European Journal of Radiology 187 (2025) 112072

Contents lists available at ScienceDirect

European Journal of Radiology

journal homepage: www.elsevier.com/locate/ejrad

Advancements in diagnosing stiffness and vascularization of synovitis in hands and wrists using shear wave elastography and power doppler ultrasound in patients with systemic lupus erythematosus

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ARTICLE INFO

Keywords:
Synovitis
Systemic lupus erythematosus
Shear wave elastography
Power doppler ultrasound
Ultrasound

ABSTRACT

Rationale and Objectives: This study aimed to compare synovial joint effusion stiffness and vascularization using shear wave elastography (SWE) and Power Doppler ultrasound (PDU) among systemic lupus erythematosus (SLE) patients with varying joint symptoms and healthy controls and to explore associations with patient characteristics.

Methods: This cross-sectional study, conducted between February 2021 and April 2023, included 60 SLE patients and a demographically matched healthy control group. The SLE patients were divided into three groups: those with active wrist/hand arthritis (G1), inflammatory arthralgia (G2), and no joint symptoms (G3). B-mode, SWE, and PDU assessments were performed on the non-dominant hand to evaluate synovial joint stiffness. Data on demographics, clinical presentations, serological markers, and patient-reported outcomes were analyzed.

Results: A total of 80 participants were included, with no significant demographic differences between groups. SLE patients exhibited significantly higher stiffness values than controls in the radiocarpal ($p = 0.004$), ulnocarpal ($p = 0.051$), and metacarpophalangeal joints ($p = 0.038$, $p = 0.002$). Among these, the ulnocarpal joint showed the highest differences in stiffness values. No significant differences in stiffness were observed among SLE groups. However, positive Doppler findings were associated with higher SLICC-SDI scores ($p = 0.005$), and a positive correlation was found between the number of Doppler-positive joints and SLICC-SDI scores ($r = 0.438$, $p < 0.001$). Importantly, subclinical synovitis was observed in asymptomatic patients (G3), as demonstrated by significantly elevated stiffness in key joints compared to controls.

Conclusions: SLE patients exhibited higher stiffness values compared to controls, indicating subclinical synovitis even in asymptomatic individuals. Key findings suggest that the radiocarpal and ulnocarpal joints are particularly affected and should be prioritized in imaging protocols. The integration of SWE and PDU into routine SLE assessments can facilitate earlier diagnosis, enabling prompt treatment and reducing the risk of cumulative joint damage. SWE and PDU are valuable for the early detection and treatment of musculoskeletal changes. By identifying subclinical synovitis, these techniques not only improve patient monitoring but also help tailor therapeutic strategies to individual disease activity.

The correlation with higher SLICC-SDI scores underscores the critical role of joint evaluation in preventing long-term damage and enhancing care management. Moving forward, refining imaging protocols to standardize SWE

Abbreviations: **SLE**, Systemic Lupus Erythematosus; **SWE**, Shear Wave Elastography; **PDU**, Power Doppler Ultrasound; **SLICC**, Systemic Lupus International Collaborating Clinics; **G1**, Group 1 (SLE patients with active wrist/hand arthritis); **G2**, Group 2 (SLE patients with inflammatory arthralgia); **G3**, Group 3 (SLE patients without symptoms); **G4**, Group 4 (Healthy control group); **US**, Ultrasound; **MRI**, Magnetic Resonance Imaging; **EULAR**, European Alliance of Rheumatology Associations; **OMERACT**, Outcome Measures in Rheumatology; **SDI**, SLICC/ACR Damage Index; **PROs**, Patient-Reported Outcomes; **HAQ**, Health Assessment Questionnaire; **FSS-9**, Fatigue Severity Scale (9-item version); **RF**, Rheumatoid Factor; **ACPA**, Anti-Citrullinated Protein Antibodies; **MCP**, Metacarpophalangeal Joint; **PIP**, Proximal Interphalangeal Joint.

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https://doi.org/10.1016/j.ejrad.2025.112072
Received 18 November 2024; Received in revised form 7 March 2025; Accepted 26 March 2025
Available online 29 March 2025

and PDU application in SLE is essential. Additionally, exploring the utility of these techniques in other joints, such as the knees and ankles, may provide further insights into the extent of subclinical involvement across the musculoskeletal system.

1. Introduction

Systemic Lupus Erythematosus (SLE) is recognized for its broad spectrum of clinical manifestations, particularly those affecting the musculoskeletal system. Despite its prevalence, the subtle inflammatory involvement of muscles and joints often goes unnoticed, posing a challenge in understanding its full impact on patients[1–4]. Among the various imaging modalities, Power Doppler Ultrasound (PDU) and Magnetic Resonance Imaging (MRI) have emerged as the most utilized tools in clinical practice[5–15]. Early diagnosis of osteoarticular involvement in SLE remains a challenge. Ozbek et al. demonstrated that although osteoarticular manifestations in SLE are the most prevalent and are usually the main initial symptom, in their study only 27 % of these cases were diagnosed with SLE during the first three years of the disease. However, patients who initially had "non-articular" and more typical manifestations of SLE (such as malar erythema, pleuritis, etc.) were diagnosed much earlier. Therefore, we can conclude that correct joint physical examination in SLE, as well as the use of imaging techniques such as ultrasound, MRI, and elastography, helps maximize an important window for the early diagnosis of patients with SLE, as well as for the initiation of early treatment to avoid future joint damage[16].

