Introduction

Systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA) are systemic rheumatic diseases that present with various musculoskeletal signs and symptoms. While RA is characterized by destructive and deforming polyarthritis, arthritis in SLE is typically non-erosive, although some patients with SLE show erosive and destructive arthropathy called “rhupus” [1,2]. The non-erosive and manually movable “Jaccoud’s deformity” in SLE can be attributed to the inflammation and subsequent damage in joint tendons and ligaments rather than those in bone and cartilage [1,3].

Recent advances in high-sensitivity imaging such as magnetic resonance imaging (MRI) and ultrasonography (US) have elucidated the arthropathy of various rheumatic diseases, particularly rheumatoid arthritis (RA) [4-6]. MRI is advantageous for its highly sensitive detection of osteitis and, with gadolinium enhancement, synovitis and tenosynovitis [7-10]. Indeed, Jaccoud’s arthropathy is identified on MRI as severe oedematous tenosynovitis and capsular swelling without bony erosions [11]. In contrast, ultrasonography (US) examination of the joints can immediately visualize various joints

without contrast medium. Therefore, it is undoubtedly useful to perform US joint examinations in patients' first referral for arthritis evaluation.

Articular symptoms develop initially in 60% of patients with SLE and eventually in 90% [12]. Although a few previous studies have compared joint US findings of patients with SLE with those of RA patients [13-15], the differences in the treatment of SLE and RA make such comparisons very complicated.

Thus, in the present study we retrospectively investigated the distribution and activity of joint synovitis and tenosynovitis/periextensor tendon inflammation (PTI) in the hands of patients with treatment-naïve early SLE compared to those with treatment-naïve early RA. Our findings suggest a relative predominance and independence of tenosynovitis/PTI over joint synovitis in SLE compared with RA.

Patients and methods

Patients

Among patients visiting the Division of Rheumatology, Toho University Ohashi

Medical Center for the first time between January 2011 and March 2014, those who met all of the following criteria were enrolled in this retrospective study: 1) presence of subjective articular symptoms in any joints such as arthralgia or joint stiffness; 2) presence of joint swelling and/or tenderness in at least one joint; 3) availability of joint US examination records of the hands before reaching a diagnosis and starting any treatments with synthetic or biological disease-modifying anti-rheumatic drugs or glucocorticoids; and 4) fulfilment of the 1997 revised American College of Rheumatology (ACR) or 2012 Systemic Lupus International Collaborating Clinics (SLICC) classification criteria for SLE [16,17] or 2010 ACR/European League Against Rheumatology (EULAR) classification criteria for RA [18] and diagnosed with SLE or RA, respectively. The exclusion criterion was disease duration > 2 years (Figure 1). This study was approved by the institutional ethical committee of Toho University Ohashi Medical Center (project approval number: 14-31), and informed consent was obtained from all participants.

Clinical assessments

The patients' medical records were reviewed and their demographic features and clinical and laboratory findings at the time of US evaluation including disease duration (from the onset of the symptom to US examination); tender and swollen joint counts of 28 joints; presence or absence of cutaneous, serosal, renal, and neuropsychiatric lupus manifestations; erythrocyte sedimentation rate (ESR; normal, ≤15 mm/hour); serum C-reactive protein (CRP; normal, ≤3 mg/L), complement (C3, C4, and/or CH50; normal, 60–130 mg/dL, 17–40 mg/dL, and 25–48 CH50 U/mL, respectively), rheumatoid factor (RF; normal, ≤15 IU/mL), anti-cyclic citrullinated peptide antibody (anti-CCP; normal, <4.5 U/mL), anti-nuclear antibody (ANA; negative titre < 1:40), anti-double-stranded DNA antibody (dsDNA; normal, <6.0 IU/mL by radioimmunoassay), and anti-Smith antibody (anti-Sm; normal, ≤10.0 IU/mL by enzyme-linked immunosorbent assay or negative by double immunodiffusion).

US examination

A Xario (Toshiba Medical Systems, Tochigi, Japan) US machine equipped with a multi-frequency linear array probe (7–14 MHz) was used. Power Doppler (PD) settings were flow range, 3.8 cm/s; PD pulse repetition frequency, 16.5 kHz [19,20]; Doppler frequency, 6.1 MHz; and low wall filter. Colour gain was set just below the level at which noise appeared. Before the diagnosis was made, the US examination was performed according to the EULAR guidelines for musculoskeletal US in rheumatology [21] by one of three rheumatologists (TO, AH, or NH). All of them were Japan College of Rheumatology board-certified ultrasonographers and not blinded to the patients' medical records. The bilateral wrist joints (radial, medial, and ulnar sides, focusing on the distal radioulnar, radiocarpal, and midcarpal joints), the first through fifth metacarpophalangeal (MCP) joints, thumb interphalangeal (IP) joints, second through fifth proximal interphalangeal (PIP) joints, first through sixth compartments of the wrist extensor tendons, wrist flexor tendons, and extensor and flexor tendons of the first through fifth finger digits on the dorsal and palmar sides were examined on longitudinal and transverse scans.

One US examiner (TO) performed the final scoring of the recorded US findings in a blinded manner according to the OMERACT definitions [22]. Grayscale (GS) was graded semiquantitatively on a scale of 0–3 (0 = absent, 1 = mild, 2 = moderate, and 3 = marked) in a combined measure of synovial hypertrophy and fluid retention of the articular recess and tendon sheath/periextensor tendon [23-25]. The periextensor tendon was used because the finger extensor tendon does not have a formal tendon sheath (Supplementary Figure 1) [7]. The intra-articular and tenosynovial/periextensor tendon PD signals were also graded on a 0–3 scale. Joints or tendons graded as GS ≥ 2 or PD ≥ 1 were judged as having joint synovitis or tenosynovitis/PTI, respectively [26].

