


## Clinical science

# The value of shear wave elastography in diagnosis and assessment of systemic sclerosis

Ruyi Cai<sup>1,2,‡</sup>, Zhuohua Lin<sup>3,‡</sup>, Dan Xu<sup>1,2</sup>, Yang Sun<sup>3</sup>, Ligang Cui<sup>3</sup>, Rong Mu <sup>1,2,\*</sup>

<sup>1</sup>Department of Rheumatology and Immunology, Peking University Third Hospital, Beijing, China

<sup>2</sup>Center for Rare Disease, Peking University Third Hospital Beijing, China

<sup>3</sup>Department of Ultrasound, Peking University Third Hospital, Beijing, China

\*Correspondence to: Rong Mu, Department of Rheumatology and Immunology, Peking University Third Hospital, Beijing 100191, China.  
E-mail: murongster@163.com

‡R.C. and Z.L. contributed equally.

## Abstract

**Objective:** The aim was to determine the efficacy of shear wave elastography (SWE) in assessing skin stiffness and aiding in the diagnosis of patients with systemic sclerosis (SSc).

**Methods:** A total of 66 patients with SSc, 100 healthy individuals and 27 patients with SSc-like disorders were included. SWE was performed at 17 modified Rodnan skin score (mRSS) measurement sites. The correlation between SWE and clinical profiles was assessed, and the diagnostic value of SSc was explored.

**Results:** The SWE values at all 17 mRSS sites were significantly higher in SSc than in the healthy group [54.95 (45.95, 66.55) vs 41.10 (39.18, 45.45) m/s,  $P < 0.001$ ]. For clinically uninvolved sites (mRSS = 0) of patients with SSc, 11 of 17 sites showed significantly higher SWE values compared with healthy controls. SWE was positively correlated with total mRSS ( $r = 0.783$ ,  $P < 0.001$ ), the European Scleroderma Study Group disease activity index ( $r = 0.707$ ,  $P < 0.001$ ) and histological collagen deposition ( $r = 0.749$ ,  $P = 0.013$ ). SWE effectively distinguished patients with SSc from patients with SSc-like disorders (area under the curve, AUC = 0.819). Use of SWE-detected skin sclerosis showed a significantly higher sensitivity compared with 1980 ACR criteria [0.818 (95% CI 0.709, 0.893) vs 0.727 (95% CI 0.610, 0.820),  $P = 0.031$ ].

**Conclusion:** SWE correlates well with disease activity and collagen deposition in the skin, provides greater reliability than mRSS and aids in the diagnosis of SSc. SWE could be considered as a convenient and reliable quantitative tool for assessing skin sclerosis and disease progression in SSc.

## Lay Summary

### What does this mean for patients?

Systemic sclerosis (SSc) is an autoimmune disease characterized by skin thickening and sclerosis. Doctors often assess skin using the modified Rodnan skin score (mRSS), a semi-quantitative method based on palpation (feeling with the fingers during physical examination), or the invasive method of skin biopsy. A quantitative and non-invasive alternative is to perform ultrasound examination with shear wave elastography (SWE), which measures tissue stiffness. Our comparison of SWE with mRSS and skin biopsy revealed that SWE demonstrates a strong correlation with disease activity and collagen deposition in the skin, offering greater reliability than mRSS and aiding in SSc diagnosis. For patients with suspected SSc, SWE is recommended, especially when clinically apparent skin lesions are not present through palpation. Anticipating the future, SWE holds promise as a quantitative and non-invasive tool for disease monitoring and evaluating the response to treatment in both clinical practice and clinical trials.

**Keywords:** SSc, skin lesion, shear wave elastography.

### Key messages

- Shear wave elastography is a potential tool for detecting skin lesions and subclinical skin involvement in SSc.
- Shear wave elastography values are correlated with disease activity and collagen deposition in skin histology.
- Shear wave elastography could effectively identify SSc and contribute to the diagnosis of SSc.

## Introduction

Systemic sclerosis (SSc), also known as scleroderma, is an autoimmune disease characterized by fibrosis of the skin and internal organs and by vasculopathy [1, 2]. Skin symptoms such

as skin thickening and sclerosis are common in SSc, and skin involvement is a crucial component of SSc classification criteria [3]. Accurate assessment of the extent and rate of progression of skin lesions is crucial because it is closely related to

Received: 25 July 2023. Accepted: 28 July 2023

© The Author(s) 2023. Published by Oxford University Press on behalf of the British Society for Rheumatology.

This is an Open Access article distributed under the terms of the Creative Commons Attribution-NonCommercial License (<https://creativecommons.org/licenses/by-nc/4.0/>), which permits non-commercial re-use, distribution, and reproduction in any medium, provided the original work is properly cited. For commercial re-use, please contact [journals.permissions@oup.com](mailto:journals.permissions@oup.com)

disease activity, severity and prognosis [4, 5]. The modified Rodnan skin score (mRSS), a semi-quantitative method that assesses skin at 17 body sites based on palpation, is a validated and recognized method to evaluate skin lesions in SSc. Although the mRSS has been generally accepted, it has several limitations, such as significant inter- and intra-rater variability owing to subjective feelings and physician inexperience, making it a heterogeneous method in skin evaluation [6, 7]. There exists a need to find a more sensitive and objective method to assess the lesions of the skin in patients with SSc.

