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

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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 to 80 years) were recruited in 23 international Outcome Measures in Rheumatology (OMERACT) ultrasound centres and clinically assessed to exclude inflammatory diseases or overt osteoarthritis before undergoing a bilateral ultrasound examination of digit flexor (DF) 1-5 and extensor carpi ulnaris (ECU) tendons to detect the presence of tenosynovial hypertrophy (TSH), power Doppler (TPD) and tenosynovial effusion (TEF), usually considered ultrasound signs of inflammatory diseases. A comparison cohort of Rheumatoid Arthritis (RA) patients was taken from the Birmingham BEACON early arthritis inception cohort.

Results 939 HS and 144 RA patients were included. The majority of HS (85%) had grade 0 for TSH, TPD and TEF in all DF and ECU tendons examined. There was statistically significant difference in the proportion of TSH and TPD involvement between HS and RA subjects (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 in newly presenting suspected RA.

Keywords

Ultrasound, healthy, tendons, rheumatoid arthritis, tenosynovitis

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 magnetic resonance imaging (MRI) and ultrasound examination is more sensitive, and has shown that the prevalence of detecting tenosynovitis 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 tenosynovitis has a role in predicting outcome in early disease and flare in clinical remission. [6 7]

Although recent studies using MRI have focussed on the prevalence of tendon abnormalities in healthy subjects (HS),[8] there is limited data on the prevalence of ultrasound detected "tenosynovitis" abnormalities in HS with data arising from small comparison cohorts (i.e. case control studies focussed on patients with rheumatic diseases). Furthermore, current studies were not focussed on the prevalence of sonographic tendon abnormalities in HS within the age range of 40 to 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) study was therefore to determine the prevalence of ultrasound detected tendon abnormalities characterizing the presence of tenosynovitis in HS according to the age range.

Methods

Recruitment

A large cohort of adult HS (age 18 to 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: joint trauma of hands or wrist in the previous month; hand or wrist pain ≥10/100 on visual analogue scale; hand osteoarthritis as defined by ACR criteria[11]; history or evidence of inflammatory/crystal arthritis; inflammatory bowel diseases; recent culture-proven bowel or genito-urinary infection; recent or concurrent use of corticosteroids, or current use of non-steroidal anti-inflammatory medications. Demographic data including body mass index (BMI) were collected. Metacarpophalangeal (MCP), proximal interphalangeal (PIP) and wrist joints were clinically examined by an independent assessor in each centre and subjects were excluded if synovitis was found.

Ultrasound

Ultrasound assessment of bilateral digit flexor (DF) 1-5 and extensor carpi ulnaris (ECU) tendons was performed using a multi-planar approach. The presence of hypoechoic tenosynovial hypertrophy (TSH) and power Doppler signal within tenosynovial hypertrophy (TPD) were defined and graded using the OMERACT ultrasound scoring system for tenosynovitis 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 pre-set parameters were used to optimise imaging for greyscale and power Doppler and reduce variability. Details of probes and machines used in all centres can be found in Supplementary Table 1. Quality and grading of recorded images were confirmed by review of all images for the primary recruit from each centre by an experienced blinded independent assessor in the hub centre. Any disagreement was then fed back to the centre and consensus achieved to ensure reliability in subsequent scans.

Data for a comparison cohort of DMARD-naive patients presenting with RA fulfilling ACR-EULAR 2010[14] and/or 1987 criteria[15] at presentation were extracted from the Birmingham Early Arthritis (BEACON) inception cohort as previously described[6], who underwent identical baseline tendon ultrasound assessment except presence of TEF was not recorded.

Statistical analysis

Statistical analysis was performed using IBM SPSS Statistics version 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, joint counts (for RA patients) were not normally distributed; significance was therefore assessed using the Kruskall Wallis test. The tendon gradings were dichotomised into either present (grade 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 RA patients.

Results

One thousand and thirty-eight HS were recruited and 939 HS were included after exclusions of subjects with present or past history of carpal tunnel syndrome, Dupuytren's contracture, hepatitis C, autoimmune keratitis, cutaneous lupus, polymyalgia rheumatica as well as current pregnancy. Baseline data for 144 RA patients 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.

