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ORIGINAL RESEARCH

Recommendations for the execution and reporting of skin ultrasound in systemic sclerosis: an international collaboration under the WSF skin ultrasound group

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ABSTRACT

Objective Ultrasound is a promising tool to foster much-needed improvement of skin assessment in systemic sclerosis (SSc). Our aim was to develop evidence and expert opinion-based recommendations to promote the standardisation and harmonisation of technical execution and reporting of skin ultrasound studies in SSc.

Methods A multidisciplinary task force of 16 members from five European countries and Japan was convened under the auspices of World Scleroderma Foundation. First, a systematic literature review (SLR) was performed. Then, each member proposed and formulated items to the overarching principles, recommendations and research agenda. Two rounds of mails exchange for consensus as well as an on-line meeting were performed to debate and refine the proposals. Two Delphi rounds of voting resulted in the final recommendations. Levels of evidence and strengths of recommendations were assigned, and task force members voted anonymously on the level of agreement with each of the items.

Results Five overarching principles and seven recommendations were developed, based on an SLR and expert opinion, through consensus procedures. The overarching principles highlight the promising role of skin ultrasound in SSc assessment, the need for standardisation of technical aspects, sufficient training and adequate equipment. The recommendations provide standards for the execution and reporting of skin ultrasound in SSc. The research agenda includes the need for more research into unmet needs according to Outcome Measures in Rheumatology Algorithm requirements.

Conclusion These are the first recommendations providing guidance on the execution and reporting of skin ultrasound in SSc patients, aiming at improving the interpretability, reliability and generalisability of skin ultrasound, thus consolidating its role in research and practice.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Ultrasound and elastography are promising tools to foster much-needed improvement of skin assessment in systemic sclerosis (SSc). However, there is a remarkable methodological heterogeneity and lack of information in a variety of technical aspects in skin ultrasound studies.

⇒ The role of skin ultrasound in clinical practice and research is not yet established.

WHAT THIS STUDY ADDS

⇒ These are the first recommendations focused on the execution and reporting of skin ultrasound in SSc to promote standardisation and harmonisation of the technical procedures.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ These recommendations aim to improve interpretability, reliability and generalisability of skin ultrasound study results.

⇒ Well-designed observational studies and randomised clinical trials are now required aiming at providing resolution to research agenda.

INTRODUCTION

Skin involvement is a cardinal feature for the diagnosis and prognosis of systemic sclerosis (SSc), and its extent and rate of progression are associated with visceral involvement, functional disability and survival.[1 2] The modified Rodnan Skin Score[3] (mRSS), a semiquantitative score based on clinical palpation, is the current gold standard for skin assessment in clinical practice and research.[3 4] However, it has limited sensitivity

to change, hampering its use in the investigation of new treatments for SSc.[5 6]

The use of ultrasound for skin assessment in SSc has been extensively investigated over the last four decades.[7 8] Ultrasound may have some advantages over mRSS,[7–9] including its higher intrarater and inter-rater reproducibility and sensitivity to change.[10] Moreover, high-frequency ultrasound can identify early subclinical skin involvement in areas with a normal mRSS.[11 12] Moreover, skin ultrasound has experienced major technological improvements, including higher-frequency probes for B-mode,[13 14] new imaging modalities, such as shear-wave elastography[15] and new models for the analysis of spatial distribution of image features.[13] Shear-wave elastography represents an advance on previous generations of 'compression' (or strain) elastography as the shear-wave is generated within the transducer head rather than by the operator. Thus, this technique is less operator-dependent, and allows the use of small adjustable sampling gates to assess discrete anatomical structures, such as skin layers.[7 8] Despite these advances, the role of skin ultrasound in clinical practice and research is not yet established.

A recent systematic literature review (SLR) has summarised all available evidence on the use of ultrasound and elastography to assess skin involvement in SSc, according to the Outcome Measures in Rheumatology (OMERACT) filter selection algorithm (OFISA).[9] This review identified significant knowledge gaps in the three pillars of evidence: truth, discrimination and feasibility. For different reasons, none of the ultrasound domains (ie, thickness, echogenicity, stiffness) fully satisfied the OMERACT criteria. Additionally, this SLR[9] confirmed a remarkable methodological heterogeneity and frequent lack of information in a variety of technical aspects, including equipment, settings, standard images, scoring systems and skin sites examined. These aspects preclude direct comparisons and combination of ultrasound studies, thus undermining the evidence of validity, according to OFISA. Standardisation of procedures is, therefore, a crucial step to further develop and consolidate the contribution of skin ultrasound evaluation in SSc.