Doppler ultrasound, with its ability to visualize blood flow, is invaluable for detecting active synovitis and guiding the assessment of inflammatory activity within joints[5,6]. Meanwhile, MRI stands out for its superior sensitivity in identifying early musculoskeletal changes, including subtle erosions and soft tissue involvement that may not be apparent in conventional radiographs or even ultrasound[7–15]. Despite the fact that in 2021 the European Alliance of Rheumatology Associations (EULAR) presented recommendations that parallel the use of ultrasound imaging studies in muscle-sensitive diseases and included for the first time the use of elastosonography[17], which allows for the measurement of the elasticity of synovial fluid, there are few reports that analyze the role of shear wave elastography (SWE) in rheumatological pathologies and none that specifically study its role in SLE[18,19].

Despite its clear advantages in the evaluation of synovitis and rheumatologic diseases, MRI has some limitations, including long acquisition times, high costs, limited availability, potential issues with claustrophobia, and incompatibility with metallic objects [20]. These factors, while not diminishing its role as a powerful imaging modality, may restrict its routine use, particularly in longitudinal studies or in patients requiring frequent assessments.

In this context, shear wave elastography (SWE) and Power Doppler ultrasound (PDU) represent highly practical alternatives. Both techniques are cost-effective, non-ionizing, and portable, making them more suitable for routine clinical practice and follow-up in patients with SLE. PDU provides real-time visualization of blood flow, which is crucial for assessing active inflammation, while SWE offers objective, quantifiable measurements of tissue stiffness that help detect subclinical synovitis. Additionally, the practical advantages of SWE and PDU align with the clinical need for rapid, repeatable, and reliable imaging in SLE patients [21,22].

The early detection of subclinical synovitis has significant implications for long-term outcomes in SLE. In particular, baseline joint ultrasound abnormalities have been shown to predict worse clinical progression in SLE patients. In a study by Corzo et al., patients with arthralgia and baseline ultrasound abnormalities were more likely to experience osteoarticular flares and require treatments commonly used for arthritis, such as methotrexate and hydroxychloroquine[23]. This highlights the importance of using ultrasound as a predictive tool for disease progression in patients with subtle musculoskeletal symptoms.

Furthermore, studies focused specifically on subclinical synovitis in SLE, such as those by Guillén-Astete et al., emphasize its prevalence and clinical significance. In a 2020 cross-sectional study, 38 % of SLE patients without overt arthritis demonstrated subclinical synovitis on ultrasound[24]. More recently, a prospective 10-year multicenter study by the same group revealed that subclinical synovitis at baseline was significantly associated with clinical progression of joint disease. Specifically, 74.9 % of patients with clinical progression had demonstrated subclinical synovitis at the start of follow-up, compared to 23.4 % in patients without clinical progression ($p < 0.01$, OR 9.44, 95 % CI 3.46–25.74). Additionally, patients with clinical progression had worse combined ultrasound scores at baseline (6.41 ± 1.45 vs. 1.15 ± 0.97, $p < 0.01$)[25].

This study sought to evaluate the stiffness of synovial fluid using SWE in kilopascals (kPa) among three different groups of SLE patients characterized by varying degrees of joint symptoms, and to compare these findings with a control group of healthy individuals. Additionally, it sought to identify any correlations between the stiffness of synovial effusion and specific patient demographics and disease manifestations, examining these relationships both across the entire cohort and within each specific joint group. We used a cut-off value of 30 kPa to evaluate the presence or absence of synovitis, as suggested in the 2023 article by Marsico et al. This current study includes the largest number of patients with lupus studied by SWE reported in the literature[19]. Furthermore, our research assesses the relationship between the presence of synovitis, as detected by PDU and various patient characteristics. This study intends to shed light on the often underappreciated ultrasound aspect of subclinical musculoskeletal involvement in SLE patients.

2. Materials and Methods

This single-center, cross-sectional study, drawing upon a retrospective collection of clinical data, was approved by our institutional ethics committee (number: 2022/10450/I), which waived the informed consent requirement.

Population: The participants were divided into distinct groups based on their clinical presentations:

- Group 1 (G1): patients with SLE exhibiting wrist and/or hand arthritis, confirmed by physical examination by a rheumatologist within the last six months. Definition of Arthritis in Group 1 (G1): Arthritis was defined as joint inflammation characterized by pain, swelling, redness, warmth, or functional limitation, with or without associated joint deformity, documented during the consultation or reported within the last six months based on medical history.
- Group 2 (G2): patients with SLE reporting wrist and/or hand inflammatory arthralgia, without any observed arthritis as determined by a rheumatologist during the same time frame.
- Group 3 (G3): SLE patients without any symptoms of arthritis or arthralgia in their wrist/hand during the past six months.
- Group 4 (HS): A control group of healthy subjects matched for sociodemographic characteristics with the SLE groups, without any wrist/hand pain or swelling, and no personal or family history of rheumatic diseases.

Exclusion criteria included Jaccoud's arthropathy, incomplete SLE, mixed connective tissue diseases, overlap syndromes, and other non-rheumatic systemic autoimmune diseases, along with RF and/or ACPA positivity, symptomatic hand osteoarthritis, previous hand surgery, or active neoplasms.