In recent years, US has emerged as a convenient and non-invasive tool for diagnosing and evaluating rheumatic diseases. Shear wave elastography (SWE), a measurement technique based on US, measures tissue stiffness quantitatively by measuring the speed of shear wave propagation and calculating Young's modulus of the tissue [8]. Previous studies indicated that SWE could effectively distinguish affected skin and healthy skin [9–11] with good intra- and inter-group consistency [12–14], and skin US can detect clinically unaffected skin lesions in SSc [9]. These findings suggest that US, particularly SWE, has the potential to be a valuable tool in assessment of the skin in SSc. However, the full potential of skin US in SSc assessment has yet to be explored.

There are several factors that limit the clinical application of SWE. First, the validity of SWE in assessing skin sclerosis and its correlation with clinical profiles needs to be established. It remains uncertain whether the abnormalities detected by SWE can accurately reflect the collagen deposition status or disease activity of SSc, which hinders the interpretation of results and restricts the widespread clinical application of SWE as a skin assessment method. Second, it is yet to be determined whether SWE can distinguish skin lesions in SSc effectively and contribute to the diagnosis. Early detection of skin lesions is crucial for diagnosis and timely treatment decisions, emphasizing the need for more sensitive and objective measures of skin involvement. Although SWE is a possible tool for the early detection of skin lesions, its effectiveness in diagnosis has not been verified fully. Third, the time-consuming process of examining all 17 sites in the mRSS assessment could potentially hinder the clinical application of SWE. Thus, optimization and standardization of the examination process are necessary to facilitate its wider adoption and utility in clinical practice.

The objective of this study was to explore the value of SWE as an imaging modality to differentiate skin sclerosis and aid in diagnosis, and its correlation with skin histological findings and disease activity. We also discuss the possibility of reducing the number of detection sites for optimization in efficiency and better clinical application.

## Methods

### Patients

This study included a total of 66 consecutive patients over >18 years of age, who were diagnosed with SSc and met the ACR/EULAR 2013 criteria for SSc [3]. These patients were admitted to Peking University Third Hospital between May 2021 and January 2023. To assess the diagnostic value of SWE in SSc, we also included 27 first-visit patients as disease controls who presented with clinical or antibody patterns resembling SSc but were later excluded from the diagnosis after thorough evaluation. Additionally, we enrolled 100 healthy

volunteers as the control group, all of whom had no previous history of rheumatic immune diseases, skin diseases, hypertension or diabetes.

Ethical approval was obtained from the ethics committee of the Peking University Third Hospital, and all participants signed a written informed consent form (M2022122).

### Clinical profiles

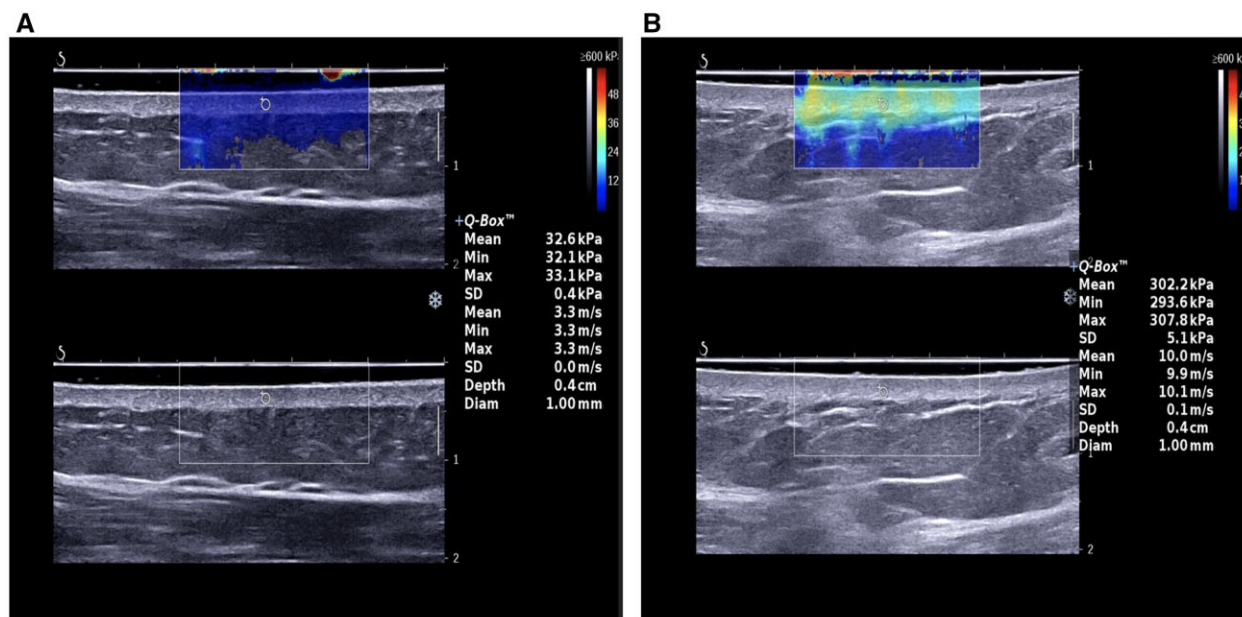
The following demographic and clinical data were collected from all subjects: characteristics including age, sex, disease duration and BMI. The following information was recorded, including the presence of RP, puffy fingers, digital ulcers, fingertip pitting scars, telangiectasia, skin thickening of the fingers proximal to the MCP joints, sclerodactyly, interstitial lung disease, pulmonary arterial hypertension and renal crisis. Laboratory examination was also conducted to assess the DAS {European Scleroderma Study Group (EScSG) disease activity index [15]}. The mRSS was assessed by two physicians (R.C. and D.X.) at all 17 mRSS sites. In the event of any discrepancies between their findings, a third physician, R.M., would act as an adjudicator.