Complete and accurate reporting is required to detect potential biases in the studies (internal validity) and to assess the generalisability and applicability of the results (external validity). Recently, EULAR developed comprehensive recommendations for the reporting of ultrasound studies in rheumatic and musculoskeletal diseases.[16] This present work is a product of the World Scleroderma Foundation Skin Ultrasound Working Group which aims at filling that gap developing recommendations on skin ultrasound. Indeed, the objective of the working group is also to promote the standardisation and harmonisation of the technical procedures to improve application of skin ultrasound in SSc studies, as well as to propose a research agenda for future development.

METHODS

We followed the methodology proposed in the updated EULAR standardised operating procedures for the production of recommendations.[17] The task force consisted of 16 individuals from 5 European countries and from Japan, including 11 rheumatologists—senior or first authors of published studies in skin ultrasound and with clinical expertise in SSc; 2 health professionals—1 podiatrist with expertise in SSc and ultrasound (LG) and 1 engineer with more than 10 years' experience in skin ultrasound (MW); 1 methodologist with accredited experience in this field (EJFS); 1 rheumatologist with expertise in musculoskeletal ultrasound and methodology of imaging (MAD'A) and 1 patient research partner (LJR).

The work was developed in two steps

Step 1: systematic review of the literature

On 22 January 2021, a first on-line meeting was performed to define the focus of the task force and the research questions for the SLR. The SLR was performed by a rheumatologist (TS) under the supervision of the methodologist (EJFS) and the steering group. A draft of the SLR results and the resulting material circulatedonline supplemental table circulatedvarious times through the group until a consensus was reached and the report submitted.

Step 2: formulation and consensus

The SLR[9] informed the recommendations. Initially, each group member provided at least three items for overarching principles, recommendations or research agenda. The first author collected, combined and rephrased all items into a draft proposal of overarching principles, recommendations and research agenda, which were sent by email to the group for feedback and improvement. An updated version of this work was finally sent to all task force members to vote on the acceptance of each statement. Statements achieving at least 75% approval were considered approved.[17] The remaining ones were discussed and amended in the second online meeting (26 January 2022) and again to vote during the meeting. An agreement of 66% was required for approval in this second round. If a third one was needed, 50% agreement was sufficient for approval. Notes were taken to capture the content of the discussions and inform the comments accompanying the individual items below.

After conclusion of voting process, an anonymised email-based voting, on the level of agreement among the task force members, was performed using a 0–10 scale (with 10 meaning full agreement). The mean and SD of the level of agreement, as well as the percentage of task force members with an agreement ≥8 were presented. Of note, 100% of the members participated in the ballots at the two voting processes.

The level of evidence and strength of recommendations was determined for each item of the recommendations, according to the Oxford evidence-based medicine categorisation.[18] In the absence of empirical evidence, recommendations

regarding the reporting of studies were based on consensus among the task force members. It was agreed not to attribute a level of evidence for these items.

Target audience and when to apply the recommendations

The target audience of this work comprises researchers participating in, reporting on or appraising observational and interventional studies using skin ultrasound evaluation in SSc. Each of the seven recommendations should be considered an essential component of the execution and reporting of skin ultrasound studies in SSc, regardless of their specific purpose.

The target population comprises individuals with very early diagnosis of SSc, early/established SSc (including diffuse and limited cutaneous subsets) as well as those with suspected/undifferentiated connective tissue diseases at-risk for SSc.

RESULTS

The results of the SLR[9] informing these recommendations are published separately and should be considered as part of this report. Based on the SLR[9] results and expert opinion, five overarching principles and seven recommendations for the execution (section A) and reporting (section B) of studies of skin ultrasound in SSc were formulated and are presented in table 1.

Overarching principles

(A) B-mode ultrasound and elastography are promising tools to assess skin involvement, but their role in the management of patients with SSc has yet to be defined

The integration of skin ultrasound into SSc clinical trials and daily practice and the full fruition of this technique's potential demands the fulfilment of the OMERACT filter requirements, as highlighted in our previous SLR.[9] Ultrasound thickness and stiffness have already demonstrated robust evidence for convergent validity against the 'gold standard' and skin histological findings[19 20] and good to excellent intrareliability and inter-reliability. The main knowledge gaps are highlighted in the research agenda, depicted in table 2.