Furthermore, the total joint or tendon US score was determined by summing all of the GS and PD scores for each patient. The mean US score for each joint region was defined by the total US score divided by the number of affected regions. The concordance of joint and tendon involvement in each joint region was also examined.

Intraobserver reliability of the final scoring (TO) was examined using the recorded US findings of 10 randomly selected patients at an interval > 6 months. Interobserver

reliability (TO, AH, or NH) was evaluated with the same set of images from six randomly selected scored patients.

Statistical analysis

The statistical analysis was performed using EZR software (version 1.25; Saitama Medical Center, Jichi Medical University, Saitama, Japan) [27], a graphical user interface for R (version 3.1.1; The R Foundation for Statistical Computing, Vienna, Austria). Continuous variables were summarized as medians and interquartile ranges (IQRs) and analysed using the Mann–Whitney U test, while binominal data from the two groups were examined by Fisher's exact test. The rate of concordance was analysed using Cohen's kappa statistic. The kappa coefficients were divided as follows: <0.0 = poor, 0–0.20 = slight, 0.21–0.40 = fair, 0.41–0.60 = moderate, 0.61–0.80 = substantial, and 0.81–1.0 = almost perfect agreement [28]. Intraobserver reliability was determined using weighted kappa statistics, while interobserver reliability was determined using Kendall's W coefficient. P values < 0.05 were considered statistically significant.

Results

Patient characteristics

Among the total 1494 patients visiting the Division of Rheumatology, Toho University Ohashi Medical Center for the first time between January 2011 and March 2014, 788 reported the presence of joint symptoms such as arthralgia and stiffness (Figure 1). A clinical joint examination revealed the presence of joint swelling and/or tenderness in 515 patients; of them, 394 were treatment-naïve. One hundred and twenty-two patients underwent US examinations of at least the bilateral hands to assess joint and tendon involvement. Fifteen and 41 patients fulfilled the classification criteria for and were diagnosed with SLE and RA, respectively. After excluding one patient with a disease duration > 2 years, we finally included 15 patients with SLE and 40 patients with RA in this study. Patients' demographic, clinical, and laboratory characteristics are shown in Table 1. A similar female predominance was observed in both groups, and patients with SLE were younger than those with RA (mean age, 53 years versus 67 years; $p = 0.040$).

The median disease durations (from symptoms) were approximately 6 months for both SLE and RA.

Hand arthritis was observed on clinical examination in most patients in the SLE and RA groups (87% and 98%, respectively; p = 0.177). As expected, tender joint count, but not swollen joint count, and (high) positivity of RF and anti-CCP were greater in RA than SLE, while ANA high-titre positivity was greater in SLE. Radiographic erosive changes were observed in zero patients with SLE and five of 40 patients with RA.

Prevalence of US findings

US joint synovitis in the hands was observed in 12 of 15 (80%) patients with SLE and 38 of 40 (95%) patients with RA (p = 0.119; Table 2). Wrist and MCP synovitis was detected in 70–80% of patients in both groups, while IP/PIP synovitis was demonstrated in <50% of patients in both groups. Interestingly, tenosynovitis/PTI was more frequently observed in the SLE than RA group (93% versus 65%; p = 0.045) and specifically, wrist tendon involvement was observed in a significantly greater proportion

of patients with SLE than those with RA (73% versus 40%; p = 0.037).

The examination of a total of 26 regions for joint synovitis per patient revealed similar occurrence rates of joint synovitis in the SLE and RA groups (90 of 390 [23%] versus 286 of 1040 [28%], respectively; p = 0.083). Joint synovitis was especially frequent in the wrists as well as the second and third MCP joints in the SLE and RA groups (>30%; Figure 2A). However, when 34 regions were examined for tenosynovitis/PTI per patient, tendon involvement was significantly more frequent in the SLE versus RA group (70 of 510 [14%] versus 112 of 1360 [8%], respectively; p = 0.022). Notably, tendon involvement in the fourth compartment of the wrist extensor, wrist flexor, and third finger flexor tendon was observed in approximately 30% of patients with SLE but was relatively rare (approximately 10%) in patients with RA (Figure 2B).

Intensity of US findings

The median total joint US score (composed of GS and PD scores) was 14 in patients with SLE and 20 in those with RA (p = 0.269), and no differences were observed

between the two groups in any joint regions including the wrist, MCP, and IP/PIP (Supplementary Table 1). However, the median wrist tendon US score was greater in the SLE group than in the RA group for both GS (2 versus 0, respectively; p = 0.031) and PD (2 versus 0, respectively; p = 0.010) as well as GS+PD (3 versus 0, respectively; p = 0.012) scores, although the total tendon US score was not significantly different between the SLE and RA groups (6 versus 3.5, respectively; p = 0.095). To clarify whether the difference or non-difference in summed US score between SLE and RA was attributable to the intensity (score per region) or extension (the number of regions) of joint/tendon inflammation, the total joint or tendon US score was divided by the number of affected (GS ≥ 2 or PD ≥ 1) regions for each patient and compared between the SLE and RA groups (Table 3). The median wrist PD score and GS+PD score per joint were significantly lower in patients with SLE than in those with RA (1.0 versus 1.4, respectively, p = 0.012; 2.0 versus 2.6, respectively, p = 0.037) along with the total GS score (1.2 versus 1.5, respectively; p = 0.038), total PD score (1.0 versus 1.4, respectively; p = 0.003), and total GS+PD score (2.0 versus 2.6, respectively; p = 0.019).

