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Applicability of shear wave elastography for the evaluation of skin strain in systemic sclerosis

Piotr Sobolewski[1] · Maria Maślińska[2] · Jakub Zakrzewski[3] · Łukasz Paluch[3] · Elżbieta Szymańska[1] · Irena Walecka[1]

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Abstract

The assessment of skin fibrosis is vital for the diagnosis and monitoring of treatment in the systemic sclerosis (SSc)—a severe autoimmune disease. The elastography is a technique of skin fibrosis assessment through the evaluation of skin strain. We compared the efficacy of the shear wave elastography (SWE) and commonly used modified Rodnan skin score (RSS) in skin fibrosis assessment in SSc. The study included 40 SSc patients and 28 healthy individuals, with the exclusion of individuals with other skin/autoimmune diseases. Skin thickness using RSS and skin strain using SWE were assessed in the same 20 body localizations**.** Subjects' informed consent and the bioethics committee approval were obtained. Elastographic skin strain correlated positively with both partial and overall RSS values, with strong positive correlation ($r \geq 0.75$) for hands and fingers localizations in particular. In SSc patients with normal RSS values, the elastographic strain was significantly higher than in healthy controls. Elastographic strain of fingers' skin evaluated in SWE is highly accurate for distinguishing SSc patients (sensitivity 0.897–0.923, specificity 0.929–0.964, positive predictive value 0.946–0.973, negative predictive value 0.867–0.900). ESW results are substantially more reproducible than those of RSS examination (intraclass correlation coefficients: 0.987 vs. 0.941). The shear wave elastography is more reproducible and has higher sensitivity than RSS in the evaluation of skin condition in SSc, especially in case of changes non-detectable on physical evaluation, indicating it might become a useful tool in SSc diagnosis**.**

Keywords Shear wave elastography · Systemic sclerosis · Rodnan skin score

Introduction

Systemic sclerosis (SSc) is a chronic autoimmune disease with a highly heterogeneous symptomatology. At the transcriptional level, the upregulated collagen (mainly type I) production by skin fibroblasts causes the deposition of collagen fibers and components of the extracellular matrix and leads to the skin fibrosis, which is a hallmark of this autoimmune disease. Skin fibrosis is very often accompanied by internal organ fibrosis [1].

In line with the current American College of Rheumatology (ACR) and European League Against Rheumatism (EULAR) classification criteria, a skin thickening of the fingers extending proximal to the metacarpophalangeal joints (MCPs) is sufficient to be classified as SSc [2]. The degree of skin thickening in SSc is also an established prognostic factor, which can be used to assess the risk of internal organ involvement, determine the activity of the disease and evaluate treatment response [3–7]. Thus, assessment of skin thickness, which is a manifestation of fibrosis, is one of the essential tests performed in SSc [8].

Currently, the Rodnan skin score (RSS) is the gold standard in the clinical evaluation of skin thickness in SSc. The Rodnan skin score is calculated as a sum of skin thickness in 20 (classic RSS) or 17 (modified RSS) anatomical sites. The skin thickness in each site is estimated by palpation and expressed on a four-grade subjective scale, ranging from 0

✉ Maria Maślińska
maslinskam@gmail.com

[1] Department of Dermatology, Center of Postgraduate Medical Education, Central Clinical Hospital of Ministry of the Interior and Administration, Warsaw, Poland

[2] Early Arthritis Clinic, National Institute of Geriatrics, Rheumatology and Rehabilitation, Warsaw, Poland

[3] Department of Radiology, Center of Postgraduate Medical Education, Gruca Orthopedic and Trauma Teaching Hospital, Otwock, Poland

(no thickening) to 3 (severe thickening). The overall score can range from 0 to 60 (classic RSS) or to 51 (modified RSS) points [9]. Although RSS is commonly used in clinical trials and everyday practice, this method has certain disadvantages: a palpation of multiple cutaneous sites is time-consuming, the scale is subjective and the final result does not necessarily reflect a true activity of SSc in patients with skin atrophy [10, 11]. These shortcomings of the method stimulated a research into novel, more objective methods, that would facilitate the assessment of skin thickness in SSc [12].