	HS Y 18-39 yr	HS M 40-59 yr	HS O ≥60 yr	HS Y/M/O p value	RA	RA vs HS [#] p value
n	405	350	184		144	
Age, yr median (IQR)	29 (25-33)	49 (44-54)	68 (62-72)	<0.001	54 (45-67)	<0.001
Females, n (%)	268 (66.2)	285 (81.4)	117 (63.6)	<0.001	106 (73.6)	0.620
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)	<0.001
ever (%)	88 (22)	109 (31)	66 (36)		75 (52)	<0.001
current (%)	47 (12)	56 (16)	12 (7)		28 (19)	0.024
EMS, mins 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
DAS 28 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

Table 1: Demographics and tendon changes (grade 1-3 tenosynovial hypertrophy and power Doppler) for healthy subjects (HS) and RA patients.

[#]RA and HS age and sex matched to compare ultrasound graded tendon findings. *RA patients had 66/68 joint counts. HS had joint counts of MCPs, PIPs, wrists and MTPs. IQR, interquartile range; BMI, body mass index; EMS, early morning stiffness; CRP, C reactive protein; DAS 28, disease activity score; DF, digit flexor tendon, ECU, extensor carpi ulnaris tendon; TSH, tenosynovial hypertrophy; PD, power Doppler. Full ultrasound grading results available in supplementary table 2.

Healthy subjects

The median age of HS was 43 years (30-57). HS were grouped into 3 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 health care 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 11237 tendons were scanned in the 939 included HS; 98% of these tendons were grade 0 for TSH, TPD and TEF (supplementary table 3). The distribution of tendon abnormalities, when found, was symmetrical with no significant difference between right and left hands (supplementary table 4). TEF was more frequently detected than TSH or TPD ($p<0.001$) (supplementary 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 DF1-5 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).

All abnormalities detected across 939 HS were of grade 1 severity, with the exception of one grade 2 for TSH in an ECU tendon. The ECU tendons had significantly more grade ≥1 for TSH than the DF1-5 tendons ($p<0.05$) (supplementary table 6).

There was no statistically significant difference in 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 (supplementary tables 7 and 8).