On the contrary, the wrist tendon PD score per joint was greater in the SLE group than in the RA group (1.0 versus 0.0, respectively; p = 0.030), although the total tendon GS+PD score was not significantly different between SLE and RA patients (2.1 versus 2.2, respectively; p = 0.738). The mean number of joints with synovitis for each patient was similar in the SLE and RA groups (5 versus 6, respectively; p = 0.602), although the mean number of joints with tenosynovitis/PTI was significantly greater in the SLE than RA group (3 versus 1, respectively; p = 0.042).

Independence of tenosynovitis/PTI from joint synovitis

Because of the relative tenosynovitis/PTI predominance in the SLE group and joint synovitis predominance in the RA group, we examined the concordance of joint synovitis and tenosynovitis/PTI in 150 and 400 fingers in the SLE and RA groups, respectively. The concordance of synovitis and tenosynovitis/PTI in the same finger was observed in 68% and 77% of SLE and RA fingers, respectively, and the kappa values were 0.201 (95% confidence interval [CI], 0.014–0.387) and 0.415 (95% CI, 0.310–

0.520), respectively (Table 4). Notably, the presence of joint synovitis was observed in only 49% (17 of 35) of fingers with tenosynovitis/PTI in the SLE group versus 74% (58 of 78) of fingers with tenosynovitis/PTI in the RA group ($p = 0.010$ by Fisher's exact test).

Intra- and interobserver reliability

The weighted kappa statistics for intraobserver reliability revealed $\kappa = 0.852$ (95% CI, 0.825–0.880) for the total GS and PD scores. Interobserver agreement was significant for the total GS and PD scores ($p < 0.001$). Kendall's W coefficient was 0.838.

Discussion

In the present study focusing on treatment-naïve patients with early disease, we demonstrated that patients with SLE had wrist tendon inflammation more frequently than those with RA. In addition, the concordance of joint and tendon involvement in the same finger was lower in SLE patients than in RA patients, suggesting non-destructive

joint deformity in hands with SLE.

Previous studies of SLE patients not focusing on treatment-naïve populations reported tendon involvement in 28–65% in addition to wrist arthritis (16–94%) and MCP arthritis (42–71%) [29-35]. Similarly, tenosynovitis of the hand flexor tendons was observed by physical examination in 55% of patients with RA [36] and noted on US examination in 47–80% of RA patients [4,7,8,37,38]. A comparison of US and MRI revealed that finger flexor and extensor tendon involvement were determined by US in 48% and 18% of treatment-naïve RA patients, respectively, and in 82% and 72% using MRI, respectively [7]. Another study of treatment-naïve RA patients also demonstrated wrist extensor and wrist/finger flexor tendon involvement in 40% and 50% of patients, respectively, on US and in 67% and 87% of patients, respectively, on MRI [8].

In a MRI comparison of RA and SLE patients, a comparable but numerically higher mean global score was observed in SLE compared to RA (7 versus 6 in the wrist and 5.7 versus 3.8 in the MCP joints, respectively) [39]. Previous US-based comparisons of patients with SLE and those with RA did not include tendon involvement [13,14]. Thus,

to our knowledge, this study is the first to use US to compare joint synovitis and tenosynovitis/PTI between treatment-naïve patients with early SLE and those with RA. Our results suggest that patients with SLE tend to develop tendon inflammation in the wrists and that inflammation in the fingers is likely to occur independently of joint synovitis compared to RA patients, which may lead to non-erosive joint deformities in patients with SLE. In contrast, the degree of joint synovitis per joint was more intense in RA than in SLE, which is likely to be associated with erosive joint destruction in RA. These findings are consistent with the concept of synovitis primary site [40]: RA synovitis is primary, whereas SLE synovitis can be secondary.

The limitations of this study include its small sample size, retrospective data analysis, and absence of other high-sensitivity imaging data such as MRI. Therefore, future prospective studies should include MRI and assess radiographic progression in patients with SLE and RA, although treatment differences between these diseases may complicate the results. Although our mean patient age seems high for treatment-naïve early disease, this may be partially attributable to the aged society in Japan, including

Tokyo. For example, the mean age of a recent cohort study of newly diagnosed RA patients was 60.9 years despite the mean disease duration of 9.1 months [41]. The age range of SLE patients in this study was 23–72 years, and we compared the hand radiographs for the presence of osteoarthritis (OA)-like changes (focal joint space narrowing, marginal osteophytes, and osteosclerosis) between SLE and RA patients. The OA-like changes in the joints we examined by US (IP/PIP and MCP joints) were observed in three of 12 (25.0%) patients with SLE (hand X-ray was missing for three patients) and 10 of 40 (25.0%) patients with RA, showing comparable results ($p = 1.000$ by Fisher's exact test). Therefore, our study population could be rather suitable for the comparing US joint findings of SLE and RA.

In conclusion, the present US-based study of treatment-naïve patients with early SLE and RA demonstrated that SLE arthropathy is characterized by tendinitis/tenosynovitis. These findings may be useful in the management of SLE arthropathy and preventing the development of Jaccoud's deformity.

Funding

This research was supported by a research grant from Takeda Pharmaceutical Company Limited.

Conflict of interest

The authors declare no conflicts of interest.

References

1. Alarcon-Segovia D, Abu-Mendoza C, Diaz-Jouanen E, Iglesias A, De los Reyes V, Hernandez-Ortiz J. Deforming arthropathy of the hands in systemic lupus erythematosus. J Rheumatol. 1988; 15: 65-69.

2. van Vugt RM, Derksen RH, Kater L, Bijlsma JW. Deforming arthropathy or lupus and rhupus hands in systemic lupus erythematosus. Ann Rheum Dis. 1998; 57: 540-544.

3. Cruickshank B. Lesions of joint and tendon sheaths in systemic lupus erythematosus. Ann Rheum Dis. 1959; 18: 111-119.

4. Backhaus M, Kamradt T, Sandrock D, et al. Arthritis of the finger joints: a comprehensive approach comparing conventional radiography, scintigraphy, ultrasound, and contrast-enhanced magnetic resonance imaging. Arthritis Rheum. 1999; 42: 1232-1245.