With a progress in diagnostic imaging, researchers focused their interest on the applicability of ultrasonography for the evaluation of the severity and extent of skin fibrosis in SSc [13, 14]. The ultrasound elastography is an ultrasonographic technique suitable for the quantification of skin fibrosis, indicating not the thickening of the skin, but its strain—a parameter, which can be considered as a more detailed marker of a change of the skin structure [15]. The elastography, used increasingly in various medical disciplines, provides information about the tissue strain, which is independent of acoustic impedance and blood perfusion. The still strain elastography (SE) is a currently very popular elastographic technique, which examines the deformability of a given tissue during its controlled compression with an ultrasonographic transducer. The result of SE is expressed on a semiquantative color scale or as a strain ratio (SR) obtained by dividing the deformability of the tissue of interest by the deformability of a prespecified reference area. Another elastographic technique, used increasingly in clinical practice, is a shear wave elastography (SWE), which measures the speed at which the transducer-generated wave is propagated across the examined tissue. The results of SWE expressed as the value of Young modulus (in kPa) or shear wave velocity (in m/s), were shown to be more accurate and reproducible than those obtained during SE [16].

The liver elastography assessment determining the degree of organ fibrosis has already entered into a daily practice, while its use in case of other parenchymal organs, such as kidney, breasts, thyroid, salivary glands and lymph nodes is currently emerging [17, 18]. Obviously, it is important to validate the method and correctly interpret the results for each type of tissue.

Application of elastography in the evaluation of skin strain has been considered problematic for a long time, because of the specific structure of the target tissue and limitations of the ultrasonographic equipment [19, 20]. However, this has changed recently due to the implementation of high-frequency transducers designated for the examination of small, superficially located regions of interest (ROIs) [21, 22]. This opened perspectives for the use of an elastography in the evaluation of a skin strain in conditions associated with a chronic inflammation and fibrosis, such as SSc. The results of a few published studies using either SE or SWE suggest, that the elastographic strain of the skin of patients with SSc is higher than those of healthy controls and that, elastographic parameters are characterized by a high repeatability and reproducibility in this setting [23–27]. However, the above-mentioned studies included only small groups of patients (no more than 26) and in two of them [23, 25] the elastographic strain of the skin was expressed on semiquantative scales.

Objectives

The aim of this study was to verify the usefulness of SWE in the assessment of the skin fibrosis in SSc compared to the classic clinical evaluation of skin changes using RSS.

Materials and methods

The study was conducted between October 31, 2018 and February 23, 2019 at the Department of Dermatology.

Study participants

Patients with a confirmed diagnosis of systemic sclerosis [both diffuse (dSSc) and limited (lSSc) type] based on the ACR and EULAR classification criteria were included into the study [2].

There were 40 SSc patients 34 (85.0%) female (F) and 6 (15.0%) male (M); F/M ratio 4:1; aged between 23 and 77 years (mean 44.4 ± 13.5 years). There were 29 (72.5%) lSSc and 11 (27.5%) dSSc patients. The median time elapsed since the diagnosis of SSc was 9 years (range 0–30 years). The control group consisted of 28 healthy sex- and age-matched individuals, 23 (82.1%) female and 5 (17.9%) male, aged between 22 and 71 years old (mean 44.9 ± 14.4 y.o.).

All examined SSc patients ($n = 40$;100.0%) and 25 (89.3%) healthy subjects used their right hand as a dominant extremity.

In both groups the co-existence of other autoimmune or skin disease was assumed as the exclusion criterion, to eliminate the influence of other phenomena on the elastographic assessment of the skin.

The protocol of the study was approved by the Institutional Bioethics Committee. All patients and healthy volunteers have given their informed consent for participation in the study.

Skin assessment

The skin fibrosis was assessed via means of evaluating the skin thickness with a classic RSS and assessing the skin strain with the shear wave elastography.

The skin thickness in patients with SSc was expressed as classic RSS, based on the palpation of 20 cutaneous sites:

face, neck, anterior chest, abdomen, upper and lower back, right and left upper arm, right and left forearm, right and left hand, finger of the right and left hand, right and left thigh, right and left leg, right and left foot. The results were scored as described elsewhere [9]. To verify the reproducibility of the results, RSS values were determined by two independent physicians.