(B) Report of ultrasound studies in rheumatic and musculoskeletal diseases, including SSc, should consider the recommendation checklist developed by EULAR

Aiming at the general standardisation of technical aspects and reports the task force recommends that the EULAR 23-item checklist, is fully considered also, where applicable, in skin ultrasound.[16]

(C) Standardisation of the technical aspects for skin ultrasound, in particular image acquisition and analysis, is essential to foster progress in this field

Our SLR[9] identified a remarkable heterogeneity and lack of information in a variety of technical aspects during image acquisition and analysis which need to be overcome to achieve the purposes of these recommendations.

(D) The level of training of the examiner and use of appropriate ultrasound equipment and settings are critical in the assessment of the skin in SSc

Ultrasound is an operator-dependent imaging technique with an inherent risk of observer bias, which can lead to an incorrect image acquisition and/or analysis. Previous studies have also shown that equipment and settings affect the reliability or accuracy of the ultrasound musculoskeletal examination.[16] Therefore, appropriate training of examiners contributing to research is essential to reduce variability and increase the quality of evidence. However, formal training of skin ultrasound is yet to be standardised. The ultrasound equipment and respective settings (including, probe frequency, gain, dynamic range and depth) need to be defined and detailed.

(E) These recommendations are designed to promote the full validation of skin ultrasound in SSC through optimised objectivity, reliability and sensitivity of evaluations

If skin ultrasound is to be used as an outcome measure in SSc research it should prioritise the knowledge gaps identified in the previous SLR[9] and presented in the research agenda, with emphasis on feasibility and discrimination (table 2).

Recommendations

Section A: Recommendations for the execution of skin ultrasound in SSc

Recommendation 1: The examination of the skin in SSc patients should, whenever possible, include B-mode ultrasound, to measure thickness and echogenicity, and also elastography to measure stiffness

Based on the evidence found in the SLR,[9] the task force considers it crucial to push research in all these three ultrasound domains to obtain further insights into its OMERACT measurement properties. Simultaneous ultrasound evaluation of skin thickness, stiffness and echogenicity may help to clarify the underlying pathological conditions and the relationship between these ultrasound features, a knowledge gap which is highlighted in the research agenda (table 2).

The task force recognises, however, that an examination protocol including the three ultrasound domains in the same study will face logistic difficulties related to current equipment specificities.

Recommendation 2: skin ultrasound should be performed at the standardised areas used in the mRSS

In general, relevant publications followed the 17-point dermal ultrasound scoring system proposed by Moore *et al*[21] in 2003, with a complete or reduced list of skin sites assessed. This approach, including exactly adherence to the examination sites, in endorsed by the task force.

In fact, ultrasound evaluations of different skin sites cannot be combined into larger databases for detailed analysis, comparison with mRSS or longitudinal evaluation. However, authors are free to analyse other sites deemed preferable for some reason.

Examining all 17 sites is time consuming and perhaps unnecessary, but the best trade-off of validity and

Table 1 WSF recommendations for the execution and reporting of skin ultrasound in systemic sclerosis