5. Goupille P, Roulot B, Akoka S, et al. Magnetic resonance imaging: a valuable method for the detection of synovial inflammation in rheumatoid arthritis. J Rheumatol. 2001; 28: 35-40.

6. Walther M, Harms H, Krenn V, Radke S, Faehndrich TP, Gohlke F. Correlation of power Doppler sonography with vascularity of the synovial tissue of the knee joint in patients with osteoarthritis and rheumatoid arthritis. Arthritis Rheum. 2001; 44: 331-338.

7. Wakefield RJ, O'Connor PJ, Conaghan PG, et al. Finger tendon disease in untreated early rheumatoid arthritis: a comparison of ultrasound and magnetic resonance imaging. Arthritis Rheum. 2007; 57: 1158-1164.

8. Navalho M, Resende C, Rodrigues AM, et al. Bilateral evaluation of the hand and wrist in untreated early inflammatory arthritis: a comparative study of ultrasonography and magnetic resonance imaging. J Rheumatol. 2013; 40: 1282-1292.

9. Østergaard M, Conaghan PG, O'Connor P, et al. Reducing invasiveness, duration, and cost of magnetic resonance imaging in rheumatoid arthritis by omitting intravenous contrast injection -- Does it change the assessment of inflammatory and destructive joint changes by the OMERACT RAMRIS? J Rheumatol. 2009; 36: 1806-1810.

10. Tamai M, Kawakami A, Uetani M, et al. Magnetic resonance imaging (MRI)

detection of synovitis and bone lesions of the wrists and finger joints in early-stage rheumatoid arthritis: comparison of the accuracy of plain MRI-based findings and gadolinium-diethylenetriamine pentaacetic acid-enhanced MRI-based findings. Mod Rheumatol. 2012; 22: 654-658.

11. Ostendorf B, Scherer A, Specker C, Mödder U, Schneider M. Jaccoud's arthropathy in systemic lupus erythematosus: differentiation of deforming and erosive patterns by magnetic resonance imaging. Arthritis Rheum. 2003; 48: 157-165.

12. D Wallace, BH Hahn. Dubois' Lupus Erythematosus and Related Syndromes. 8th ed. Philadelphia: Elsevier/Saunders, 2013, p. 305-307.

13. Tani C, D'Aniello D, Delle Sedie A, et al. Rhupus syndrome: assessment of its prevalence and its clinical and instrumental characteristics in a prospective cohort of 103 SLE patients. Autoimmun Rev. 2013; 12: 537-541.

14. Buosi AL, Natour J, Machado FS, Takahashi RD, Furtado RN. Hand ultrasound: comparative study between "no rhupus" lupus erythematosus and rheumatoid arthritis. Mod Rheumatol. 2014; 24: 599-605.

15. Ball EM, Gibson DS, Bell AL, Rooney MR. Plasma IL-6 levels correlate with clinical and ultrasound measures of arthritis in patients with systemic lupus erythematosus. Lupus. 2014; 23: 46-56.

16. Hochberg MC. Updating the American College of Rheumatology revised criteria for the classification of systemic lupus erythematosus. Arthritis Rheum. 1997; 40: 1725.

17. Petri M, Orbai AM, Alarcón GS, et al. Derivation and validation of the Systemic Lupus International Collaborating Clinics classification criteria for systemic lupus erythematosus. Arthritis Rheum. 2012; 64: 2677-2686.

18. Aletaha D, Neogi T, Silman AJ, et al. 2010 Rheumatoid arthritis classification criteria: an American College of Rheumatology/European League Against Rheumatism collaborative initiative. Arthritis Rheum. 2010; 62: 2569-2581.

19. Seo Y. Method and system for controlling ultrasound scanning sequence. U.S. Patent 4,993,417. Feb. 19, 1991.

20. Sakano R, Kamishima T, Nishida M, Horie T. Power Doppler signal calibration between ultrasound machines by use of a capillary-flow phantom for pannus vascularity

in rheumatoid finger joint. Radiol Phys Technol 2015; 8: 120-124.

21. Backhaus M, Burmester GR, Gerber T, et al. Guidelines for musculoskeletal ultrasound in rheumatology. Ann Rheum Dis 2001; 60: 641-649.

22. Wakefield RJ, Balint PV, Szkudlarek M, et al. Musculoskeletal ultrasound including definitions for ultrasonographic pathology. J Rheumatol. 2005; 32: 2485-2487.

23. Naredo E, D'Agostino MA, Wakefield RJ, et al. Reliability of a consensus-based ultrasound score for tenosynovitis in rheumatoid arthritis. Ann Rheum Dis. 2013; 72: 1328-1334.

24. Szkudlarek M, Court-Payen M, Jacobsen S, Klarlund M, Thomsen HS, Ostergaard M. Interobserver agreement in ultrasonography of the finger and toe joints in rheumatoid arthritis. Arthritis Rheum. 2003; 48: 955-962.

25. Scheel AK, Hermann KG, Kahler E, et al. A novel ultrasonographic synovitis scoring system suitable for analyzing finger joint inflammation in rheumatoid arthritis. Arthritis Rheum. 2005; 52: 733-743.

26. Nakagomi D, Ikeda K, Okubo A, et al. Ultrasound can improve the accuracy of the

2010 American College of Rheumatology/European League against rheumatism classification criteria for rheumatoid arthritis to predict the requirement for methotrexate treatment. Arthritis Rheum. 2013; 65: 890-898.

27. Kanda Y. Investigation of the freely available easy-to-use software 'EZR' for medical statistics. Bone Marrow Transplant. 2013; 48: 452-458.