All the anatomical sites used for the RSS evaluation were also assessed with SWE. Each anatomical site was examined separately, with the individual in a supine or prone position. Sonographic scans were obtained with Toshiba iAplio 900 ultrasonograph (2019 Malaysia) with a 5–18 MHz transducer. Elastographic results (strain) were expressed with the Young's modulus value (kPa).

During the examination, the skin was covered with a 10-mm hydrogel pad and a thick layer of gel. The transducer was placed perpendicularly to the skin, and transverse scans were obtained. Upon visualization of the area of interest, SWE was performed, after stabilizing the elastographic image. The region of interest (ROI) was placed in the center of the screen, to cover approximately 80% of the examined structure.

Three measurements were taken for each ROI, and the average result was recorded. To verify the reproducibility of the results, the examination was conducted by two independent operators with a 5-year experience in elastographic studies.

Both palpation and elastographic examinations were carried out between 9:00 AM and 3:00 PM, in a room with an ambient temperature (20–25 °C), with the patient lying in a supine or prone position.

Statistical analyses

The normal distribution of continuous variables was verified with the Shapiro–Wilk test. Statistical characteristics of continuous variables were presented as arithmetic means and their standard deviations (SD) or medians and ranges. The significance of between-group differences in the values of quantitative parameters was verified with Mann–Whitney *U* test. The direction and power of associations between pairs of quantitative variables were estimated on the basis of Spearman's rank correlation coefficients (*r*). The diagnostic accuracy of selected elastographic parameters as the predictors of SS was verified on receiver operating characteristic (ROC) analysis, based on their sensitivity, specificity, positive (PPV) and negative predictive value (NPV), and AUC along with its 95% confidence interval (95% CI). The reproducibility of RSS values and elastographic parameters obtained by two independent researchers was estimated on the basis of intraclass correlation coefficients (ICC). All calculations were carried out with Statistica 13.3 package (StatSoft, United States), statistical significance was set up $p \leq 0.05$.

Results

Compared with healthy controls, patients with SSc presented a significantly higher elastographic strain of the skin in all examined sites except for the anterior chest, abdomen, upper and lower back (Table 1).

The body mass index (BMI) of patients with SSc ranged between 16.4 and 29.9 kg/m^2 (mean 24.1 ± 3.4 kg/m^2). The BMI was shown to correlate inversely with the elastographic strain of the skin on the neck, anterior chest, abdomen, right and left hand. Moreover, statistically significant inverse correlations were observed between the age of SSc patients and elastographic strain of the skin on the anterior chest, abdomen, right and left upper arms, and right forearm. No significant correlations were found between the elastographic strain of the skin and the time elapsed since the diagnosis of SSc.

Overall RSS values for the patients studied ranged between 0 and 20 points (median 5.25 points). There were no significant correlations between the strain of the skin on the anterior chest, abdomen, right and left upper arm, right forearm, left thigh and left leg and the overall RSS value. The elastography results for other body regions correlated positively with the overall RSS values, with the strong correlations ($r = 0.75$and higher) found for the right and left hand and fingers of both hands. Moreover, the elastographic strain of the skin in all sites—except for the abdomen, upper back, left upper arm, and both thighs—showed moderately strong or strong correlations with partial Rodnan scores for the same sites. Again, the highest values of the correlation coefficients ($r = 0.8$ and higher) were found between the strain and the thickness of the skin of the right and left hand and fingers of both hands. In Table 2 the correlations between SWE-determined elastographic skin strain values, age, BMI, time elapsed since the SSc diagnosis, overall RSS and partial Rodnan scores for the same anatomical site were presented.

The elastographic evaluation of the skin strain in patients in whom the skin thickness in a given site was considered normal (partial Rodnan score 0) was compared with the elastographic strain of the corresponding sites of healthy controls. In 10 out of 20 examined sites (face, neck, left upper arm, right and left forearm, finger of the left hand, right and left thigh, right leg and left foot) of SSc patients, elastographic strain of the skin, which thickness was classified on subjective evaluation as normal, turned out to be significantly higher than the skin strain of corresponding sites in healthy controls, whereas the strain in one site (anterior chest) was significantly lower than in the control group (Table 3).