### US examination

US examination was performed using a Doppler US diagnostic apparatus (Supersonic Imagine), equipped with a linear array high-frequency probe (SL15-4), with a detection frequency of 4–15 MHz. Ultrasonography was performed on 17 mRSS sites throughout the body by Z.L., an experienced US physician with 5 years of expertise in musculoskeletal sonography who was blinded to the mRSS. The 17 sites included the dorsal segment of the middle finger on both sides; the bilateral dorsal hand, the interspace between index/middle finger, nearly 2 cm from the MCP joint; bilateral dorsal forearms, 10 cm from the ulnar styloid process; both upper arms, 10 cm proximal to the medial epicondyle; the chest wall between the sternal angle and the sternal notch; the abdominal wall at ~10 cm below the xiphoid process; the forehead; bilateral thighs, 10 cm from the upper patella; bilateral anterolateral calves, 10 cm from the lateral malleolus; bilateral dorsum of the foot, first webbed space, 2 cm from the MTP joint.

The arrangement of skin collagen fibres is directional, leading to the differences in Young's modulus of the skin in different directions [16]. To avoid the influence of skin anisotropy on the results, the US probe was placed in the same direction as the long axis of the body. Patients were examined in relaxed positions to prevent changes in skin stiffness caused by exertion. Skin measurements were taken in different positions depending on the location being examined. The skin of the upper limbs, trunk and forehead was measured in the supine position, and the thighs were assessed in a sitting position with the legs straightened. The lateral leg and dorsum of the foot were assessed with the knee bent and both feet flat on the examination bed.

To perform SWE, the skin at the measurement site should be fully exposed, and the probe should be placed perpendicular to the skin surface. A coupling space is filled between the probe and the skin to avoid direct pressure on the skin. After displaying the epidermis, dermis and s.c. soft tissue layers in greyscale mode, the examination mode can be switched to SWE, and images are frozen after stabilizing for 3–5 s (Fig. 1). The shear wave velocity (in metres per second) is measured three times by selecting a region of interest in the dermis layer, and the average value is recorded. All measurements were



**Figure 1.** US-measured skin stiffness of an SSc patient and a healthy individual. The mean shear wave velocity for a single subject was 3.3 m/s in the healthy controls (A) and 10.0 m/s in SSc patients (B)

performed in the afternoon between 17.00 and 20.00 h at a room temperature of 20–25°C.

### Skin biopsy and semi-quantification of collagen density

Skin biopsies were collected from the forearm at the location of SWE assessment in 10 of 66 SSc patients who had undergone skin biopsies for the need of clinical assessment. The collected tissue samples were fixed in formalin and embedded in paraffin. The embedded tissue sections were then stained for collagen using Masson's Trichrome (SOLARBIO, G1340), and the collagen volume fraction was calculated by quantifying the ratio of the collagen-stained area to the total stained area using ImageJ software.

### Threshold of SWE values in different sites

We assessed SWE at the 17 mRSS sites in 100 healthy controls, using the 95th percentile of SWE value as the upper threshold (Supplementary Table S1, available at *Rheumatology Advances in Practice* online). There were variations in the thresholds across different sites, with the highest thresholds observed in the fingers and dorsum of the feet, and the lowest thresholds observed in the thighs. We defined SWE-detected skin sclerosis as skin with SWE values that exceeded the 95th percentile upper threshold of the 100 healthy controls at each individual site.

### Incorporation of SWE-detected skin sclerosis for the classification of SSc patients

The 1980 ACR classification criteria [17] were applied to all patients with established SSc ( $n = 66$ ) and with SSc-like disorders ( $n = 27$ ). We evaluated the impact of using SWE-detected skin sclerosis as a substitute for the skin involvement assessment items in the original 1980 ACR criteria (proximal scleroderma, sclerodactyly) on the diagnostic performance of the classification criteria.

### Statistical analysis

Statistical analysis was performed using SPSS v.26.0, with a significance level of  $P < 0.05$ . The age, BMI and SWE values of the study subjects were analysed descriptively, and normality was tested using the single-sample Kolmogorov–Smirnov test. Continuous variables with a normal distribution were expressed as the mean (s.d.), and continuous variables with a non-normal distribution were expressed as the median (interquartile range). Categorical variables were expressed as the frequency (percentage). Student's  $t$ -test or the Mann–Whitney  $U$ -test was used to compare the SWE values of SSc patients and healthy controls. The McNemar test and the area under the receiver operating characteristic curve (AUC) were used to evaluate the diagnostic value. Pearson's correlation or Spearman's correlation was used to analyse the correlation between SWE, mRSS, collagen volume fraction and European Scleroderma Study Group disease activity index (EScSG-DAI). Logistic regression was used to assess the value of different SSc detection sites.