28. Landis JR, Koch GG. The measurement of observer agreement for categorical data. Biometrics. 1977; 33: 159-174.

29. Iagnocco A, Ossandon A, Coari G, Conti F, Priori R, Alessandri C, et al. Wrist joint involvement in systemic lupus erythematosus. An ultrasonographic study. Clin Exp Rheumatol. 2004; 22: 621-624.

30. Wright S, Filippucci E, Grassi W, Grey A, Bell A. Hand arthritis in systemic lupus erythematosus: an ultrasound pictorial essay. Lupus. 2006; 15: 501-506.

31. Delle Sedie A, Riente L, Scire CA, et al. Ultrasound imaging for the rheumatologist. XXIV. Sonographic evaluation of wrist and hand joint and tendon involvement in systemic lupus erythematosus. Clin Exp Rheumatol. 2009; 27: 897-901.

32. Iagnocco A, Ceccarelli F, Rizzo C, et al. Ultrasound evaluation of hand, wrist and foot joint synovitis in systemic lupus erythematosus. Rheumatology (Oxford). 2014; 53: 465-472.

33. Gabba A, Piga M, Vacca A, et al. Joint and tendon involvement in systemic lupus erythematosus: an ultrasound study of hands and wrists in 108 patients. Rheumatology (Oxford). 2012; 51: 2278-2285.

34. Mosca M, Tani C, Carli L, et al. The role of imaging in the evaluation of joint involvement in 102 consecutive patients with systemic lupus erythematosus. Autoimmun Rev. 2015; 14: 10-15.

35. Zayat AS, Md Yusof MY, Wakefield RJ, Conaghan PG, Emery P, Vital EM. The role of ultrasound in assessing musculoskeletal symptoms of systemic lupus erythematosus: a systematic literature review. Rheumatology (Oxford). 2016; 55: 485-494.

36. Gray RG, Gottlieb NL. Hand flexor tenosynovitis in rheumatoid arthritis. Prevalence, distribution, and associated rheumatic features. Arthritis Rheum. 1977; 20: 1003-1008.

37. Grassi W, Tittarelli E, Blasetti P, Pirani O, Cervini C. Finger tendon involvement in rheumatoid arthritis. Evaluation with high-frequency sonography. Arthritis Rheum. 1995; 38: 786-794.

38. Filippucci E, Gabba A, Di Geso L, Girolimetti R, Salaffi F, Grassi W. Hand tendon involvement in rheumatoid arthritis: an ultrasound study. Semin Arthritis Rheum. 2012; 41: 752-760.

39. Boutry N, Hachulla E, Flipo RM, Cortet B, Cotten A. MR imaging findings in hands in early rheumatoid arthritis: comparison with those in systemic lupus erythematosus and primary Sjögren syndrome. Radiology. 2005; 236: 593-600.

40. McGonagle D, Gibbon W, Emery P. Classification of inflammatory arthritis by enthesitis. Lancet. 1998; 352: 1137-1140.

41. Kaneko Y, Kuwana M, Kondo H, Takeuchi T. Discordance in global assessments between patients and estimator in patients with newly diagnosed rheumatoid arthritis: associations with progressive joint destruction and functional impairment. J Rheumatol. 2014; 41: 1061-1066.

Table 1. Clinical characteristics of SLE and RA patients

Characteristics	SLE	RA	p
Number of patients (female)	15 (12)	40 (29)	0.734
Age, years	53 (42-66)	67 (49-78)	0.040
Disease duration, years	0.6 (0.4-1.4)	0.4 (0.2-0.6)	0.089
Clinical examination			
Hand	13 (87)	39 (98)	0.177
Wrist	7 (47)	30 (75)	0.059
MCP	10 (67)	31 (78)	0.493
IP/PIP	8 (53)	25 (63)	0.533
Swollen joint count[a]	2 (1-5)	4 (2-10)	0.115
Tender joint count[a]	2 (0-4)	4 (2-9)	0.017
Cutaneous lupus	4 (27)	-	-
Lupus serositis	4 (27)	-	-
Lupus nephritis	4 (27)	-	-

Neuropsychiatric lupus	1 (7)	-	-
CRP, mg/dl	0.29 (0.05-1.20)	0.77 (0.12-2.32)	0.281
ESR, mm/h	41 (27-76)	45 (17-75)[b]	0.746
RF positive	8 (53)	35 (88)	0.011
low-positive[c]	6 (40)	12 (30)	0.529
high-positive[d]	2 (13)	23 (58)	0.005
Anti-CCP positive	1 (7)	27 (68)	<0.001
low-positive[e]	0 (0)	1 (3)	1.000
high-positive[f]	1 (7)	26 (65)	<0.001
ANA positive	15 (100)	31 (78)	0.051
Low-titer positive[g]	1 (7)	29 (73)	<0.001
High-titer positive[h]	14 (93)	3 (8)	<0.001
Anti-DNA and/or -Sm positive	10 (67)	-	-
Low complement[i]	7 (47)	-	-
SLEDAI	7 (5-12)	-	-

DAS28-CRP	-	4.06 (3.37-5.37)[j]	-

The values are expressed as median (IQR) and number (%). Fisher's exact test or Mann–Whitney U test was used for group comparisons. SLEDAI: Systemic Lupus Erythematosus Disease Activity Index; DAS28-CRP: Disease Activity Score 28-CRP. [a]Tender and swollen joint count from 28-joint count. [b]ESR data were not obtained from 3 RA patients (n=37). [c]RF low-positive: >15 to ≤45 IU/ml. [d]RF high-positive: >45 IU/ml. [e]ACPA low-positive: ≥4.5 to <13.5 U/ml, [f]ACPA high-positive: ≥13.5 U/ml. [g]ANA low-titer positive: titer of ≥1:40 to ≤1:80. [h]ANA high-titer positive: titer of ≥1:160. [i]Low complement: C3 < 60 mg/dl, C4 < 17 mg/dl,and/or CH50 < 25 CH50 U/ml. [j]DAS28-CRP were not obtained from 2 RA patients (n=38).