Table 1 Statistical characteristics of SWE-determined elastographic strain of the skin in various anatomical sites in patients with SSc and healthy controls

Site	Systemic sclerosis ($n=40$)			Healthy controls ($n=28$)			p
	Median (kPa)	Mean (kPa)	SD (kPa)	Median (kPa)	Mean (kPa)	SD (kPa)	
Face	19.475	23.71	11.91	14.875	15.02	4.11	< 0.001
Neck	17.30	19.02	8.96	11.625	13.16	4.19	0.002
Anterior chest	16.50	20.11	13.00	20.350	21.62	5.02	0.563
Abdomen	13.725	16.02	8.39	13.025	13.34	4.12	0.124
Upper back	16.20	19.39	11.28	18.025	18.95	5.68	0.851
Lower back	14.20	17.95	12.13	13.775	14.04	3.38	0.103
Right upper arm	22.90	27.82	17.77	20.775	20.26	5.86	0.034
Right forearm	30.65	36.32	20.65	23.70	24.05	6.00	0.003
Right hand	45.70	49.10	25.37	27.70	28.28	7.02	< 0.001
Right hand1	2.87	2.89	1.75	1.33	1.35	0.40	< 0.001
Right hand2	2.557	2.86	1.65	1.55	1.60	0.57	< 0.001
Right-hand finger	58.00	68.87	30.63	29.70	28.34	6.87	< 0.001
Right-hand finger[a]	3.265	4.15	2.43	1.235	1.36	0.41	< 0.001
Right-hand finger[b]	3.649	4.00	2.00	1.558	1.60	0.57	< 0.001
Left upper arm	24.50	26.79	11.72	18.525	19.22	4.20	0.002
Left forearm	32.70	37.42	20.42	24.025	25.13	5.76	0.003
Left hand	41.05	47.98	26.35	26.35	27.08	7.17	< 0.001
Left hand[a]	2.556	2.75	1.54	1.268	1.28	0.34	< 0.001
Left hand[b]	2.509	2.77	1.53	1.356	1.52	0.56	< 0.001
Left-hand finger	64.10	63.65	23.69	27.525	28.19	6.75	< 0.001
Left-hand finger[a]	3.617	3.81	1.88	1.226	1.38	0.48	< 0.001
Left-hand finger[b]	3.253	3.78	1.83	1.532	1.60	0.58	< 0.001
Right thigh	16.95	19.02	6.84	14.375	15.24	4.23	0.012
Right leg	38.625	45.13	21.14	33.90	34.30	9.02	0.013
Right foot	41.625	50.37	26.75	30.65	33.94	13.37	0.004
Left thigh	16.90	18.12	7.33	13.825	14.96	4.30	0.045
Left leg	35.60	46.17	24.63	33.25	33.56	7.75	0.011
Left foot	43.60	52.42	25.90	33.55	33.99	11.92	0.001

[a]Values normalized by dividing by the elastographic strain of the chest skin

[b]Values normalized by dividing by the elastographic strain of the or upper back skin

The elastographic strain of the skin of the right and left hand and fingers of both hands were subjected to ROC analysis as potential predictors of SSc. The cut-off values identified in ROC analysis, together with the parameters of a diagnostic accuracy and areas under curve (AUC) are shown in Table 4 and Fig. 1.

The diagnostic accuracy of the elastographic parameters for the right- and left-hand fingers turned out to be substantially higher than in the case of the elastographic strains for the right and left hand. Similar results of ROC analysis were also obtained when the values of elastographic strains of the skin of hands and fingers were normalized by dividing them by the value of strains of skin covering the chest and upper back; mean values of the normalized elastographic strains in patients and controls are shown in Table 1 and parameters of their diagnostic accuracy are summarized in Table 4.

Comorbidities, such as type 2 diabetes mellitus/disorders of carbohydrate metabolism ($n=5$), ischemic heart disease ($n=2$), myocardial infarction ($n=2$), arterial hypertension ($n=11$), pulmonary complications ($n=23$) and complications within the central nervous system ($n=2$), were present in a total of 27 (67.5%) patients with SSc. Patients with and without concomitant diseases did not differ significantly in terms of their elastographic parameters, except for the elastographic strain of the skin on the left upper arm, significantly lower in persons with comorbidities (Table 5).

The analysis of ICCs demonstrated that the reproducibility of the SWE results was higher than that of RSS, with the ICC values of 0.987 and 0.941, respectively.