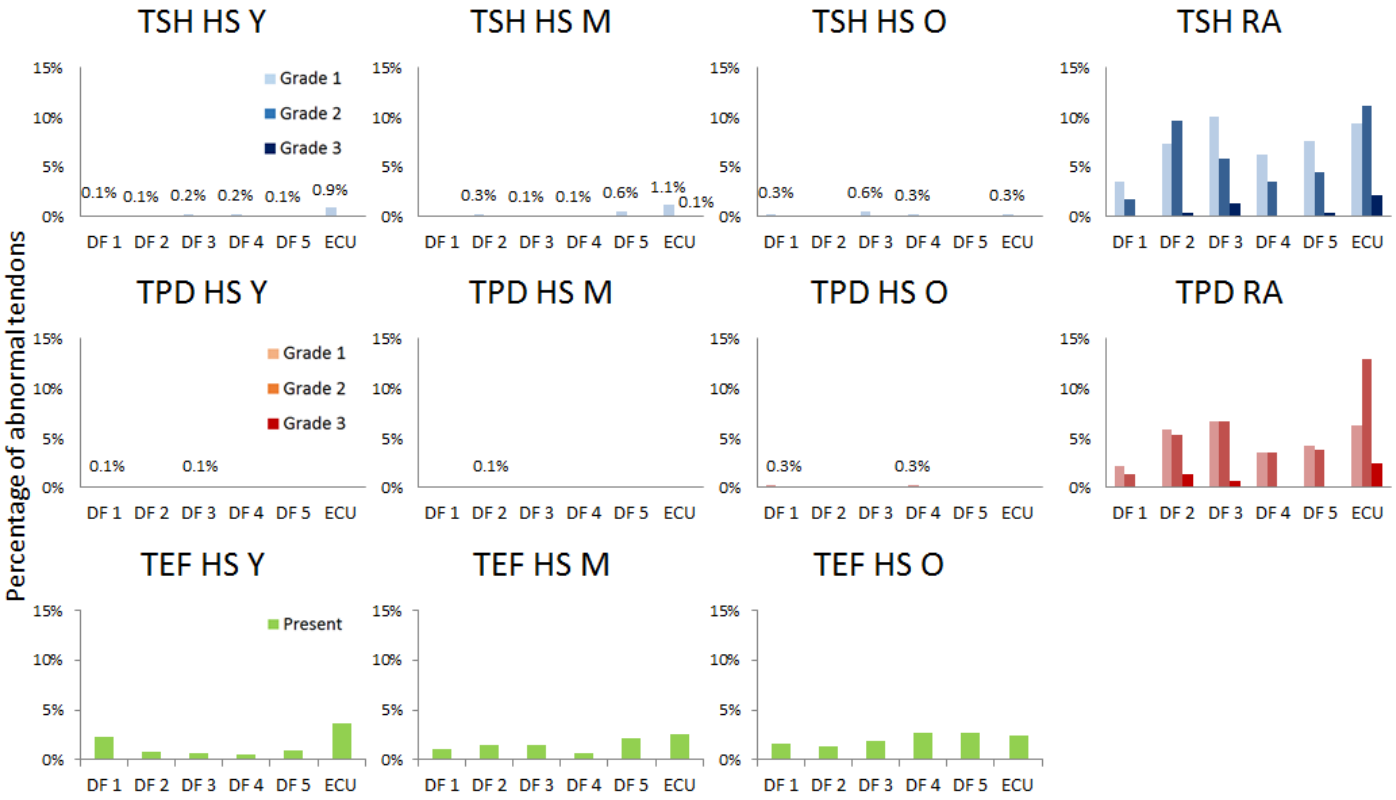

Figure 1: Percentage of tendons with detected tenosynovial hypertrophy (TSH), tendon sheath power Doppler (TPD) and tenosynovial effusion (TEF) in digit flexor (DF) tendons 1-5 and extensor carpi ulnaris tendons (ECU) for healthy subjects (HS) and rheumatoid arthritis (RA) patients according to age groups. TSH and TPD quantified as grades 0 -3, with grade 0 being absent; TEF measured only in HS, and as either present or absent. HS Y, 18-39 years; HS M, 40-59 years; HS O, 60-80 years.

RA patients

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

Discussion

The aim of this large international study of over 900 HS was to determine the extent of sonographic abnormalities of tendons compatible with ultrasound detected inflammation in HS across a broad age range encompassing the age incidence of RA. There was very low prevalence of TSH and Power Doppler in all DF and ECU tendons across the age range. The few abnormalities observed were almost exclusively grade 1 in severity. Due to the large population studied, this study provides conclusive data validating and expanding upon the findings of existing studies with less than 50 healthy controls.[16 17,18]

Despite a low mean age (44.4 (+/-15.5) years), our study assessed large numbers in the older age range, with 367 healthy subjects over the age of 50 years. Remarkably, very low numbers of ultrasound abnormalities were seen even in the older age group of 60-80 year olds.

TEF was more prevalent than TSH or TPD in HS. Although MRI studies have suggested tenosynovial effusion to be almost ubiquitous in digit flexor tendons in HS[19], we have shown that ultrasound detects smaller numbers, with less than 2% of digit flexor tendons having effusion even in the older age group.

Compared to a smaller earlier study[6] we show in a larger cohort that tenosynovial abnormalities on ultrasound are significantly more prevalent in early RA compared to matched HS.

By explicitly selecting only patients with minimal joint pain and without overt osteoarthritis, HS in this cohort may have fewer tendon changes than an unselected general population of 60-80 year olds. However it was not the purpose of this study to document the presence of tendon abnormalities in individuals with clinically evident osteoarthritis. Similarly, although less than 10% of HS in this study were manual workers, no significant difference was found between these 68 HS and the larger cohort.

Importantly, the very low prevalence of TSH and TPD across the age range in HS suggests that gradable findings can be regarded as clinically significant in the absence of obvious confounding regional pain syndromes. Therefore rheumatologists, radiologists or health professionals performing ultrasound in early arthritis or disease management clinics should feel confident in interpreting mild TSH and TPD as significant in patients of all ages presenting with possible early inflammatory arthritis or with ambiguous symptoms and clinical findings. Digit flexor and ECU tendons can be easily examined during routine ultrasound examination, so could be included in abbreviated scanning protocols.

Key Messages

What is already known about this subject?

Little was known about the prevalence of sonographic tenosynovial abnormalities in healthy subjects across the age range

What does this study add?

This is the largest cohort of healthy subjects' tendons scanned by ultrasound

There was very low prevalence of tendon synovial hypertrophy or power Doppler abnormalities in tendons of healthy subjects 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 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 rheumatoid arthritis

Acknowledgements and affiliations

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.