	Overarching principles	LoE	GoR	LoA*
A.	B-mode ultrasound and elastography are promising tools to assess skin involvement, but their role in the management of patients with SSc has yet to be defined	n.a.	n.a.	9.1 (2.3) 87.5%
B.	Report of ultrasound studies in rheumatic and musculoskeletal diseases, including systemic sclerosis, should consider the recommendation checklist developed by EULAR	n.a.	n.a.	9.0 (1.7) 81.3%
C.	Standardisation of the technical aspects for skin ultrasound, in particular image acquisition and analysis, is essential to foster progress in this field	n.a.	n.a.	8.8 (2.4) 87.5%
D.	The level of training of the examiner and use of appropriate ultrasound equipment and settings, are critical in the assessment of the skin in SSc	n.a.	n.a.	9.9 (2.0) 87.5%
E.	These recommendations are designed to promote the full validation of skin ultrasound in SSc through optimised objectivity, reliability and sensitivity of evaluations	n.a.	n.a.	9.2 (2.2) 93.8%
	Recommendations for the execution of skin ultrasound in SSc			
1.	The examination of the skin in patients with SSc should, whenever possible, include B-mode ultrasound, to measure thickness and echogenicity; and elastography, to measure stiffness	3b	B	9.3 (1.1) 87.5%
2.	Skin ultrasound should be performed at the standardised areas used in the modified Rodnan skin score	3b	B	8.7 (1.2) 81.3%
3.	Skin ultrasound should be performed with a high-frequency linear probe (≥18 MHz), and with the probe perpendicular to skin surface. Operators should use a generous amount of gel and minimal pressure to avoid tissue compression	3b	B	9.7 (0.6) 100.0%
4.	Stands-offs should not be used in skin ultrasound in SSc	5	D	8.6 (2.6) 86.6%
5.	Skin ultrasound should only be performed by well-trained examiners	3b	B	9.3 (1.4) 87.5%
	Recommendations for the reporting of skin ultrasound in SSc			
6.	Regarding image acquisition, always specify			
	(A) The quality criteria for acceptance of an ultrasound image	n.a.	n.a.	8.6 (1.9) 87.5%
	(B) The skin layers evaluated (epidermis, dermis, hypodermis, subcutaneous layers, others)	n.a.	n.a.	9.6 (0.8) 93.8%
	(C) The exact location of the skin site/area assessed	n.a.	n.a.	9.6 (0.7) 100.0%
	(D) The no of images acquired per skin site	n.a.	n.a.	8.6 (1.8) 81.3%
7.	Regarding image analysis always specify:			

Continued

Table 1 Continued

Overarching principles	LoE	GoR	LoA*
(A) The no of measurements per skin image/scan and their location within the image	n.a.	n.a.	8.9 (1.5) 81.3%
(B) With shear-wave elastography, the size and shape of the region of interest	n.a.	n.a.	9.1 (1.8) 93.8%
(C) How individual measures were processed to calculate the site value	n.a.	n.a.	9.2 (1.2) 93.8%

These recommendations should be interpreted in the light of the clarifications provided in the body of the text and by the supporting SLR.
*Numbers in column 'LoA' indicate the mean and SD (in parentheses) of the LoA, as well as the percentage of task force members with an agreement ≥8.
GoR, grade of recommendation; LoA, level of agreement; LoE, level of evidence; n.a, not applicable; SSc, systemic sclerosis.

feasibility regarding the number of sites is still unclear. This was prioritised on the research agenda (table 2).

Recommendation 3: Skin ultrasound should be performed with a high-frequency linear probe (≥18 mHz), and with the probe perpendicular to skin surface. Operators should use a generous amount of gel and minimal pressure to avoid tissue compression.

All the studies evaluating exclusively the dermis used frequency probes ≥18 mHz, excepted one study. Several authors argue that lower frequency probes were not able to discern the epidermis-dermis interface, and thus hindered the measurement accuracy and reliability.[15 20–23] To avoid anisotropy, the probe should be continuously adjusted to maintain the beam perpendicular to the skin surface.[16] Applying a generous layer of gel is important to minimise probe compression on the skin when performing ultrasound.

The task force, therefore, unanimously agreed that the above-mentioned technical requirements and procedures are essential for a valid skin ultrasound assessment. We acknowledge, however, that high-frequency probes for shear-wave elastography are not yet widely available.[15 19 20] Thus, skin ultrasound for SSc, to date, may require two different probes.

Recommendation 4: Stands-offs should not be used in skin ultrasound in SSC

This recommendation was mainly based on expert opinion. In our SLR[9] we did not identify any studies that directly evaluated the use of stands-offs.

The task force considered that the use of high-frequency probes and a generous amount of gel provide the best image resolution and avoid image artefacts, making the use of stand-offs unnecessary and risky due to increased tissue deformation from the appliance weight on the surrounding skin.

Recommendation 5: Skin ultrasound should only be performed by well-trained examiners

This recommendation specifically applies to skin ultrasound examinations performed for research or clinical purposes, not for training. Ultrasound requires focused learning of both basic physics and technical skill. It is increasingly part of Rheumatology training,[24] at least in Europe, and healthcare professionals are increasingly undertaking accredited ultrasound training, qualified to perform ultrasound examinations as part of clinical care and research purposes.[25] Although acquiring the skills to assess skin is arguably easier than assessing the musculoskeletal system or major organs.[16 26] Of note, skin ultrasound has been addressed in some previous EULAR Ultrasound Courses (advanced level), but there are currently no official training programmes specifically designed for skin ultrasound. Despite this, and the lack of consensus on the optimal level of ultrasound experience, the task force considered wise to underline the importance of safe-guarding this requirement for examinations.