## Results

### Demographic data of enrolled participants

The study included 66 patients with SSc, of whom 63 were females and 3 males, with an average age of  $51.4 \pm 13.7$  years. Sixteen patients were classified with dcSSc and 50 with lcSSc. The characteristics of patients and healthy individuals are presented in Supplementary Table S2, available at *Rheumatology Advances in Practice* online.

### SWE values were elevated in SSc and in sites that showed subclinical skin involvement upon detection

In patients with SSc, the value of SWE in all 17 mRSS sites was significantly higher than that of the healthy control group [ $54.95$  (45.95, 66.55) vs  $41.10$  (39.18, 45.45) m/s,  $P < 0.001$ ], and the most significant differences were observed in the middle fingers [right:  $6.50$  (4.50, 9.40) vs  $3.70$  (3.45, 3.95) m/s,

**Table 1.** Shear wave elastography values of the SSc patients and controls in our study

Site	Patients ( <i>n</i> = 66) SWE (m/s)	HC ( <i>n</i> = 100) SWE (m/s)	Difference SWE (m/s)	P-value
Right middle finger	6.50 (4.50, 9.40)	3.70 (3.45, 3.95)	2.80 (2.00, 3.40)	<0.001
Left middle finger	5.80 (3.95, 7.15)	3.15 (2.78, 3.55)	2.50 (1.70, 3.00)	<0.001
Right hand dorsum	3.20 (2.60, 4.50)	2.30 (2.20, 2.53)	0.70 (0.50, 1.00)	<0.001
Left hand dorsum	2.70 (2.30, 4.20)	2.20 (2.00, 2.65)	0.50 (0.20, 0.80)	<0.001
Right forearm	3.10 (2.65, 3.70)	2.30 (2.18, 2.63)	0.60 (0.40, 0.80)	<0.001
Left forearm	3.00 (2.65, 3.80)	2.30 (2.10, 2.70)	0.70 (0.50, 1.00)	<0.001
Right upper arm	2.80 (2.30, 3.30)	2.30 (1.88, 2.50)	0.40 (0.20, 0.70)	0.001
Left upper arm	2.80 (2.40, 3.60)	2.30 (2.10, 2.63)	0.40 (0.20, 0.70)	<0.001
Forehead	3.10 (2.60, 3.50)	2.25 (2.08, 2.50)	0.60 (0.40, 0.80)	<0.001
Anterior chest	2.60 (2.20, 2.85)	2.10 (1.78, 2.50)	0.30 (0.10, 0.50)	0.001
Anterior abdomen	2.20 (1.80, 2.65)	1.90 (1.60, 2.30)	0.20 (0.10, 0.40)	0.006
Right thigh	1.90 (1.80, 2.10)	1.75 (1.60, 2.10)	0.10 (0.00, 0.30)	0.026
Left thigh	2.00 (1.80, 2.25)	1.80 (1.60, 2.10)	0.20 (0.10, 0.30)	0.005
Right calf	2.40 (2.10, 2.85)	2.40 (2.08, 2.73)	0.20 (0.00, 0.30)	0.025
Left calf	2.50 (2.10, 3.15)	2.40 (2.20, 2.65)	0.20 (0.00, 0.40)	0.044
Right foot dorsum	3.60 (2.90, 4.15)	2.80 (2.28, 3.45)	0.40 (0.10, 0.80)	0.010
Left foot dorsum	3.70 (2.80, 4.50)	2.80 (2.50, 3.53)	0.50 (0.10, 0.80)	0.010
Total	54.95 (45.95, 66.55)	41.10 (39.18, 45.45)	12.9 (9.60, 16.30)	<0.001

HC: healthy control; SWE: shear wave elastography.

**Table 2.** Statistical characteristics of shear wave elastography in the skin sites of patients with a modified Rodnan skin score of zero and healthy controls

Site	SSc (mRSS = 0)		HC		P-value
	<i>n</i>	SWE	<i>n</i>	SWE	
Right middle finger	17	3.60 (3.10, 5.05)	100	3.70 (3.45, 3.95)	0.762
Left middle finger	18	3.65 (3.23, 4.15)	100	3.15 (2.78, 3.55)	0.088
Right hand dorsum	37	2.70 (2.40, 3.45)	100	2.30 (2.20, 2.53)	0.003
Left hand dorsum	36	2.50 (2.30, 3.07)	100	2.20 (2.00, 2.65)	0.128
Right forearm	46	2.90 (2.50, 3.23)	100	2.30 (2.18, 2.63)	<0.001
Left forearm	49	2.90 (2.60, 3.40)	100	2.30 (2.10, 2.70)	<0.001
Right upper arm	57	2.80 (2.28, 3.20)	100	2.30 (1.88, 2.50)	0.002
Left upper arm	57	2.70 (2.40, 3.40)	100	2.30 (2.10, 2.63)	0.001
Forehead	53	3.10 (2.55, 3.50)	100	2.25 (2.08, 2.50)	<0.001
Anterior chest	57	2.50 (2.20, 2.80)	100	2.10 (1.78, 2.50)	0.003
Anterior abdomen	63	2.10 (1.80, 2.60)	100	1.90 (1.60, 2.30)	0.011
Right thigh	64	1.90 (1.80, 2.10)	100	1.75 (1.60, 2.10)	0.036
Left thigh	62	2.00 (1.80, 2.20)	100	1.80 (1.60, 2.10)	0.014
Right calf	56	2.40 (2.13, 2.70)	100	2.40 (2.08, 2.73)	0.064
Left calf	57	2.50 (2.10, 3.00)	100	2.40 (2.20, 2.65)	0.118
Right foot dorsum	57	3.50 (2.90, 4.00)	100	2.80 (2.28, 3.45)	0.037
Left foot dorsum	56	3.50 (2.73, 4.00)	100	2.80 (2.50, 3.53)	0.069