Table 2. Ultrasonographic findings of joint and tendon involvement

	SLE	n=15	RA	n=40	p
Region	number	(%)	number	(%)	
Joint involvement	12	(80)	38	(95)	0.119
Wrist	11	(73)	32	(80)	0.716
MCP	11	(73)	29	(73)	1.000
IP/PIP	4	(27)	19	(48)	0.224
Tendon involvement	14	(93)	26	(65)	0.045
Wrist	11	(73)	16	(40)	0.037
Finger extensor tendons	7	(47)	15	(38)	0.553
Finger flexor tendons	10	(67)	18	(45)	0.227

Fisher's exact test was used for group comparisons.

Table 3. Comparison of US score at each single region between SLE and RA patients.

Region	Score range	US mode	SLE	RA	p
Joint					
Wrist	(0–3)	GS	1.0 (0.5-1.5)	1.3 (1.0-2.0)	0.317
		PD	1.0 (0.0-1.0)	1.4 (1.0-1.8)	0.012
	(0–6)	GS+PD	2.0 (1.0-2.4)	2.6 (2.0-3.7)	0.037
MCP	(0–3)	GS	1.0 (0.5-1.3)	1.0 (0.0-1.8)	0.352
		PD	1.0 (0.5-1.4)	1.0 (0.0-1.6)	0.640
	(0–6)	GS+PD	2.0 (1.0-2.7)	2.0 (0.0-3.1)	0.438
PIP	(0–3)	GS	0.0 (0.0-0.5)	0.0 (0.0-1.0)	0.215
		PD	0.0 (0.0-0.3)	0.0 (0.0-1.0)	0.106
	(0–6)	GS+PD	0.0 (0.0-1.0)	0.0 (0.0-2.1)	0.175
Total	(0–3)	GS	1.2 (1.0-1.4)	1.5 (1.1-1.8)	0.038
		PD	1.0 (0.4-1.3)	1.4 (1.1-1.8)	0.003
	(0–6)	GS+PD	2.0 (1.9-2.3)	2.6 (2.0-3.5)	0.019

Tendon					
Wrist	(0–3)	GS	1.0 (0.0–1.0)	0.0 (0.0-1.0)	0.200
		PD	1.0 (0.5–1.3)	0.0 (0.0-1.0)	0.030
	(0–6)	GS+PD	2.0 (0.5–2.5)	0.0 (0.0-2.0)	0.082
Extensor	(0–3)	GS	0.0 (0.0–0.9)	0.0 (0.0-1.0)	0.800
(finger)		PD	0.0 (0.0–1.2)	0.0 (0.0-1.5)	0.957
	(0–6)	GS+PD	0.0 (0.0–2.0)	0.0 (0.0-2.5)	0.898
Flexor	(0–3)	GS	1.0 (0.0–1.0)	0.0 (0.0-1.0)	0.206
(finger)		PD	1.0 (0.0–1.0)	0.0 (0.0-1.0)	0.638
	(0–6)	GS+PD	2.0 (0.0–2.0)	0.0 (0.0-2.0)	0.478
Total	(0–3)	GS	1.0 (0.7–1.0)	1.0 (0.0-1.0)	0.482
		PD	1.2 (1.0–1.3)	1.0 (0.0-1.5)	0.645
	(0–6)	GS+PD	2.1 (2.0–2.4)	2.2 (0.0-2.5)	0.738

GS: gray-scale score, PD: power-Doppler score. The values were median (IQR). Mann–Whitney U test used for group comparisons.

Table 4. The concordance of joint synovitis and tenosynovitis/PTI in the same region

	SLE (n=150 fingers) Number (%)		RA (n=400 fingers) Number (%)	
	TS (+)	TS (-)	TS (+)	TS (-)
JS (+)	17 (11)	30 (20)	58 (15)	72 (18)
JS (-)	18 (12)	85 (57)	20 (5)	250 (62)
κ	0.201		0.415	

JS: joint synovitis, TS: tendinitis/tenosynovitis

MCP and PIP joint synovitis were compared to extensor and flexor tendinitis/tenosynovitis in the same finger by applying Cohen's kappa coefficient.

Figure legends

Figure 1. A flow chart depicting the enrollment of study participants

Figure 2. The involvement of each joint and tendon (compartment).

Histograms show the frequency of involvement at each joint (A) and tendon (B). DRU: distal radio-ulnar joint, RC: radiocarpal joint, MC: midcarpal joint.

Figure 1.