2.1. Recruitment Process

All patients that fulfilled the inclusion and exclusion, accepted to participate in the study and signed the informed consent, were consecutively recruited from the outpatient SLE clinic in the rheumatology department at our institution. Patients were referred for ultrasound and MRI assessments based on clinical findings from their routine evaluations. The rheumatologist performing clinical assessments classified the participants into groups (G1, G2, G3, G4) according to their physical examination findings and reported symptoms. Once the minimum sample size calculated for each group was included, we stopped the recruitment of patients of that group and continued with those of the other groups until the final sample size was achieved. Control subjects (G4) were also recruited consecutively from the same clinic, ensuring they were age- and gender-matched to the SLE patient groups. The electronic medical records of each patient were examined to retrieve the appropriate demographics and clinical data. Patients that did not have data of the physical examination, ultrasound or MRI exam were removed from the study due to missing data. Those with those last 3 completed and with less than 80 % of missing data on the rest of variables were included.

2.2. Ultrasound Technique

Baseline B-mode Ultrasound (US), SWE, and PDU assessments were conducted on the non-dominant hand/wrist of participants. A flat-panel LOGIQ E9 ultrasound machine from General Electric (GE), equipped with a high-frequency linear transducer (4–15 Hz), was operated by a radiologist with extensive expertise in musculoskeletal ultrasound and SWE. An initial B-mode evaluation was conducted at time zero, using both axial and longitudinal scans as per EULAR guidelines to identify and quantify significant synovitis. The analysis covered the dorsal aspect of the radiocarpal, ulnocarpal, intercarpal, 2nd to 5th metacarpophalangeal (MCP) joints, and the 2nd to 5th proximal interphalangeal (PIP) joints (22 joints per individual). A B-mode assessment in accordance with EULAR OMERACT guidelines was then carried out, using a grading system to assess synovial hypertrophy. Multiple measurements across the surface were conducted to detect any intrasynovial differences (Figs. 1–2). Given the absence of sufficient joint fluid to facilitate proper evaluation in all joints, kPa values and Doppler measurements were performed on 145 joints out of the 660 potentially evaluable joints in patients (G1, G2, G3). In the control group (G4), kPa values and Doppler measurements were carried out on 32 joints out of 220 potentially evaluable joints. The analysis of SWE data was conducted on the three patient groups combined (G1, G2, G3) versus the control group (G4), among the patient groups themselves (G1, G2, G3),

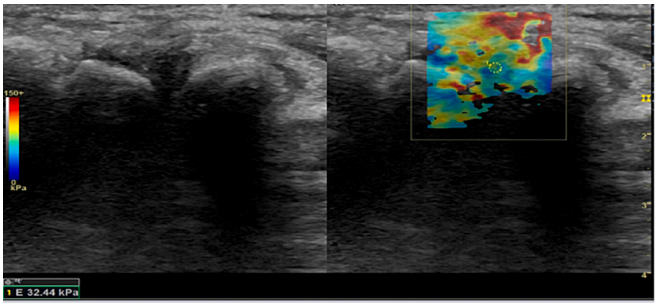

Fig. 1. Shear wave elastosonography (SWE) analysis of the third metacarpophalangeal joint in the sagittal plane of a 59-year-old female patient with a history of SLE and suspected active arthritis based on clinical rheumatological evaluation. The left image shows diffuse synovial hypertrophy, with hypoechoic tissue extending beyond the joint margins. The right image illustrates the measurement of synovial tissue stiffness using a Region of Interest (RoI) circle, with the quantitative stiffness value displayed in the lower left corner.

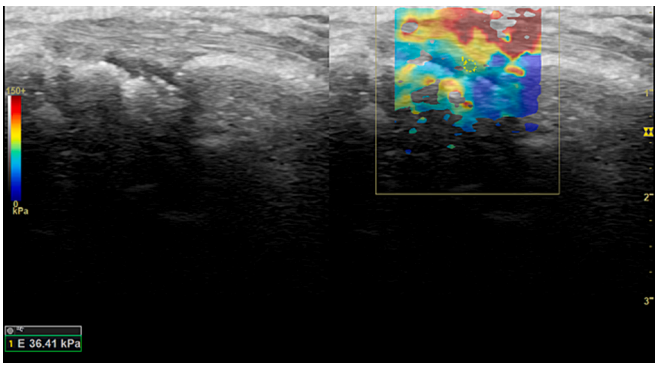

Fig. 2. Shear wave elastosonography (SWE) analysis of the radiocarpal joint in the sagittal plane of a 45-year-old asymptomatic female patient with a history of SLE and suspected active arthritis based on clinical rheumatological evaluation. The left image shows mild synovial hypertrophy, with hypoechoic synovial tissue extending slightly beyond the joint margins. The right image illustrates the stiffness measurement of the mildly hypertrophic synovial tissue, with the RoI circle marking the analyzed area and the corresponding stiffness value displayed in the lower left corner.

and among all groups collectively, including individual joints. Additionally, Doppler uptake was assessed for each joint to evaluate any vascular activity associated with inflammation (Fig. 3).

To address inter-observer variability during imaging and analysis, several measures were implemented. All ultrasound examinations were performed by a single radiologist with extensive expertise in musculoskeletal imaging to ensure consistency during image acquisition. Additionally, a second radiologist independently reviewed 100 % of the images in a blinded manner to assess reproducibility. Discrepancies between the two observers were resolved through consensus discussions, and inter-observer agreement was quantified using the intraclass correlation coefficient (ICC). The ICC values demonstrated excellent agreement (ICC $>$ 0.85) for both SWE and PDU evaluations, further ensuring the reliability of the imaging and analysis process.

The non-dominant hand was chosen for evaluation to minimize potential confounding factors related to overuse or repetitive stress. It is well known that patients with immune-mediated diseases, including SLE, can experience synovitis induced by physical stress or overexertion. This phenomenon, often observed in dominant hands, can lead to localized inflammation and disease flares, potentially biasing the assessment of joint involvement in SLE.