HC: healthy control; mRSS: modified Rodnan skin score; SWE: shear wave elastography.

$P < 0.001$ ; left: 5.80 (3.95, 7.15) vs 3.15 (2.78, 3.55) m/s,  $P < 0.001$ ], as shown in Table 1.

SWE values of clinical uninvolved sites (with mRSS of zero) in 66 patients with SSc were investigated. Of the 17 examined sites, 11 sites (right hand, bilateral forearms, bilateral upper arms, forehead, chest, abdomen, bilateral thighs and right foot dorsum) showed significantly higher SWE values compared with healthy controls, as shown in Table 2.

### SWE was correlated with collagen deposition in skin and disease activity in SSc

There were positive correlations between SWE values and mRSS in most measurement sites, except for the forehead and bilateral calves. Specifically, we observed significant correlations between SWE and mRSS in bilateral fingers, dorsal hands, forearms, upper arms, anterior chest, abdomen, thigh

and dorsal foot, and in total scores in 17 sites ( $r = 0.783$ ,  $P < 0.001$ ; Table 3).

To confirm the reliability of SWE to assess the skin lesions in SSc, a histochemical stain (Masson's Trichrome) was applied. A total of 10 patients at an early stage of SSc, with a disease duration of <3 years, had undergone skin biopsies in the same site as SWE measurements on their forearms and were included for the comparison. The collagen content of the skin, as measured by collagen volume fraction, was correlated with SWE measurements of local skin ( $r = 0.749$ ,  $P = 0.013$ ), which was higher than that of local mRSS ( $r = 0.624$ ,  $P = 0.054$ ; Fig. 2).

We also assessed the correlation between SWE and disease activity in SSc. SWE values of 17 sites were positively correlated with disease activity assessed by EScSG-DAI ( $r = 0.710$ ,  $P < 0.001$ ; Table 3), which was higher compared with mRSS ( $r = 0.685$ ,  $P < 0.001$ ).

**Table 3.** Correlation between shear wave elastography values and both modified Rodnan skin score and European Scleroderma Study Group disease activity index in all 17 sites

Site	mRSS		EScSG-DAI	
	<i>r</i>	<i>P</i> -value	<i>r</i>	<i>P</i> -value
Right middle finger	0.762	<0.001	0.458	0.001
Left middle finger	0.690	<0.001	0.481	<0.001
Right hand dorsum	0.600	<0.001	0.448	0.001
Left hand dorsum	0.454	<0.001	0.433	0.002
Right forearm	0.488	<0.001	0.428	0.002
Left forearm	0.536	<0.001	0.547	<0.001
Right upper arm	0.362	0.004	0.382	0.006
Left upper arm	0.375	0.003	0.339	0.016
Forehead	0.168	0.196	0.232	0.106
Anterior chest	0.307	0.016	0.430	0.002
Anterior abdomen	0.301	0.018	0.126	0.382
Right thigh	0.325	0.006	0.071	0.626
Left thigh	0.358	0.005	0.198	0.167
Right calf	0.242	0.061	0.363	0.010
Left calf	0.240	0.062	0.253	0.064
Right foot dorsum	0.269	0.036	0.271	0.057
Left foot dorsum	0.354	0.005	0.172	0.232
Total	0.783	<0.001	0.710	<0.001

EScSG-DAI: European Scleroderma Study Group disease activity index; mRSS: modified Rodnan skin score; SWE: shear wave elastography.

### SWE could effectively distinguish SSc from other diseases and aid in the diagnosis

To explore whether SWE could aid in the diagnosis, receiver operating characteristic curve analysis was performed using SWE values of 17 sites. SWE could effectively distinguish SSc patients from healthy controls, with an AUC of 0.851 (95% CI 0.787, 0.915), and from patients with other diseases, with an AUC of 0.819 (95% CI 0.733, 0.904), which suggests that SWE might be a valuable diagnostic tool for SSc (Fig. 3).

We also evaluated the diagnostic value of SWE in enhancing the performance of classification criteria. The use of SWE-detected skin sclerosis instead of the original skin involvement assessment items in the 1980 ACR criteria significantly increased the sensitivity of the criteria for diagnosis (81.8 vs 72.7%,  $P = 0.031$ ), with no significant impact on specificity (85.2 vs 88.9%,  $P = 1.00$ ).