Table 2 Spearman's coefficients of rank correlation (r) between SWE-determined elastographic strain of the skin and: age, BMI, time elapsed since the SSc diagnosis, overall RSS and partial Rodnan scores established for the same anatomical site

Site	Age (years)		BMI (kg/m^2)		Time from diagnosis (years)		Overall RSS (pts)		Rodnan score for the same region (pts)	
	r	p	r	p	r	p	r	p	r	p
Face	− 0.078	0.630	− 0.111	0.494	− 0.048	0.774	0.385	0.014	0.764	< 0.001
Neck	− 0.105	0.519	− 0.356	0.024	0.070	0.671	0.494	0.001	0.592	< 0.001
Anterior chest	− 0.419	0.008	− 0.319	0.048	− 0.314	0.055	0.204	0.213	0.564	< 0.001
Abdomen	− 0.318	0.046	− 0.468	0.002	0.046	0.779	0.187	0.249	0.271	0.091
Upper back	0.079	0.632	− 0.044	0.789	− 0.279	0.090	0.363	0.023	0.274	0.092
Lower back	− 0.042	0.801	− 0.024	0.887	− 0.133	0.426	0.475	0.002	0.525	0.001
Right upper arm	− 0.357	0.026	− 0.252	0.121	0.043	0.800	0.226	0.167	0.462	0.003
Right forearm	− 0.319	0.048	− 0.238	0.144	− 0.091	0.588	0.087	0.597	0.453	0.004
Right hand	− 0.128	0.438	− 0.322	0.046	− 0.072	0.666	0.759	< 0.001	0.869	< 0.001
Right-hand finger	0.039	0.813	− 0.196	0.231	0.064	0.701	0.869	< 0.001	0.903	< 0.001
Left upper arm	− 0.476	0.002	− 0.243	0.137	− 0.153	0.358	0.214	0.192	0.274	0.092
Left forearm	− 0.258	0.113	− 0.240	0.141	− 0.132	0.429	0.347	0.031	0.441	0.005
Left hand	− 0.196	0.232	− 0.399	0.012	0.070	0.674	0.75	< 0.001	0.828	< 0.001
Left-hand finger	− 0.035	0.831	− 0.306	0.058	0.106	0.528	0.776	< 0.001	0.823	< 0.001
Right thigh	− 0.071	0.663	− 0.063	0.698	− 0.112	0.499	0.341	0.031	n/a	
Right leg	0.041	0.800	− 0.091	0.577	0.203	0.216	0.366	0.020	0.349	0.027
Right foot	0.112	0.491	0.053	0.744	0.090	0.586	0.362	0.022	0.704	< 0.001
Left thigh	− 0.012	0.944	− 0.078	0.636	0.046	0.784	0.019	0.910	n/a	
Left leg	− 0.007	0.965	− 0.166	0.314	0.202	0.225	0.288	0.075	0.528	0.001
Left foot	0.180	0.272	0.097	0.557	0.062	0.711	0.568	< 0.001	0.634	< 0.001

n/a not applicable, partial Rodnan scores in all patients equaled 0

Table 3 Statistical characteristics of SWE-determined elastographic strain of the skin in various anatomical sites of healthy controls and patients with SSc, in whom skin thickness in a given site was considered normal (partial Rodnan score 0),

Site	Systemic sclerosis/partial Rodnan score = 0				Healthy controls				p
	n	Median (kPa)	Mean (kPa)	SD (kPa)	n	Median (kPa)	Mean (kPa)	SD (kPa)	
Face	28	18.35	18.08	4.42	28	14.875	15.02	4.11	0.010
Neck	34	16.975	16.36	4.07	28	11.625	13.16	4.19	0.003
Anterior chest	34	15.30	16.13	4.93	28	20.350	21.62	5.02	< 0.001
Abdomen	39	13.70	15.07	5.95	28	13.025	13.34	4.12	0.190
Upper back	38	16.20	17.87	6.18	28	18.025	18.95	5.68	0.470
Lower back	35	13.05	14.29	4.44	28	13.775	14.04	3.38	0.810
Right upper arm	36	22.075	23.36	8.79	28	20.775	20.26	5.86	0.113
Right forearm	33	28.45	31.22	13.22	28	23.70	24.05	6.00	0.010
Right hand	17	26.75	29.14	8.21	28	27.70	28.28	7.02	0.710
Right-hand finger	5	30.80	33.77	4.77	28	29.70	28.34	6.87	0.102
Left upper arm	38	24.425	25.63	9.35	28	18.525	19.22	4.20	0.001
Left forearm	30	28.725	30.69	9.81	28	24.025	25.13	5.76	0.012
Left hand	16	24.975	28.74	9.62	28	26.35	27.08	7.17	0.517
Left-hand finger	5	29.15	36.83	11.60	28	27.525	28.19	6.75	0.025
Right thigh	40	16.85	19.02	6.84	28	14.375	15.24	4.23	0.012
Right leg	38	37.525	42.70	18.36	28	33.90	34.30	9.02	0.029
Right foot	27	33.05	38.29	19.96	28	30.65	33.94	13.37	0.345
Left thigh	39	16.90	18.12	7.33	28	13.825	14.96	4.30	0.045
Left leg	34	34.975	39.42	16.12	28	33.25	33.56	7.75	0.083
Left foot	30	39,075	43.03	20.10	28	33,55	33.99	11.92	0.044