SECTION B: Recommendations for reporting specific aspects of skin ultrasound in SSc studies

Table 2 Research agenda

I.	Validity
a.	Does ultrasound echogenicity have convergent validity against mRSS and/or skin histological findings?
b.	Does ultrasound stiffness have convergent validity against mRSS and/or skin histological findings and/or durometer?
c.	What is the correlation between skin ultrasound domains and different clinical scorings (mRSS)?
d.	What is the correlation between skin ultrasound domains and skin histological findings in different disease clinical phases?
e.	What is the correlation between skin ultrasound domains and patient reported outcome measures, such as Scleroderma Skin Patient-Reported Outcome?
f.	Is there an association between skin ultrasound domains and disease activity?
g.	Is there a relation between skin ultrasound domains and hand function?
h.	What is the best core of parameters/settings for image acquisition and analysis?
II.	Reliability
a.	What is the test–retest reliability of skin ultrasound in the different SSc subsets?
b.	What is the intra and inter-reader reliability of skin ultrasound in the different SSc subsets?
III.	Discriminatory capacity
a.	Does skin ultrasound domains discriminate between:
1.	Early phases of the disease and normal controls
2.	Disease subsets, that is, VEDOSS vs early inflammatory and dcSSc vs lcSSc vs sine?
3.	Phase of cutaneous involvement, that is, edematous versus fibrotic versus atrophic?
IV.	Responsiveness to change
a.	What is the sensitivity to change over time/treatment of skin ultrasound in SSc, in different disease subsets, in observational studies and randomised clinical trials?
b.	What is the correlation between changes in skin ultrasound measurements and in mRSS/skin histology over time/treatment?
c.	Can skin ultrasound separate between the effects of normal ageing and that of the disease and treatments on the skin?
d.	How frequently should skin ultrasound be repeated in SSc patients?
V.	Threshold of meaning
a.	What is the smallest detectable change and minimal clinically important difference for the diverse skin ultrasound domains (with stratification based on disease subsets)?
VI.	Feasibility
a.	What is the feasibility of skin ultrasound, in particular: cost of equipment and software, time taken for image acquisition and analysis?
b.	What is the best trade-off of validity and feasibility regarding of the minimum number (and sites) of skin regions examined by ultrasound in SSc?
c.	Is there an advantage in performing skin ultrasound examination in symmetrical Rodnan skin sites?
d.	Is skin ultrasound useful in a combined multi-organ ultrasound approach (eg, digital ulcers, lung, vascular, joints)?
e.	What is the availability and current practice of skin ultrasound in SSc worldwide?
VII.	Contextual factors
a.	What is the impact of patient factors (age, gender, BMI, smoking, sun exposure,) on skin ultrasound domains?

Continued

Table 2 Continued

I.	**Validity**
b.	What is the impact of ambient contextual factors (hour of the day, room temperature, time of acclimatisation, patient position,) on skin ultrasound domains?
VIII.	Educational agenda
a.	Ultrasound courses and process of certification of competencies, specifically focused on skin ultrasound in SSc

mRSS, modified Rodnan Skin Score; SSc, systemic sclerosis; VEDOSS, very early diagnosis of SSc.

The items listed below are considered mandatory for the reporting of skin ultrasound studies in SSc, in addition to the general guidance provided by the EULAR recommendations 23-item checklist.[16]

Recommendation 6: Regarding image analysis, always specify

1. The quality criteria for acceptance of an ultrasound image.
2. The skin layers evaluated (epidermis, dermis, hypodermis, subcutaneous layers, others).
3. The exact location of the skin site/area assessed.
4. The number of images acquired per skin site.

Item R6 (a) demands a clear description of the quality criteria used to accept each of the ultrasound images. The task force considers that B-mode images should only be accepted for analysis if an adequate depiction of epidermis, dermis and subcutis, with distinct and parallel interfaces between them is achieved.[9] In the case of elastography, the majority of softwares provides an automated image quality factor to allow clinicians to select the highest quality image.[15] The use of this image quality factor should also be reported in the studies. Another important criterion, for both techniques, is the identification of a gel film over the skin surface indicating that the sonographer is applying minimal or no pressure on the skin.