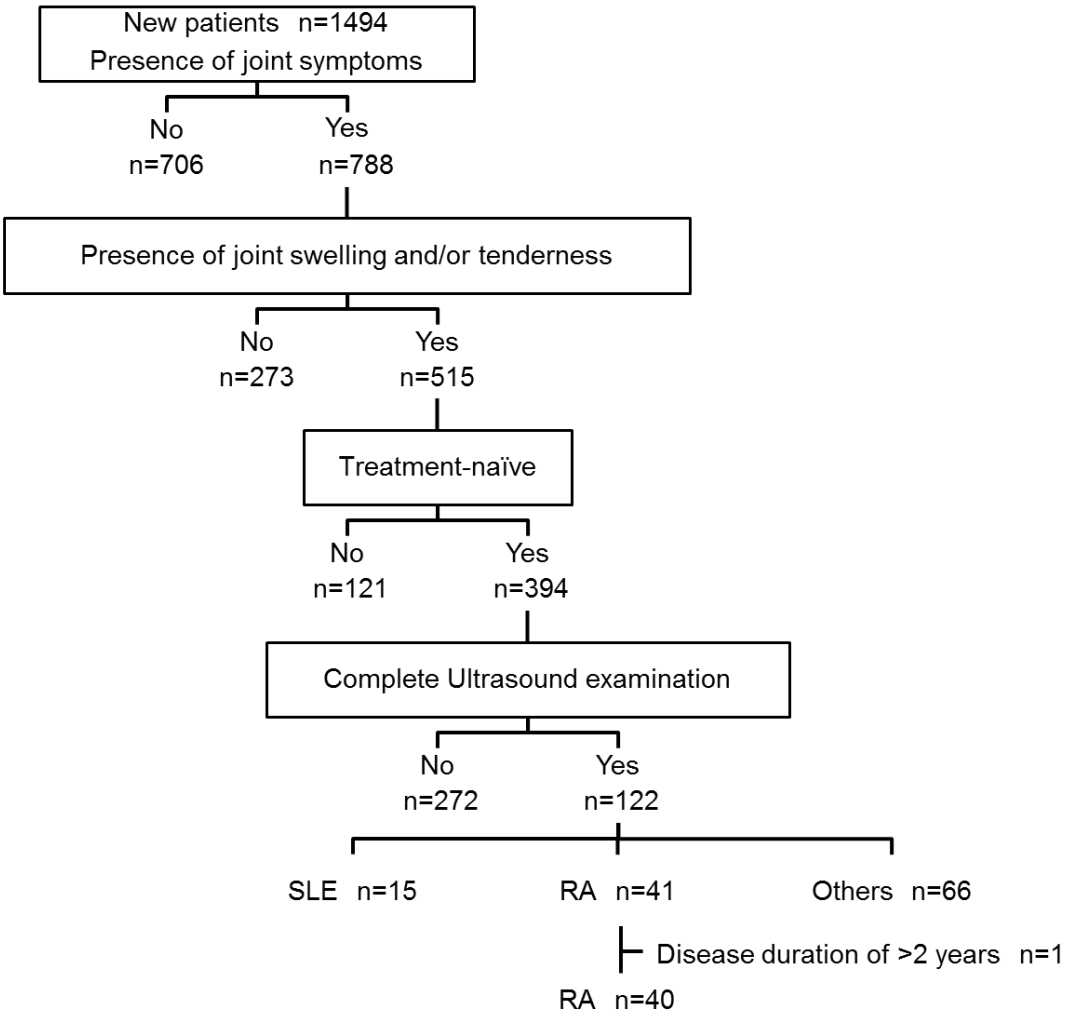
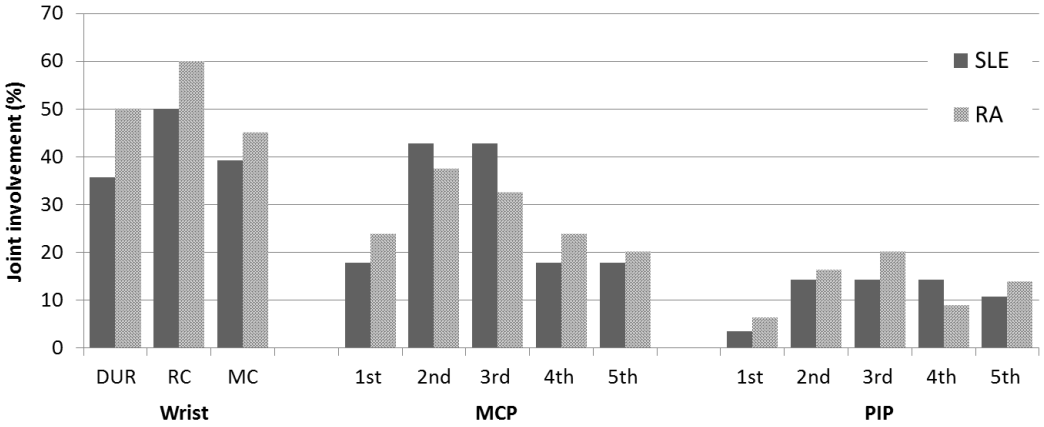
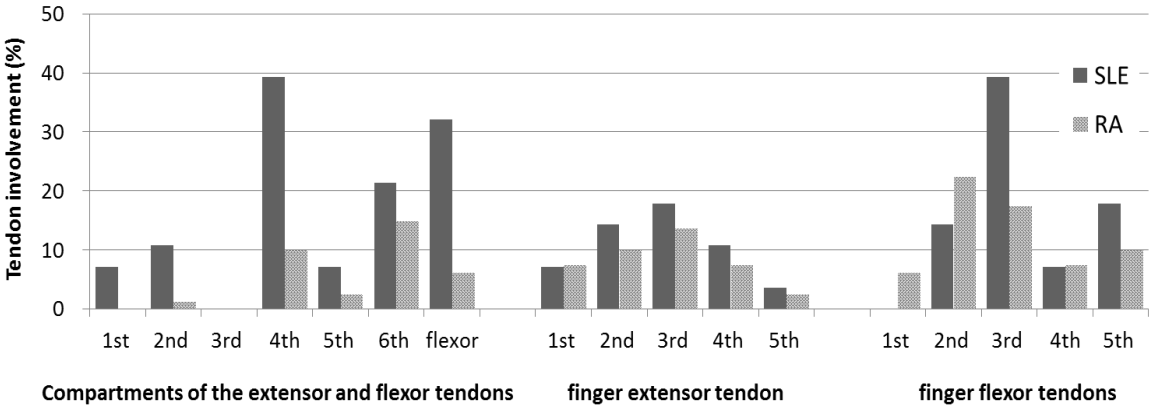