Table 4 The parameters of diagnostic accuracy of SWE examination in distinction between SSc patients and healthy controls, presented for selected anatomic areas

Parameter	Cut-off value (kPa)	Sensitivity	Specificity	PPV	NPV	AUC
Right hand	37.90	0.590	0.929	0.920	0.619	0.752 (0.637–0.868)
Right-hand finger	38.50	0.923	0.964	0.973	0.900	0.961 (0.918–1.000)
Left hand	39.35	0.590	0.964	0.958	0.628	0.758 (0.644–0.873)
Left-hand finger	40.40	0.897	0.929	0.946	0.867	0.948 (0.897–0.999)
Right hand[a]	1.702	0.744	0.857	0.879	0.706	0.813 (0.710–0.917)
Right-hand finger[a]	2.240	0.872	1.000	1.000	0.848	0.945 (0.886–1.000)
Left hand[a]	1.628	0.821	0.893	0.914	0.781	0.851 (0.749–0.953)
Left-hand finger[a]	1.922	0.923	0.821	0.878	0.885	0.926 (0.858–0.994)
Right hand[b]	1.850	0.744	0.750	0.806	0.677	0.773 (0.661–0.885)
Right-hand finger[b]	2.277	0.872	0.893	0.919	0.833	0.911 (0.839–0.983)
Left hand[b]	1.711	0.744	0.750	0.806	0.677	0.755 (0.637–0.872)
Left-hand finger[b]	2.179	0.872	0.857	0.895	0.828	0.903 (0.828–0.979)

[a]Parameters normalized by dividing by the elastographic strain of the chest skin

[b]Parameters normalized by dividing by the elastographic strain of the upper back skin

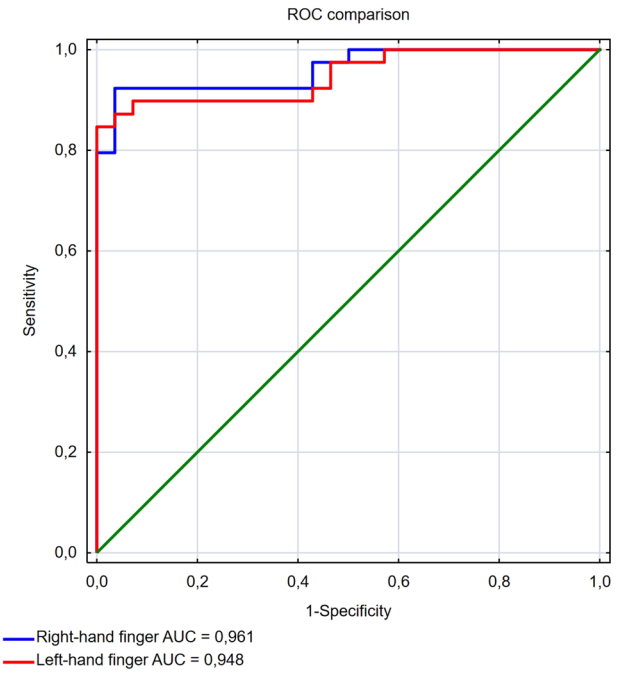

Fig. 1 The ROC comparison of the right and left hand SWE assessment results, together with the parameters of diagnostic accuracy and areas under curve (AUC)

Discussion

The established diagnostic value and prognostic significance of skin fibrosis in SSc justify a search for more objective methods to evaluate skin status in patients with this condition. The present study demonstrates, that SWE should be considered as a one of such methods.