### Optimization of measuring sites

Measuring SWE at 17 sites, like mRSS, can be time consuming, taking ~15–20 min for image acquisition and analysis per patient for an experienced doctor, which could limit its clinical application owing to inconvenience. To optimize the method and select appropriate measurement sites, univariate logistic regression was applied to all 17 mRSS sites (Supplementary Table S3, available at *Rheumatology Advances in Practice* online). The results showed that bilateral thighs (left: odds ratio = 3.63,  $P = 0.051$ ; right: OR = 3.46,  $P = 0.058$ ) and bilateral calves (left: odds ratio = 1.98,  $P = 0.055$ ; right: odds ratio = 1.51,  $P = 0.188$ ) were not significant contributors to the diagnosis of the disease. Therefore, the sum of the SWE scores from the other 13 sites was used instead.

This reduced the measurement time to 10 min and showed the same diagnostic accuracy as using all 17 sites, as demonstrated by the comparable AUC and the same effect aiding in diagnosis (Supplementary Table S4 and Supplementary Fig. S1, available at *Rheumatology Advances in Practice* online).

Furthermore, the correlation with EScSG-DAI was also the same compared with all 17 sites, further confirming the reliability of using only these 13 sites ( $r = 0.698$ , 95% CI 0.549, 0.804, vs  $r = 0.707$ , 95% CI 0.561, 0.810,  $P = 0.920$ ).

### Discussion

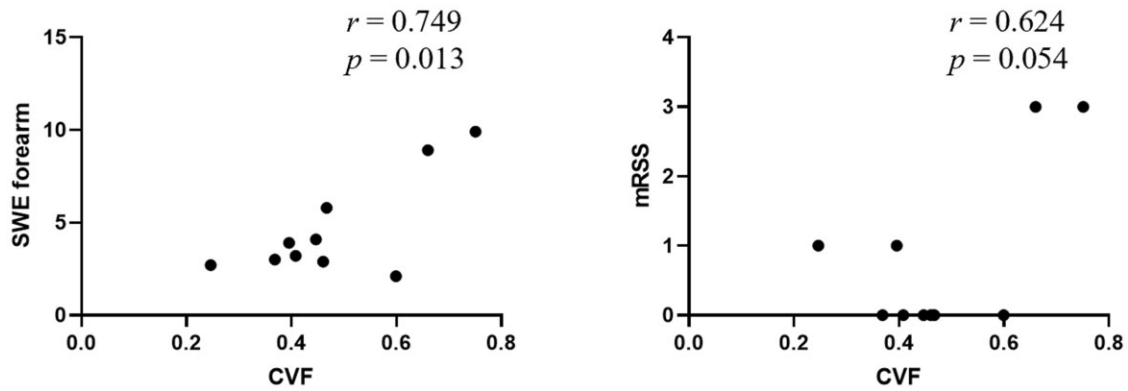
Our study showed that SWE is a valuable tool for detecting skin lesions and also subclinical skin involvement in SSc patients. It is a reliable quantitative measure for assessing collagen deposition and disease activity in SSc. Moreover, SWE holds promise as a diagnostic tool for SSc, because it differentiates SSc from healthy controls and other diseases effectively, while also improving the sensitivity of the 1980 ACR criteria for SSc.

Here, we found that SWE is effective in detecting skin sclerosis and also subclinical skin involvement in clinically uninvolved sites with an mRSS of zero, which is consistent with previous studies [11, 12, 18]. This suggests that SWE is a useful tool for the assessment of skin lesions in SSc and that it might have the potential to detect early changes in skin fibrosis that might not be apparent clinically. This expands our understanding of the diagnostic utility of SWE in SSc, because it might allow for earlier detection and monitoring of skin involvement in SSc patients, leading to improved disease management and better prognosis.

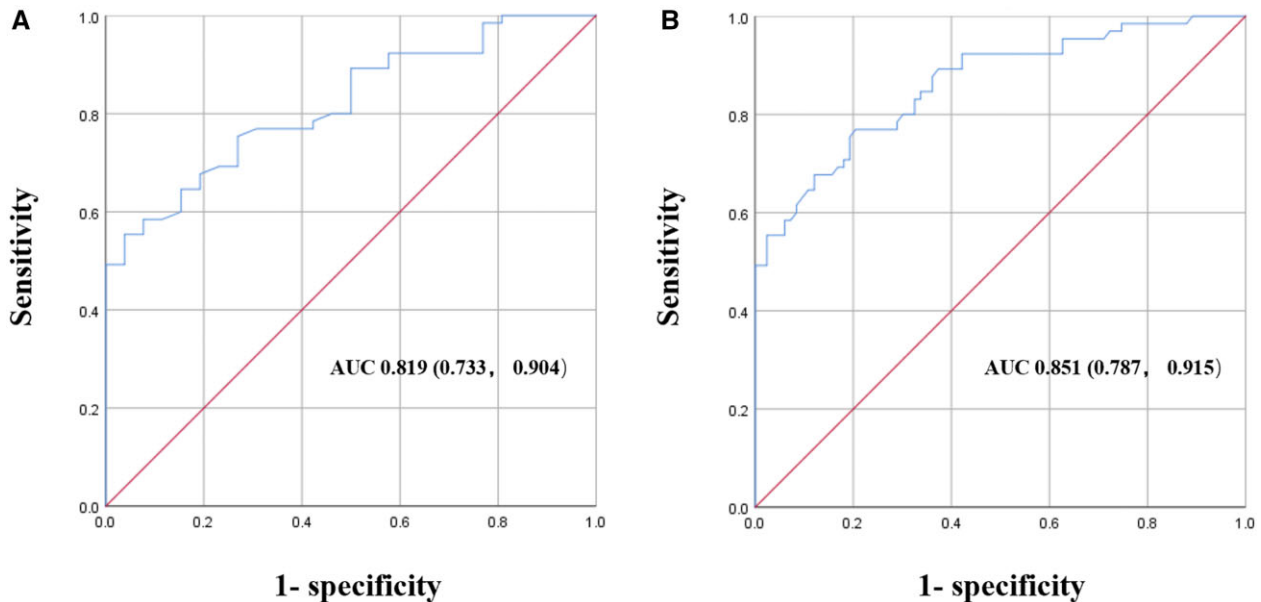
To validate SWE as an assessment tool for skin sclerosis and its correlation with collagen content, we investigated the relationship between SWE and skin pathology. We found a significant correlation between SWE values and skin collagen deposition, consistent with the findings of Flower *et al.* [19]. Moreover, compared with mRSS, SWE could evaluate skin collagen deposition and reflect the degree of skin sclerosis better. Chen *et al.* [11] demonstrated that skin thickness measured by US correlated well with that measured by histology, whereas no correlation was found between histological skin thickness and US-measured skin stiffness. Combining the results, it appeared that skin stiffness measured by US primarily reflected tissue collagen deposition rather than skin thickness. As a non-invasive assessment method, SWE has the advantage of being convenient and well tolerated by patients compared with skin biopsy. Through SWE evaluation, the degree of collagen deposition can be well reflected, which makes it a promising alternative to skin biopsy.