The 30 kPa cutoff for synovitis detection was selected based on findings from a 2023 retrospective study, where joint stiffness was assessed in 29 cases and 29 controls using Shear Wave Elastography (SWE). The study highlighted significant differences in stiffness values between cases and controls, particularly in inflammatory conditions

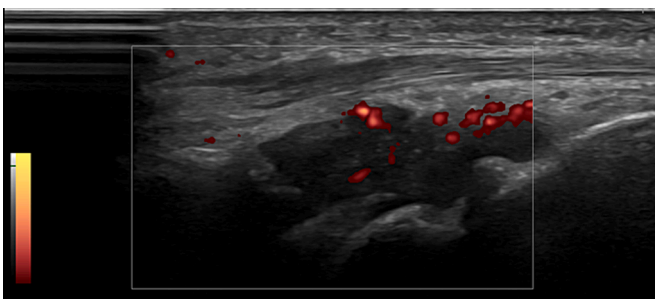

Fig. 3. Power-Doppler Ultrasound image of the radio carpal joint in the sagittal plane of a 61 -year-old asymptomatic female patient who had a history of SLE and was suspected of having active arthritis based on a rheumatological clinical evaluation. A diffuse increase in vascularization in the context of synovial hypertrophy.

such as SLE, rheumatoid arthritis, and psoriatic arthritis[19]. The 30 kPa threshold was chosen as it represents a value sufficiently high to distinguish pathological synovitis from normal joint structures, reducing the risk of overestimating synovial abnormalities. While the literature on SWE cutoffs remains limited, this approach provides a preliminary, reliable and specific benchmark for detecting true inflammatory changes.

2.3. Clinical data collection

A retrospective observational data collection was conducted for SLE patients between February 2021 and April 2023. The patient medical records of SLE individuals were reviewed retrospectively to gather baseline demographic and clinical data, including age, gender, and findings from SWE and PDU. Follow-up clinical variables included disease evolution (predominance of joint/systemic involvement), baseline visit date, presence and type of arthritis. Data on SLE-related synthetic disease-modifying antirheumatic drugs (DMARDs) such as hydroxychloroquine, azathioprine, methotrexate, leflunomide, mycophenolate mofetil, rituximab, and belimumab were collected. Disease and damage severity scores, including the SLE Disease Activity Index (SLEDAI)[26] and the Systemic Lupus International Collaborating Clinic/ACR Damage Index (SLICC/ACR)[27], as well as disability based on the modified Health Assessment Questionnaire (mHAQ)[28], were recorded. Regular blood tests from our reference laboratory were performed to assess SLE serological markers, including anti-DNA antibodies (CLIF method), antinuclear antibodies (ANA), and complements C3 and C4. Other serological variables included the presence/absence of antiphospholipid autoantibodies (anticardiolipin IgG/IgM, anti-β2-glycoprotein IgG/IgM, or lupus anticoagulant), cyclic citrullinated peptide antibody (CCPA), rheumatoid factor, anti-Ro, and anti-Smith antibodies, if applicable. Patient-reported outcomes (PROs) were gathered through standardized questionnaires, covering aspects such as pain (numeric rating scale 0–10), the Health Assessment Questionnaire (HAQ), and the Fatigue Severity Scale (FSS-9) (29).

Cases with incomplete data or missing essential clinical information were not included in the final analysis. Of the initial 74 patients considered for the study, 14 were excluded due to unmet inclusion criteria or incomplete data.

2.4. Statistical analysis

The distribution of the continuous variables studied was evaluated and failed the test of normality (Shapiro-Wilk test). However, evaluation of the Q-Q plots for SWE data showed a minor deviation. Therefore, using this as the dependent variable, we performed an analysis using both parametric (T-student, ANOVA) and non-parametric tests (Mann-Whitney and H-Kruskal-Wallis). For categorical variables, a chi-squared or Fisher's exact test (for 2x2 tables) were performed. When evaluating differences in variables including more than 2 categories, post-hoc analyses were performed to assess the differences by pairs. The post-hoc analysis performed were Tukey HSD (for significant results after ANOVA analysis) and the Z test (for significant results after Chi-square test).

First, we contrasted the baseline characteristics among the 4 groups (for demographic variables) or the 3 groups of patients (for clinical variables) using ANOVA and the H Kruskal-Wallis test. Then, SWE and PDU data were evaluated comparing patients (G1,G2 and G3 combined) and controls (G4) via the t-student/Mann-Whitney test, and Fisher's exact test, respectively. These analyses were performed taking into account all of the joints assessed (22 joints per individual) and also each joint separately. The same analyses were performed evaluating only the differences between the three groups of patients. In these cases, an ANOVA/H-Kruskal-Wallis test and a Chi-squared were performed.

Finally, the association between SWE and PDU data, and the clinical variables were determined using the Spearman correlation test and Fisher's exact test, respectively.

All statistical analyses were carried out using IBM® SPSS® Statistics version 23.0.0.0.

3. Results

From February 2021 to April 2023, we enrolled a cohort of 80 participants (74 women, 6 men; mean age 49.13 years ± 11.66) in the study, with participants distributed equally across four groups (G1: 20, G2: 20, G3: 20, G4: 20). *Baseline evaluation.*

No demographic differences were found between the four groups (Table 1). Among SLE patients, we observed significant differences between groups in the following variables: hand pain VAS (p-value = 0.000); SLEDAI (p-value = 0.000) and SLICC-SDI (p-value = 0.050). The post-hoc analysis showed that P1′s hand pain VAS, and SLEDAI scores were significantly higher than those from P2 (mean differences 1.95 (95 % IC 0.30–3.50), p value = 0.016; 2.2 (95 % IC 0.67–3.73) p-value = 0.003, respectively) and P3 (mean differences 3.70 (95 % IC 2.10–5.30), p value = 0.000; 3.95 (95 % IC 2.42–5.50) p-value = 0.000, respectively). On the other hand, SLICC-SDI post-hoc analysis did not show any specific differences between groups.