Our comparative analysis showed that, aside from a few anatomical regions (anterior chest, upper and lower back, abdomen), the elastographic strain of the skin in patients with SSc was significantly higher than that in healthy controls. This observation is consistent with the results of previous studies using elastography, whether SWE or SE, evaluating the skin strain in patients with SSc [23–27].

The lack of statistically significant between-group differences in the elastographic strain of the skin in some sites might be associated with the fact, that in the case of two of such areas (anterior chest, abdomen), the results of SWE showed moderately strong inverse correlations with age and BMI of the studied patients. Hence, it cannot be excluded that those two variables might act as confounders during the comparative analysis. An age-progressive decrease in the skin strain in some anatomical regions, e.g. face, and an inverse correlation between elastographic parameters of the skin and BMI were also documented in some previous SWE-based studies of healthy persons [28–31]. Aside from potential confounding effects of age and BMI, another reason behind the lack of significant between-group differences in the elastographic strain of the abdomen, anterior chest and back skin might be a less frequent occurrence of skin thickening in these regions. This explanation is supported by the distribution of Rodnan scores in our SSc patients; partial Rodnan score considered normal (pRSS = 0) was found on anterior chest wall in $n = 34$, on abdomen in $n = 39$, upper back $n = 38$ and lower back $n = 35$ of patients.

This finding is consistent with the results of previous studies in which the involvement of the skin in those anatomical areas was observed less often than in the case of the face and distal parts of the limbs [32].

The analysis of correlation of the obtained data demonstrated strong or moderately strong associations between

Table 5 Statistical characteristics of SWE-determined elastographic strain of the skin in various anatomical sites in SSc patients with comorbidities and without

Site	Comorbidities ($n=27$)			No comorbidities ($n=13$)			p
	Median (kPa)	Mean (kPa)	SD (kPa)	Median (kPa)	Mean (kPa)	SD (kPa)	
Face	20.45	24.02	11.37	19.30	23.06	13.42	0.815
Neck	17.50	19.30	9.80	17.10	18.44	7.21	0.781
Anterior chest	16.10	19.06	10.69	16.50	22.22	17.03	0.481
Abdomen	14.70	15.16	4.74	11.70	17.82	13.22	0.355
Upper back	16.20	19.75	12.72	16.60	18.67	8.04	0.782
Lower back	15.05	15.84	7.00	13.05	22.16	18.30	0.127
Right upper arm	21.55	26.56	18.07	25.80	30.34	17.60	0.538
Right forearm	26.47	34.01	19.07	34.25	40.94	23.62	0.330
Right hand	42.72	48.46	27.09	47.40	50.39	22.49	0.826
Right-hand finger	59.55	72.27	29.24	46.85	62.09	33.40	0.335
Left upper arm	20.70	24.07	9.64	26.75	32.22	13.90	0.039
Left forearm	31.67	35.14	17.20	33.30	41.98	25.89	0.330
Left hand	44.92	47.04	25.52	40.75	49.86	28.92	0.757
Left-hand finger	65.60	65.38	22.53	59.70	60.20	26.47	0.528
Right thigh	16.85	18.23	6.45	18.20	20.67	7.59	0.297
Right leg	33.80	44.81	23.46	43.25	45.80	16.12	0.892
Right foot	50.90	53.14	27.63	34.00	44.62	24.86	0.352
Left thigh	16.60	18.42	7.79	17.25	17.53	6.55	0.726
Left leg	32.80	43.63	25.84	42.75	51.27	22.09	0.368
Left foot	51.43	55.79	27.05	40.05	45.70	22.94	0.257

