grade ≥1 n (%)	0 (0)	10 (3.5)	0.002
DF 2 TPD grade ≥1 n (%)	0 (0)	36 (12.5)	< 0.001
DF 3 TPD grade ≥1 n (%)	0 (0)	40 (13.9)	< 0.001
DF 4 TPD grade ≥1 n (%)	0(0)	20 (6.9)	< 0.001
DF 5 TPD grade ≥1 n (%)	0 (0)	23 (8.0)	< 0.001
ECU TPD grade ≥1 n (%)	0 (0)	58 (20.3)	< 0.001

HS, healthy subject; THS, tenosynovial hypertrophy; TPD, power Doppler within the tendon sheath; TEF, tenosynovial effusion; DF, digit flexor tendon; ECU, extensor carpi ulnaris tendon. * Fisher's exact test.

Supplementary Figure 1: Flow chart diagram of inclusion and exclusion of healthy subjects

Supplementary Figure 2: Example images of tenosynovial hypertrophy, tenosynovial effusion within the tendon sheath in healthy subjects and patients with Rheumatoid Arthritis

1. Transverse section of left digit flexor 3 in a healthy subject showing tenosynovial hypertrophy and effusion
2. Longitudinal section of left digit flexor 3 in a healthy subject showing tenosynovial hypertrophy and effusion
3. Transverse section of right digit flexor 2 in a patient with Rheumatoid arthritis showing tenosynovial hypertrophy and effusion
4. Longitudinal section of right digit flexor 2 in a patient with Rheumatoid arthritis showing tenosynovial hypertrophy and effusion