Item R6 (b): The skin layers evaluated in the ultrasound studies must be clearly identified. Moore *et al*[21] and Naredo *et al*, Flower *et al*[13 19] proposed that evaluation of the dermis is essential, not only because it is the main focus of pathological disease changes, but also because reliability of epidermis measurements was poor (interobserver ICC <0.35). Recently, Naredo *et al*[13] using a 50MHz probe underlined the importance of also measuring the hypodermis, separately, particularly in early disease. Therefore, the task force reiterated that report of which skin layer is exactly being measured is decisive for the quality of skin US reports.

Item R6 (c): When examining the Rodnan skin sites, the exact location described by Moore *et al*[21] should be respected and confirmed in the publication. For sites other than the Rodnan, an exact description should be provided with distances relative to anatomical landmarks.

Finally, the number of images acquired per skin site—item R6 (d)—should always be clearly reported for standardisation purposes.

Recommendation 7: Regarding image analysis always specify:

1. The number of measurements per skin image/scan and their location within the image.
2. With shear-wave elastography, the size and shape of the region of interest.
3. How individual measures were processed to calculate the site value.

These aspects have been scarcely or not reported in previous skin ultrasound studies.[9] Choices made here may affect ultrasound measures and jeopardise reproducibility and generalisability of the results. Therefore,

reporting details of the image analysis and scoring system employed is mandatory.

Research agenda

Table 2 presents the research agenda proposed by the taskf orce, based on areas with only weak or limited evidence. An item for educational agenda is also presented, which encourages the development of training programmes to enhance and support skin ultrasound educational competencies. Of note, a full validation of skin ultrasound will be completed through a randomised clinical trial or sensitivity to change over time. These further insights will be crucial for the evaluation of new fibrotic and immunosuppressive treatments in this field.

DISCUSSION

These are the first recommendations for the execution and reporting of studies using ultrasound of the skin in the assessment of skin involvement of SSc patients. The recommendations were formulated by a multidisciplinary group based on an exhaustive SLR[9] and on SSc experts' opinions.

We recognise that many topics in which evidence is limited, or lacking are crucially important. Therefore, they have been the object of expert consensus and they populate the research agenda designed to convey the path necessary to support the full endorsement of skin ultrasound in clinical practice and research. Our ratings of key aspects of reporting directly relevant to ultrasound assessment of the skin in SSc reflect the strong endorsement within our task force for the EULAR recommendations.

The need for the standardisation of procedures and reporting in skin ultrasound studies has been voiced by numerous authors over recent years.[13 19 20 23]

We acknowledge that there is still a large amount of research required to optimise the use of the ultrasound before its implementation in clinical practice, in particular what skin sites should be used for disease assessment and monitoring, consideration of the feasibility, contextual factors impact on ultrasound measures, responsiveness to change and appropriate threshold of meaning. Good quality and well-designed observational studies and randomised clinical trials are now required to provide an answer to these questions.

We hope that these recommendations will inspire and be widely adopted by researchers, an essential step to empower them to represent a significant step forward in the much-needed progress in skin assessment in SSc. We believe that their implementation will improve research, and consequently the interpretability, reproducibility and generalisability of the study results. This will represent a major advance in topics such as identification of subclinical or early disease, and assessment of response to immunosuppressive or antifibrotic therapies.[27] This is especially important when, finally, promising new agents are being investigated in the treatment of SSc, highlighting the need for sensitive and reliable measurement tools.

In summary, we have developed seven recommendations on various aspects of the execution and reporting of skin ultrasound in SSc. They were based on the best available evidence along with hands-on expertise, and we expect that this can foster much needed progress in this field, as reported in the research agenda. We will carefully follow developments, assuming that an amendment of these recommendations may be needed within a few years.