3.1. Comparisons between the control group and patients

The analysis of SWE data on patients (groups G1, G2 and G3 combined) versus the control group (HS), showed a significant disparity in stiffness measurements, as indicated by shear wave elastography (kPa), with cases exhibiting a mean stiffness increase of 24.06 kPa (95 % CI: 19.77–28.36, $p < 0.001$). When this analysis was performed separately on the different joints assessed, we were only able to detect significantly higher values in patients versus controls in 4 joints: radiocarpal joint (mean difference 26.600, 95 % CI: 19.22–33.98, p-value: 0.000) ulnocarpal joint (mean difference 30.81, 95 % CI: 31.24–40.37, p-value: 0.000), second metacarpophalangic (MCP) joint (mean difference 12.74, 95 % CI: 12.74–23.46, p-value: 0.022) and third MCP joint (mean difference 23.11, 95 % CI: 6.60–39.62, p-value: 0.008).

Regarding the presence of synovitis (defined by a SWE > 30 kPa), when all of the joints were considered together, we observed a significantly higher proportion in patients than in controls (53.1 % vs 3.1 %, p-value = 0.000). This difference was only observed in two joints: the radiocarpal (38.3 % vs 0 %, p-value = 0.000) and ulnocarpal joints

Table 1
Demographic Variables. This table presents the demographic variables of the study participants.

Variable	**Group 1** (SLE w/ arthritis)	**Group 2** (SLE w/ arthralgia)	**Group 3** (SLE w/o arthritis/ arthralgia)	**Group 4** (Healthy subjects)	***P-value***
	n: 20	n = 20	n:20	n:20	
Age (years)	48.5 (11.98)	48.48 (12.20)	49.37(11.79)	43.35 (13.53)	0.162
Sex (n female)	16 (80 %)	20 (100 %)	17 (85 %)	17 (85 %)	0.249
Disease duration (in years)	9.16 (8.09)	8.06 (6.66)	9.48 (8.60)		0.722
Body Mass Index (kg/m^2)	25.22 (4.34)	25.63 (4.30)	26.18(6.12)		0.232
Tobacco use (yes)	5 (25 %)	8 (40 %)	6 (20.69 %)		0.341
Ethnicity					0.352
White	11 (55 %)	10 (50 %)	8 (40 %)		
Black	0 (0 %)	0 (0 %)	0 (0 %)		
Latino	7 (35 %)	7 (35 %)	10 (50 %)		
Asian	2 (10 %)	3 (15 %)	1 (5 %)		
Arab	0 (0 %)	0 (0 %)	1 (5 %)		

(26.70 % vs 0.00 %, p-value = 0.008).

3.2. Comparisons between SLE patient groups

Among the SLE groups (G1, G2, G3), no notable differences in stiffness values were observed. A higher frequency of cases showed kPa values greater than 30 kPa compared to controls, with a significant difference (53.1 % in cases vs. 3.1 % in controls, p-value 0.000). No significant differences were found in the frequency of high kPa > 30 values among the different case groups, although a higher frequency was observed in group 3. Comparing the combined G1 and G2 groups to G3 group, no statistically significant differences in stiffness values were observed (P = 0.157). Comparing the stiffness data in SWE among all of the groups, significant differences were found in the radiocarpal joint (p = 0.004) and the ulnocarpal joint (p = 0.051) (Table 2).

Specifically, significantly different stiffness values were observed, with higher values in patient groups in the radiocarpal joint between G1 and G4 (p = 0.033), between G2 and G4 (p = 0.005), and between G3 and G4 (p = 0.006), as well as in the ulnocarpal joint between G1 and G4 (p = 0.038). Significant differences in kPa values were observed in specific joints (radiocarpal, ulnocarpal, second and third metacarpophalangeal joints) between cases and controls (radiocarpal joint p = 0.000, ulnocarpal joint p = 0.008, and second and third metacarpophalangeal joints p = 0.038 and 0.002, respectively), with the ulnocarpal joint showing the highest difference in kPa values (30.80 kPa higher in cases).

3.3. Associations between SWE and PDU data with clinical variables

No significant differences were found in clinical variables (HAQ, pain scales, SLEDAI, SLICC-SDI, ANA, DNA) between patients with kPa values above and below 30, although SLEDAI approached significance (p = 0.056). Clinical differences between patients with positive Doppler in any joint that showed significant differences (p-value 0.005) were only observed in the SLICC-SDI variable, with higher values among patients with at least one Doppler-positive joint (mean 0.652, 95 % CI 0.317–0.987) compared to those with no affected joints (mean 0.135, 95 % CI 0.02–0.251). Associations between clinical features and positive Doppler findings in each joint were observed, with significant associations found in the radiocarpal joint (BMI, p-value 0.041), ulnocarpal joint (SLICC-SDI, p-value 0.032), intercarpal joint (SLICC-SDI, p-value 0.045), and the second metacarpophalangeal joint (SLICC-SDI, p-value 0.002 and SM, p-value 0.008). A significant positive correlation was found between the number of PDU joints and SLICC-SDI scores (correlation coefficient of 0.438, p = 0.000) (Table 3).