most elastographic strain values and either partial Rodnan scores or overall RSS. The strongest correlations were observed in the case of the skin covering distal segments of the limbs, especially hands and fingers. The lack of statistically significant correlations between the elastographic strain of the skin and Rodnan scores seen in some of the other anatomical areas might be associated with the absence of skin lesions severe enough to be detected by clinical palpation only. This hypothesis seems to be confirmed by the comparison of the elastographic strains in healthy controls and SSc patients whose skin thickness in various sites was classified as normal (partial Rodnan scores 0). Significant between-group differences in the elastographic strain of the skin were found in 4 out of 7 sites in which this parameter did not correlate with the overall RSS, as well as in 3 out of 5 areas in which no associations were observed between the elastographic parameters and partial Rodnan scores. Although on clinical palpation the thickness of their skin was considered normal, patients with SSc presented significantly higher values of elastographic parameters than the controls in all but one anatomical region mentioned above. This implies, that SWE might provide greater sensitivity in the identification of less advanced skin fibrosis, non-detectable on subjective palpation. An opposite result in the case of the anterior chest might be associated with a confounding effect of at least two factors, age and BMI, on the elastographic strain of the skin in this region.

Another argument for the usefulness of SWE in SSc in the evaluation of skin fibrosis is a greater reproducibility of the elastographic results as compared to RSS. The evidence from sparse previous studies also suggests that the reproducibility of SWE results in patients with SSc can be very high [24–27].

Taken altogether, the results of the present study imply, that the evaluation of skin fibrosis with RSS might be, to a various extent, replaced or at least complemented by the assessment of skin strain by means of SWE. As ROC analysis reveals, the laborious and time-consuming determination of RSS, results of which are subjective and thus—not necessarily accurate, could be substituted by the measurement of a single elastographic parameter, the strain of the finger skin. This variable showed the strongest correlations with either overall RSS or partial Rodnan scores. Additionally, elastographic results concerning finger skin remained independent of two potential confounding factors identified in this study: the age and BMI. Furthermore, ROC analysis demonstrated, that values of the elastographic strain of the finger skin, provided an excellent (~90–95%) accuracy in distinguishing between patients with SSc and healthy controls. However, a question arises whether the strain of the skin in this site, distal from the MCP and hence, not satisfying the ACR and EULAR classification criteria, might be considered a marker of SSc. These concerns could be resolved by a case–control study involving a larger number of patients with various stages of SSc. Such a study might also explain whether the

elastographic strain of the finger skin correlates not only with the presence of the disease, but also with its activity, and hence, with the prognosis.

An alternative solution could be the development of an elastographic equivalent of RSS, being a sum of the elastographic strains of the skin in all examined sites. However, development of such a scoring system would require the identification of the reference ranges for the skin strain in various anatomical regions, whenever necessary corrected for the age, body weight and other confounders, as well as the determination of cut-off values accurately distinguishing between the presence of SSc and lack thereof. While with no doubt time-consuming, this task seems to be manageable, especially in the era of the increasing availability of ultrasonographic equipment and the growing possibility of international cooperation and big data analysis.

The primary potential limitation of this study is a relatively small the size of the SSc group ($n = 40$), at least from the perspective of statistical power. Nevertheless, to the best of our knowledge, this was the largest study to analyze the applicability of elastography in the evaluation of a skin strain in patients with this condition; previous studies dealing with the problem in question included between one [27] and 26 patients with SSc [26]. Secondly, our group was relatively heterogeneous in terms of the time elapsed since the SSc diagnosis; although this parameter did not correlate significantly with the elastographic strain of the skin, we still cannot conclude unequivocally that SWE is suitable for the evaluation of patients with SSc of any stage, including those with skin atrophy. The same also refers to the medication history of our patients, which was too heterogeneous to be considered in statistical analysis. Finally, it needs to be stressed, that we tested SWE in comparison to classic RSS rather than against the modified scale—as in previous studies. Nevertheless, the results are unlikely to change after the exclusion of the three regions, that are not considered in the modified RSS (neck, upper and lower back), as these sites are rarely involved during the course of SSc.

Conclusions

This study showed, that, in comparison to healthy subjects, patients with SSc presented a significantly higher elastographic strain of the skin determined by means of SWE. Considering the strong correlation of elastographic parameters with RSS, their high reproducibility and excellent diagnostic accuracy, sensitivity and specificity, SWE has a potential to become a primary test to evaluate skin condition in patients with SSc, especially those presenting subtle fibrotic changes of the skin, non-detectable on clinical palpation. This method seems to have superiority over RSS also because of its objectivity in the analysis of tissue parameters.

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Compliance with ethical standards

Conflict of interest The authors have declared no conflicts of interest.

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