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REFERENCES

1 Krieg T, Takehara K. Skin disease: a cardinal feature of systemic sclerosis. *Rheumatology* 2009;48 Suppl 3:iii14–18.
2 Clements PJ, Hurwitz EL, Wong WK, *et al*. Skin thickness score as a predictor and correlate of outcome in systemic sclerosis: high-dose versus low-dose penicillamine trial. *Arthritis & Rheumatism* 2000;43:2445–54.
3 Khanna D, Furst DE, Clements PJ, *et al*. Standardization of the modified rodnan skin score for use in clinical trials of systemic sclerosis. *J Scleroderma Relat Disord* 2017;2:11–18.
4 Merkel PA, Clements PJ, Reveille JD, *et al*. Current status of outcome measure development for clinical trials in systemic sclerosis. report from OMERACT 6. *J Rheumatol* 2003;30:1630–47.
5 Khanna D, Lin CJF, Furst DE, *et al*. Tocilizumab in systemic sclerosis: a randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet Respir Med* 2020;8:963–74.
6 Khanna D, Spino C, Johnson S, *et al*. Abatacept in early diffuse cutaneous systemic sclerosis: results of a phase IIinvestigator-initiated, multicenter, double-blind, randomized, placebo-controlled trial. *Arthritis Rheumatol* 2020;72:125–36.
7 Santiago T, Santiago M, Ruaro B, *et al*. Ultrasonography for the assessment of skin in systemic sclerosis: a systematic review. *Arthritis Care Res* 2019;71:563–74.
8 Michael Hughes CB, Cuomo G, Sedie AD. The role of ultrasound in systemic sclerosis: on the cutting edge to foster clinical and research advancement. *J Scleroderma Relat Disord* 2020.
9 Santiago T, Santos E, Ruaro B, *et al*. Ultrasound and elastography in the assessment of skin involvement in systemic sclerosis: systematic literature review focusing on validation and standardization - WSF Skin Ultrasound Group. *Semin Arthritis Rheum* 2022;52:151954.
10 Kaldas M, Khanna PP, Furst DE, *et al*. 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* 2009;48:1143–6.
11 Sulli A, Ruaro B, Alessandri E, *et al*. AB0486 high frequency ultrasound and laser doppler flowmetry for the evaluation of digital dermal thickness and fingertip blood perfusion in systemic sclerosis patients. *Ann Rheum Dis* 2013;72
12 Hesselstrand R, Scheja A, Wildt M, *et al*. High-frequency ultrasound of skin involvement in systemic sclerosis reflects oedema, extension and severity in early disease. *Rheumatology* 2008;47:84–7.
13 Naredo E, Pascau J, Damjanov N, *et al*. Performance of ultra-high-frequency ultrasound in the evaluation of skin involvement in systemic sclerosis: a preliminary report. *Rheumatology* 2020;59:1671–8.
14 Ruaro B, Sulli A, Smith V, *et al*. The impact of transducer frequency in ultrasound evaluation of subclinical skin involvement in limited cutaneous systemic sclerosis patients. *Clin Exp Rheumatol* 2019;37 Suppl 119:147–8.
15 Santiago T, Alcacer-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.
16 Costantino F, Carmona L, Boers M, *et al*. EULAR recommendations for the reporting of ultrasound studies in rheumatic and musculoskeletal diseases (RMDs). *Ann Rheum Dis* 2021;80:840–7.
17 van der Heijde D, Aletaha D, Carmona L, *et al*. 2014 update of the EULAR standardised operating procedures for EULAR-endorsed recommendations. *Ann Rheum Dis* 2015;74:8–13.
18 CEBM. *Oxford centre for evidence-based Medicine—Levels of evidence (March 2009)*, 2009.
19 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.
20 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.
21 Moore TL, Lunt M, McManus B, *et al*. Seventeen-point dermal ultrasound scoring system--a reliable measure of skin thickness in patients with systemic sclerosis. *Rheumatology* 2003;42:1559–63.
22 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.
23 Vanhaecke A, Cutolo M, Heeman L, *et al*. High frequency ultrasonography: reliable tool to measure skin fibrosis in SSC? a systematic literature review and additional pilot study. *Rheumatology* 2021;61:42–52.
24 Mandl P, Ciechomska A, Terslev L, *et al*. Implementation and role of modern musculoskeletal imaging in rheumatological practice in member countries of EULAR. *RMD Open* 2019;5:e000950.
25 Siddle HJ, Mandl P, Aletaha D, *et al*. The EULAR points to consider for health professionals undertaking musculoskeletal ultrasound for rheumatic and musculoskeletal diseases. *Ann Rheum Dis* 2018;77:311–3.
26 Iagnocco A, Porta F, Cuomo G, *et al*. The Italian MSUS study group recommendations for the format and content of the report and documentation in musculoskeletal ultrasonography in rheumatology. *Rheumatology* 2014;53:367–73.
27 omeract handbook. *Chapter 5: Instrument selection for core outcome measurement sets - Workbook*, 2019. https://omeracthandbook. org/workbooks-%26-resources