4. Discussion

Our study aimed to evaluate synovial joint effusion stiffness in SLE patients using SWE and PDU, seeking to delineate the relationship between joint effusion stiffness and various patient characteristics, including any correlation between the presence of synovitis and patient demographics and disease manifestations. To our knowledge, this was the first study to specifically explore the use of SWE in assessing joint symptoms in SLE. The early detection of synovitis is essential for improving patient outcomes, as it enables prompt treatment and reduces the risk of cumulative damage. Tissue elasticity plays a crucial role in the pathological states of tissues[30]. Elastography provides insights into biomechanical properties like stiffness and elasticity through the analysis of radiofrequency signals produced by the tissue's elastic reaction to specific ultrasound waves emitted perpendicularly by the transducer. This technique produces a qualitative representation, depicted on a color scale in kilopascals (kPa), from 0 (soft tissue, depicted as dark blue) to 180 kPa (hard tissue, shown as red). By employing SWE, it is possible to measure tissue stiffness with relative precision using a non-invasive and objective method, which reduces dependence on the

Table 2
Joint Stiffness Measured by SWE (kPa). Joint stiffness values measured in kilopascals (kPa) using ultrasound "Shear-Wave" elastography, compared across different groups (1, 2, 3, 4) and specific joints.

Articulation	Number of exanimated articulations	Mean stiffness (kPa)	Standard Deviation	P-value
Radiocarpal joint				
Group 1 (SLE w/ arthritis)	18	30.22	22.808	0.004
Group 2 (SLE w/ arthralgia)	13	37.23	20.861	
Group 3 (SLE w/o arthritis/arthralgia)	14	36.71	19.157	
Group 4 (Healthy subjects)	9	7.67	5.766	
Total	54	29.83	21.676	
Ulnocarpal joint				
Group 1 (SLE w/ arthritis)	7	43.571	25.9863	0.051
Group 2 (SLE w/ arthralgia)	7	31.200	18.1809	
Group 3 (SLE w/o arthritis/arthralgia)	10	37.200	21.2069	
Group 4 (Healthy subjects)	4	6.500	3.1091	
Total	28	32.907	22.6909	
Intercarpal joint				
Group 1 (SLE w/ arthritis)	4	35.50	31.214	0.398
Group 2 (SLE w/ arthralgia)	3	27.33	15.308	
Group 3 (SLE w/o arthritis/arthralgia)	4	45.25	21.960	
Group 4 (Healthy subjects)	2	10.00	2.828	
Total	13	32.69	23.496	
Second metacarpophalangic joint				
Group 1 (SLE w/ arthritis)	5	30.20	4.324	0.175
Group 2 (SLE w/ arthralgia)	3	29.33	8.083	
Group 3 (SLE w/o arthritis/arthralgia)	9	30.00	10.062	
Group 4 (Healthy subjects)	5	17.20	16.006	
Total	22	27.05	11.274	
Third metacarpophalangic joint				
Group 1 (SLE w/ arthritis)	4	37.50	30.610	0.071
Group 2 (SLE w/ arthralgia)	8	32.13	13.217	
Group 3 (SLE w/o arthritis/arthralgia)	7	31.29	19.371	
Group 4 (Healthy subjects)	6	9.83	7.574	
Total	25	27.40	19.489	
Fourth metacarpophalangic joint				
Group 1 (SLE w/ arthritis)	1	5.00	–	0.360
Group 2 (SLE w/ arthralgia)	3	28.00	8.000	
Group 3 (SLE w/o arthritis/arthralgia)	4	29.00	17.758	
Group 4 (Healthy subjects)	1	5.00	–	
Total	9	23.33	15.572	
Fifth metacarpophalangic joint				

(continued on next page)

Table 2 (*continued*)

Articulation	Number of exanimated articulations	Mean stiffness (kPa)	Standard Deviation	P-value
Group 1 (SLE w/ arthritis)	1	25.00	–	0.953
Group 2 (SLE w/ arthralgia)	1	24.00	–	
Group 3 (SLE w/o arthritis/arthralgia)	2	30.50	19.092	
Group 4 (Healthy subjects)	0	–	–	
Total	4	27.50	11.561	
Second proximal interphalangic joint				
Group 1 (SLE w/ arthritis)	2	56.50	21.920	0.256
Group 2 (SLE w/ arthralgia)	1	20.00	–	
Group 3 (SLE w/o arthritis/arthralgia)	2	27.00	21.213	
Group 4 (Healthy subjects)	2	10.50	7.775	
Total	7	29.71	23.357	
Third proximal interphalangic joint				
Group 1 (SLE w/ arthritis)	2	32.00	22.627	0.414
Group 2 (SLE w/ arthralgia)	1	64.00	–	
Group 3 (SLE w/o arthritis/arthralgia)	2	33.00	7.071	
Group 4 (Healthy subjects)	0	–	–	
Total	5	38.80	18.417	
Fourth proximal interphalangic joint				
Group 1 (SLE w/ arthritis)	1	12.00	–	0.172
Group 2 (SLE w/ arthralgia)	0	–	–	
Group 3 (SLE w/o arthritis/arthralgia)	3	56.00	15.524	
Group 4 (Healthy subjects)	1	12.00	–	
Total	5	38.40	26.482	
Fifth proximal interphalangic joint				
Group 1 (SLE w/ arthritis)	0	–	–	0.181
Group 2 (SLE w/ arthralgia)	1	22.00	–	
Group 3 (SLE w/o arthritis/arthralgia)	2	34.50	2.121	
Group 4 (Healthy subjects)	2	11.50	10.607	
Total	5	22.80	12.716	