Additionally, it was found that SWE values showed a positive correlation with disease activity, as assessed by the EScSG-DAI, which includes evaluation items for skin and organ involvement, in addition to laboratory examinations. The involvement of skin is associated with the active stage of SSc, as reported previously [20]. The skin, being the most commonly affected and observable organ in SSc, provides a convenient window for evaluating fibrosis and disease activity in SSc patients. The assessment of SWE, as a reflection of collagen deposition in the skin, is a good tool for the assessment of skin and can reflect the stage of disease activity.

Early diagnosis is important for SSc, which allows the initiation of therapy before irreversible damage is established. This highlights the need for more sensitive and objective measures of skin involvement. Based on the results above, we explored the diagnostic value of SWE further and found that SWE could distinguish SSc from its mimics effectively, and the replacement of the skin assessment item with SWE-detected skin sclerosis in the original 1980 ACR classification criteria could increase the sensitivity of the diagnosis, with comparable specificity. These



**Figure 2.** Correlations between shear wave elastography and skin histology in a local site of the forearm. CVF: collagen volume fraction; mRSS: modified Rodnan skin score; SWE: shear wave elastography



**Figure 3.** The receiver operating characteristic curve of shear wave elastography in the diagnosis of SSc. **(A)** Comparison of 66 patients with SSc and 27 patients with an SSc-like disorder. **(B)** Comparison of 66 patients with SSc and 100 healthy controls. AUC: area under the receiver operating characteristic curve

findings support the potential of SWE as a tool for the early detection of skin lesions and aiding in diagnosis.

The 1980 ACR classification criteria provide a relatively simple diagnostic tool that uses only four evaluation items to classify SSc, which has the advantage of being simple and convenient in clinical practice. However, owing to its low sensitivity in early SSc, it is difficult to meet the needs of early diagnosis of SSc. The criteria include symptoms of sclerosis in the skin; however, early changes can occur before patients develop clinically observed skin thickening. SWE provides a convenient and rapid method for the assessment of skin sclerosis, thus assisting in the diagnosis of SSc. In future revisions of the classification criteria, the feasibility of incorporating SWE as one of the evaluation items could be considered, and modifications can be made to the items and weightings based on the 2013 ACR/EULAR criteria, in order to achieve a more sensitive and convenient diagnosis of SSc.

Application of SWE in all 17 mRSS sites was time-consuming, which might influence the use of SWE in clinical application;

therefore, we explored the reduction of detection sites. This study indicated that the detection of thighs and calves might not necessarily contribute to SSc diagnosis, and detection stiffness in these areas was inconvenient and time-consuming for exposure of the testing sites. Currently, skin US studies vary greatly in measurement sites, ranging from only fingers to all 17 mRSS sites, leading to huge heterogeneity. We have found, for the first time, that reducing the number of sites measured to 13 has the same effect as all 17 sites, thus achieving a win-win situation of both efficiency and effect.

To our knowledge, this is the first study to address the additional value of US variables contributing to diagnosis in SSc and to discuss the optimization of detection sites. However, there are a few limitations in our study. First, the sample size was limited by the relatively low prevalence of SSc. Nevertheless, to the best of our knowledge, this was the largest study to analyse the applicability of SWE in patients with SSc and with clinical manifestations similar to SSc. In the future, studies with a larger sample size and long-term follow-up are needed to confirm the results. Second, the frequency of

15 MHz of the detection probe was relatively low. However, high-frequency probes for SWE are not yet widely available [18, 19]. Compared with high-frequency US, the 15 MHz probe might offer better accessibility, making it more suitable for widespread use and clinical promotion. The frequency of the probe might have more influence on the detection of skin thickness rather than stiffness. Third, an assessment of reliability was not performed in our study.