New patients n=1494
Presence of joint symptoms
No
n=706
Yes
n=788
Presence of joint swelling and/or tenderness
No
n=273
Yes
n=515
Treatment-naïve
No
n=121
Yes
n=394
Complete Ultrasound examination
No
n=272
Yes
n=122
SLE n=15
RA n=41
Others n=66
Disease duration of >2 years n=1
RA n=40

Figure 2

A


70
60
50
40
30
20
10
0
Joint involvement (%)
SLE
RA
DUR
RC
MC
1st
2nd
3rd
4th
5th
1st
2nd
3rd
4th
5th
Wrist
MCP
PIP

B


50
40
30
20
10
0
Tendon involvement (%)
SLE
RA
1st
2nd
3rd
4th
5th
6th
flexor
1st
2nd
3rd
4th
5th
1st
2nd
3rd
4th
5th
Compartments of the extensor and flexor tendons
finger extensor tendon
finger flexor tendons

Supplementary Table 1. Comparison of US score between SLE and RA patients

Region	Score range	US mode	SLE	RA	p
Joint					
Wrist	(0–18)	GS	3.0 (2.0-5.5)	5.5 (1.8-10.0)	0.247
		PD	2.0 (0.0-4.0)	4.5 (1.0-9.0)	0.073
	(0–36)	GS+PD	5.0 (2.5-10.0)	9.0 (2.8-18.5)	0.161
MCP	(0–30)	GS	4.0 (3.0-6.5)	2.0 (1.8-9.0)	0.641
		PD	3.0 (0.5-6.0)	2.0 (0.0-6.0)	0.833
	(0–30)	GS+PD	8.0 (4.0-12.5)	4.0 (2.0-15.0)	0.648
PIP	(0–30)	GS	0.0 (0.0-2.0)	0.0 (0.0-3.0)	0.664
		PD	0.0 (0.0-0.5)	0.0 (0.0-3.0)	0.201
	(0–30)	GS+PD	0.0 (0.0-2.5)	0.0 (0.0-6.0)	0.522
Total	(0–78)	GS	8.0 (6.5-14.5)	10.5 (6.8-14.3)	0.460
		PD	5.0 (1.0-11.0)	9.0 (4.0-13.5)	0.167
	(0–165)	GS+PD	14.0 (7.5-25.5)	20.0	0.269

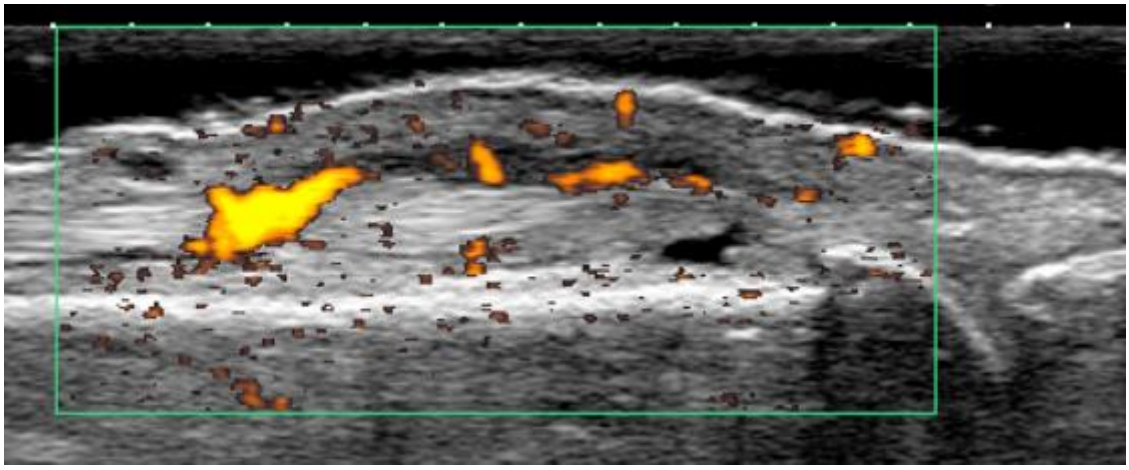
				(10.8-27.5)	
Tendon					
Wrist	(0–42)	GS	2.0 (0.0-3.0)	0.0 (0.0-1.0)	0.031
		PD	2.0 (0.5-5.0)	0.0 (0.0-1.0)	0.010
	(0–84)	GS+PD	3.0 (0.5-8.0)	0.0 (0.0-2.3)	0.012
Extensor	(0–30)	GS	0.0 (0.0-1.0)	0.0 (0.0-1.0)	0.957
(finger)		PD	0.0 (0.0-1.5)	0.0 (0.0-2.0)	0.765
	(0–60)	GS+PD	0.0 (0.0-2.5)	0.0 (0.0-3.0)	0.798
Flexor	(0–30)	GS	1.0 (0.0-2.5)	0.0 (0.0-2.0)	0.315
(finger)		PD	1.0 (0.0-2.5)	0.0 (0.0-2.0)	0.322
	(0–60)	GS+PD	2.0 (0.0-5.5)	0.0 (0.0-4.0)	0.303
Total	(0–102)	GS	2.0 (1.5-8.5)	1.0 (0.0-5.3)	0.089
		PD	4.0 (2.5-8.5)	2.5 (0.0-6.0)	0.088
	(0–204)	GS+PD	6.0 (3.5-17.0)	3.5 (0.0-10.8)	0.095

GS: gray-scale score, PD: power-Doppler score. The values were median (IQR). Mann–Whitney U test used for group comparisons.

Supplementary Figure 1. US images of extensor digitorum tendon involvement (PTI).

(A) longitudinal scan and (B) transverse scan of the MCP joint from dorsal side. This tendon involvement is gray-scale score: grade 2, power-Doppler score: grade 2

A



B