operator's technique. Its effectiveness and validation have been demonstrated in conditions such as chronic liver disease, as well as in liver masses, thyroid, breast, prostate, skin, and eye pathologies [31–40]. Additionally, SWE has emerged as an innovative tool in musculoskeletal imaging, offering insights into early inflammatory changes that may not be apparent on conventional imaging[31,32]. Its application in assessing superficial musculoskeletal structures has emerged as an innovative and promising tool in clinical settings[41–43]. In clinical practice, the integration of PDU has become widespread. Despite its proven potential for diagnosing and detecting synovitis, it varies in sensitivity and specificity, making it unsuitable as a "gold standard" test for this condition[44–46]. Evidence shows that the presence of inflammatory infiltration within synovial fluid is more common in individuals with inflammatory joint diseases[44].

This accumulation affects the visual characteristics of certain hyperechoic structures observed in synovial fluid ultrasounds and

Table 3
Differences in Joint Stiffness and Doppler Vascularization. Summary of key findings on significant differences in joint stiffness and Doppler vascularization among groups. Detailed comparisons highlight the variations in stiffness and vascularization detected between groups, with notations for significant differences and clinical relevance.

Comparisons	Mean Difference in Stiffness (kPa)	95 % CI	p-value	Number of Joints Evaluated
Patient Groups (G1, G2, G3) vs Control Group (G4)	24.06530	19.76655–28.36405	<0.001	G1: 45, G2: 41, G3: 59, G4: 32 (Total:177)
Radiocarpal Joint (Cases vs Controls)	22.7	19.5–25.9	0.000	G1: 18, G2: 13, G3: 14, G4: 9 (Total: 54)
Ulnocarpal Joint (Cases vs Controls)	22.5	19.1–25.9	0.008	G1: 7, G2: 7, G3: 10, G4: 4 (Total: 28)
Second MCP Joint (Cases vs Controls)	22.3	19.8–24.8	0.038	G1: 5, G2: 3, G3: 9, G4: 5 (Total: 22)
Third MCP Joint (Cases vs Controls)	23.6	21.2–26.0	0.002	G1: 4, G2: 8, G3: 7, G4: 6 (Total: 25)
Radiocarpal Joint (G1 vs G4)	22.7	18.9–26.5	0.033	G1: 18, G4: 9 (Total: 27)
Radiocarpal Joint (G2 vs G4)	23.4	19.6–27.2	0.005	G2: 13, G4: 9 (Total: 22)
Radiocarpal Joint (G3 vs G4)	23.0	19.2–26.8	0.006	G3: 14, G4: 9 (Total: 23)
Ulnocarpal Joint (G1 vs G4)	24.1	20.3–27.9	0.038	G1: 7, G4: 4 (Total: 11)
CDU-positive vs CDU-negative (SLICC-SDI values)	–	–	0.005	–
Correlation (CDU-positive joints and SLICC-SDI scores)	–	Correlation Coefficient:0.438	0.000	–

G1: Group 1 G2: Group 2 G3: Group 3 G4: Group 4; CDU (Color-Doppler-Ultrasound); SLICC-SDI (Systemic Lupus International Collaborating Clinics).

correlates with symptoms of joint stiffness[47]. While the literature describes SWE studies on the musculoskeletal system, the quantification of synovial fluid stiffness in healthy controls and those with a history of inflammatory pathology remains substandard[28,49,29–48]. The positive correlation between inflammatory activity and increased joint stiffness has already been documented, albeit using conventional elastography techniques instead of SWE[28,29].

In a 2023 retrospective study, 29 cases and 29 controls were assessed to explore differences in tissue stiffness within joint areas using SWE [19]. The case group's inflammatory conditions were primarily SLE at 61 %, followed by RA, seronegative undifferentiated arthritis, psoriatic arthritis, and polymyalgia rheumatica. Significant statistical differences were found in stiffness measurements, with the case group displaying considerably higher values compared to the control group. The dorsal radiocarpal joint was the most affected by synovitis, showing a marked difference in patients versus controls, underscoring the relevance of joint stiffness in assessing disease activity.

Chandel et al.[49]conducted a prospective study evaluating the role of SWE in differentiating RA from tubercular (TB) arthritis. The study demonstrated that SWE could effectively distinguish between these

conditions based on synovial stiffness, reporting a cutoff of 43.6 kPa with high sensitivity (86.7 %) and specificity (80 %) for differentiating RA from TB arthritis. These findings underscore the potential of SWE to provide quantitative and objective measures of synovial stiffness, aiding in differential diagnoses that are often challenging with conventional imaging modalities.

Similarly in 2023, Almolla et al.[50]explored the use of SWE in RA and emphasized its value in detecting synovial changes earlier than conventional ultrasonography. The study found that SWE not only detected synovial stiffness but also correlated with markers of disease activity, such as softer synovium being associated with increased disease activity. This suggests that SWE could play a role not only in diagnosis but also in monitoring treatment responses, offering clinicians a more dynamic tool for managing RA. Additionally, Almolla et al. highlighted the limitations of grey scale and power Doppler ultrasonography (PDUS), such as limited sensitivity for detecting erosions and potential diagnostic overlap with osteoarthritis. SWE, by contrast, provides additional quantitative information that could address these gaps.