In conclusion, this study underscores the diagnostic value of SWE as a substitute for skin sclerosis assessment and as an aid in early diagnosis of SSc. The non-invasive nature of SWE provides a more convenient and less painful method of evaluating skin lesions with good reliability in reflecting collagen deposition when compared with skin biopsy. Furthermore, reducing the number of measured sites from 17 to 13 did not affect the accuracy of SWE in assessing skin lesions, making it more efficient and effective for clinical practice.

### Supplementary material

Supplementary material is available at *Rheumatology Advances in Practice* online.

### Data availability

The data underlying this article will be shared on reasonable request to the corresponding author.

### Funding

This work was supported by the National Natural Science Foundation of China (no. 82271836).

*Disclosure statement:* The authors have declared no conflicts of interest.

### References

- Denton CP, Khanna D. Systemic sclerosis. *Lancet* 2017;390:1685–99.
- Volkman ER, Andréasson K, Smith V. Systemic sclerosis. *Lancet* 2023;401:304–18.
- van den Hoogen F, Khanna D, Fransen J *et al.* 2013 classification criteria for systemic sclerosis: an American College of Rheumatology/European League Against Rheumatism collaborative initiative. *Ann Rheum Dis* 2013;72:1747–55.
- Zheng B, Nevskaya T, Baxter CA *et al.*; Canadian Scleroderma Research Group. Changes in skin score in early diffuse cutaneous systemic sclerosis are associated with changes in global disease severity. *Rheumatology (Oxford)* 2020;59:398–406.
- Herrick AL, Assassi S, Denton CP. Skin involvement in early diffuse cutaneous systemic sclerosis: an unmet clinical need. *Nat Rev Rheumatol* 2022;18:276–85.
- Kaldas M, Khanna PP, Furst DE *et al.*; Investigators of the human recombinant relaxin and oral bovine collagen clinical trials. Sensitivity to change of the modified Rodnan skin score in diffuse systemic sclerosis—assessment of individual body sites in two large randomized controlled trials. *Rheumatology (Oxford)* 2009;48:1143–6.
- Czirják L, Foeldvari I, Müller-Ladner U. Skin involvement in systemic sclerosis. *Rheumatology (Oxford)* 2008;47(Suppl 5):v44–5.
- Taljanovic MS, Gimber LH, Becker GW *et al.* Shear-wave elastography: basic physics and musculoskeletal applications. *Radiographics* 2017;37:855–70.
- Santiago T, Santiago M, Coutinho M, Salvador MJ, Da Silva JAP. How much of skin improvement over time in systemic sclerosis is due to normal ageing? A prospective study with shear-wave elastography. *Arthritis Res Ther* 2020;22:50.
- Di Geso L, Filippucci E, Girolimetti R *et al.* Reliability of ultrasound measurements of dermal thickness at digits in systemic sclerosis: role of elastosonography. *Clin Exp Rheumatol* 2011;29:926–32.
- Chen C, Cheng Y, Zhu X *et al.* Ultrasound assessment of skin thickness and stiffness: the correlation with histology and clinical score in systemic sclerosis. *Arthritis Res Ther* 2020;22:197.
- Sobolewski P, Maślińska M, Zakrzewski J *et al.* Applicability of shear wave elastography for the evaluation of skin strain in systemic sclerosis. *Rheumatol Int* 2020;40:737–45.
- Yang Y, Yan F, Wang L *et al.* Quantification of skin stiffness in patients with systemic sclerosis using real-time shear wave elastography: a preliminary study. *Clin Exp Rheumatol* 2018;36(Suppl 113):118–25.
- Iagnocco A, Kaloudi O, Perella C *et al.* Ultrasound elastography assessment of skin involvement in systemic sclerosis: lights and shadows. *J Rheumatol* 2010;37:1688–91.
- Melsens K, De Keyser F, Decuman S *et al.* Disease activity indices in systemic sclerosis: a systematic literature review. *Clin Exp Rheumatol* 2016;34(Suppl 100):186–92.
- Xiang X, Yan F, Yang Y *et al.* Quantitative assessment of healthy skin elasticity: reliability and feasibility of shear wave elastography. *Ultrasound Med Biol* 2017;43:445–52.
- Masi AT. Preliminary criteria for the classification of systemic sclerosis (scleroderma). Subcommittee for scleroderma criteria of the American Rheumatism Association Diagnostic and Therapeutic Criteria Committee. *Arthritis Rheumatol* 1980;23:581–90.
- Santiago T, Alcaccer-Pitarch B, Salvador MJ *et al.* A preliminary study using virtual touch imaging and quantification for the assessment of skin stiffness in systemic sclerosis. *Clin Exp Rheumatol* 2016;34(Suppl 100):137–41.
- Flower VA, Barratt SL, Hart DJ *et al.* High-frequency ultrasound assessment of systemic sclerosis skin involvement: intraobserver repeatability and relationship with clinician assessment and dermal collagen content. *J Rheumatol* 2021;48:867–76.
- Martin P, Teodoro WR, Velosa AP *et al.* Abnormal collagen V deposition in dermis correlates with skin thickening and disease activity in systemic sclerosis. *Autoimmun Rev* 2012;11:827–35.