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Supplementary table 1: Ultrasound machines and transducers used by centres

Centre	Contributers	Machine	Linear Transducer
Institute of Inflammation and Ageing, University of Birmingham, UK	Andrew Filer, Jeanette Trickey, Ilfita Sahbudin	GE Logiq E9	8-18MHz; 6-15MHz
University College London, UK	Coziana Ciurtin	GE Logiq E8	8-15MHz
Hôpital Ambroise Paré, Paris, France	Maria-Antonietta D'agostino, Hélène Gouze	ESAOTE MyLab70 XVG	6-18MHz PD 11 MHz, PRF 750Hz
Cliniques Universitaires Saint-Luc, Institut de recherche expérimentale et clinique (IREC), Université catholique de Louvain Bruxelles, Belgium.	Maria Stoenoiu, Mihaela Maruseac		
Ghent University, Belgium	Ruth Wittoek, Philippe Carron	ESAOTE MyLab 60	
University of Ferrara, Italy	Alessandra Bortoluzzi	ESAOTE MyLab 70XVG	14–18 MHz
University of Ferrara, Italy	Georgios Filippou	Samsung RS80A	4-18 MHz; 3-12MHz
Università degli Studi di Torino, Turin, Italy	Annamaria Iagnocco, Teodora Șerban, Irene Azzolin	ESAOTE MyLab8	L4-15 (4-15 MHz); LA435 (6-18MHz)
University of Pavia, Italy	Garifallia Sakellariou	ESAOTE Mylab 70 XVG	ESAOTE LA435 (6-18 MHz) Power Doppler: PRF 0.75; Doppler frequency 7.7 MHz
Sacro Cuore Hospital, Negrar, Verona, Italy	Ilaria Tinazzi	ESAOTE MyLabClassC	10-18 MHz Power Doppler (PD): 750 Hz PRF, wall filter 3, persistence 4, colour gain 50-55%.

Copenhagen University Hospital, Denmark	Lene Terslev, Mads Ammitzball Danielsen	GE Logiq E9	ML 6-15 Colour Doppler (CD) frequency 7.5 MHz, PRF 0.4
Aarhus University Hospital, Denmark	Ellen-Margrethe Hauge, Mads Nyhuus Bendix Rasch	Hitachi Noblus	18-5 L64 Colour Doppler (CD) frequency 6.5 MHz
Diakonhjemmet Hospital, Oslo, Norway	Hilde Berner Hammer	GE Logiq E9	6-15 MHz
Leiden University Medical Center, The Netherlands.	Marion Kortekaas, Sarah Ohrndorf	GE logic E9	5-18 MHz
Pomeranian Medical University, Szczecin, Poland	Marcin Milchert, Jacek Fliciński	Phillips Epiq 5	18 MHz
Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania	Daniela Fodor	GE S7	L8-18I
University of Medicine and Pharmacy, Craiova, Romania	Florentin Vreju	ESAOTE Mylab 25 Gold	18MHz
Medical University of Plovdiv, Bulgaria.	Rositsa Karalilova	ESAOTE MyLab 7	3-18 MHz
Hospital Universitario Fundación Jiménez Díaz, Madrid, Spain.	Esperanza Naredo, Cesar Sifuentes-Cantu, Giuliana M.C. La Paglia	GE Logiq E9	ML6-15 (6-15MHz)
Instituto Nacional de Rehabilitacion, Mexico City, Mexico	Carlos Pineda, Marwin Gutierrez, Gustavo Leon, Cristina Reategui-Sokolova	GE Logiq e	8-18 MHz
Zagazig University, Egypt	Mohamed Mortada	Hitachi Aloka F37	18 MHz
Japanese Red Cross Medical Center, Tokyo, Japan	Takeshi Suzuki	HI VISION Avius	5-18 MHz PD frequency 7.5MHz, PRF 800Hz
Chiba University Hospital, Japan	Kei Ikeda	HI VISION Avius HI VISION Ascendus	EUP-L75 (5-18MHz)

Supplementary table 2: Ultrasound grades for healthy subjects and RA patients

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 3: 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 4: 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 5: 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 6: 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 7: 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 8: 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 9: Ultrasound tendon finding s 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.