Our current study provides compelling evidence for the utility of SWE and PDU in the assessment of musculoskeletal alterations in SLE patients, particularly in detecting subclinical synovitis. The findings reveal that SLE patients exhibit significantly higher stiffness in synovial joint effusion, as measured in kilopascals (kPa), compared to healthy controls, with no notable differences in stiffness among the SLE patient groups differentiated by types of joint symptoms (non-arthritis, arthralgia, arthritis). This indicates a broader prevalence of musculoskeletal changes in SLE that might not be evident through clinical examination alone. Our study has identified the radiocarpal, ulnocarpal, second and third metacarpophalangeal joints as key areas for assessing synovitis in SLE, providing a quantitative measure of inflammation through increased stiffness values. Higher stiffness values were found across the various patient groups (G1, G2, G3) compared to the control group (G4), including in groups G2-G3, which was comprised of patients with wrist and/or hand inflammatory arthralgia (G2) or asymptomatic patients (G3). Specifically, significant differences in stiffness were observed in the radiocarpal joint between G1 and G4 ($p = 0.033$), between G2 and G4 ($p = 0.005$), and between G3 and G4 ($p = 0.006$), as well as in the ulnocarpal joint between G1 and G4 ($p = 0.038$). Moreover, comparing the combined G1 and G2 groups to the G3 group, no statistically significant differences in stiffness values were observed ($p = 0.157$). This would suggest that the presence of increased stiffness, even in pauci-symptomatic or asymptomatic patients, could correlate with subclinical synovitis, in line with the elevated subclinical synovitis values reported in an MRI study by Corzo et al. in 2024[51]. These findings would be consistent with the existing literature[28,29], highlighting the potential relevance of SWE and PDU in the early detection of synovitis, and thereby facilitating timely intervention.

Moreover, the research highlights the clinical significance of elastography and the Doppler findings, notably the SLICC/ACR Damage Index (SDI) in capturing the heterogeneity of SLE-related musculoskeletal disease and the correlation with disease severity. The SDI is a score of accumulated irreversible damage in patients with SLE secondary to lupus activity or its treatments. In our study, the positive Doppler signal correlated with the SDI index of cumulative damage. The Doppler signal revealed acute and active joint involvement, and the SDI indexes showed chronic damage, leading us to the realization that those patients with chronic damage in the cohort had still been experiencing inflammatory joint activity at the time of study inclusion. It is well known that musculoskeletal joint involvement can cause irreversible damage, which occurs during the initial stages of the disease. Moreover, there is an association in the literature with a worse disease prognosis and mortality, which is why it is so important to detect the presence of synovitis and Doppler in these patients to prevent damage, diagnose early, and begin treatment at the earliest opportunity[46].

Our study presents certain limitations. Ultrasound imaging is inherently operator-dependent and has intrinsic sensitivity limits, making it less effective in terms of diagnostic sensitivity compared to MRI. The threshold of 30 kPa for defining synovitis in SWE is based on the limited available literature, and it will be necessary to expand upon the elastographic evaluation of synovitis to other inflammatory pathologies in order to establish it as a reliable cutoff measure. Patients with joint involvement probably received more corticosteroids during the follow-up of their disease, thus increasing the irreversible damage. However, this is something that we have not been able to demonstrate as we lack the cumulative dose of corticosteroids, a limitation of our study. Another limitation concerns the fact that the joints in which a significant difference in stiffness and Doppler evaluation was found were those with a higher frequency of joint fluid. As such, these joints have a larger number of evaluable samples. Additionally, although this study represents the largest SLE cohort examined with SWE to date, the sample size, particularly the number of control joints assessed, remains relatively small. This limitation should be addressed in future research with larger cohorts and expanded joint evaluations to strengthen the findings. The study was conducted under routine clinical practice conditions, leading to potential variations in clinical outcomes and results, and influenced by factors such as the delay in obtaining imaging tests, adjustments in treatments, and the inherent cyclical nature of SLE flares and remissions. Concerning the anatomical focus, our investigation concentrated on the wrist and hand, aligning with the emphasis of previous studies. Consequently, the detected abnormalities may not be directly applicable to other joints.

5. Conclusions

Our study indicates that SLE patients have higher kPa values than healthy controls, suggesting the presence of subclinical synovitis even in asymptomatic individuals. Key joints such as the radiocarpal, ulnocarpal, and metacarpophalangeal are important for obtaining a proper assessment. The integration of SWE and PDU into routine SLE assessments can facilitate earlier diagnosis, enabling prompt treatment and reducing the risk of cumulative joint damage. SWE and PDU are valuable for the early detection and treatment of musculoskeletal changes. By identifying subclinical synovitis, these techniques not only improve patient monitoring but also help tailor therapeutic strategies to individual disease activity.

The correlation with higher SLICC-SDI scores underscores the critical role of joint evaluation in preventing long-term damage and enhancing care management. Moving forward, refining imaging protocols to standardize SWE and PDU application in SLE is essential. Additionally, exploring the utility of these techniques in other joints, such as the knees and ankles, may provide further insights into the extent of subclinical involvement across the musculoskeletal system.

CRediT authorship contribution statement

Salvatore Marsico: Writing – original draft, Project administration, Conceptualization. **Laura Tío:** Formal analysis, Data curation. **Irene Carrión-Barberà:** Resources, Project administration, Investigation. **Patricia Corzo:** Writing – review & editing, Visualization, Validation. **José María Maiques Llácer:** Software, Resources, Funding acquisition, Formal analysis. **Albert Solano:** Visualization, Validation, Supervision. **Jordi Monfort:** Writing – review & editing, Writing – original draft, Data curation, Conceptualization. **Tarek Carlos Salman-Monte:** Writing – review & editing, Writing – original draft, Validation, Supervision, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

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