Multi-Organ System Screening, Care, and Patient Support in Systemic Sclerosis

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KEYWORDS

• Interstitial lung disease • Pulmonary hypertension • Ischemic
• Health-related quality of life • Patient-centred • Gastrointestinal disease
• Renal crisis • Shared decision-making

KEY POINTS

- Systemic sclerosis is a multi-organ system disease portending high risk of severe disability and death; and thus requires a global approach to prevention and management of complications.
- Standardized screening, anticipatory guidance and counselling are needed for early detection and appropriate treatement of SSc organ involvement.
- Screening for psycho-social well-being, includng sexual health, may reveal the most pressing biophysical influences for a person living with SSc.
- This article provides a reference to support a global approach to caring for people living with SSc.

INTRODUCTION

Systemic sclerosis (SSc) is a relatively rare heterogenous systemic autoimmune disease with complex multi-organ manifestations. Greater than 50% of deaths are directly attributable to SSc. The patient journey is commonly fraught with severe, diverse, and diffuse physical impairment as well as multiple causes impacting psychological burden, and greatly diminishing health-related quality of life (HRQoL).

The intricacies of care and guidance required in SSc remain unfamiliar territory for many clinicians; leaving patients feeling further isolated and unsupported. Delayed

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diagnosis, misdiagnosis, inadequate screening for common complications as well as insufficient recognition of and attention to common disabling features frequently occur contributing to potentially preventable disability and death.

This review outlines actionable standards in SSc care including screening, anticipatory guidance, and counseling in the context of patient-centered care. A reverse perspective to that traditionally found in disease state publications is presented here with a patient-forward sequence of SSc-relevant concerns. This sequence emphasizes psycho-social health as the underlying and overall central goal of care, whereas robust vigilance and efforts to improve biophysical health and survival are imperatives that support this goal.[1,2] This perspective naturally maintains shared decision-making (SDM; **Box 1**) in counseling and providing anticipatory guidance in treatment, preventive SSc care, and "red flag" situations (**Table 1**). The following are overall reference companions we hope will be useful: (a) **Fig. 1** is an aide memoire for a biophysical organizational approach for SSc's complex multi-organ system involvement. (b) Though SSc portends a high risk of severe disability and death for all patients—including those with an indolently progressive phenotypes—**Table 2** outlines biophysical factors that confer even higher risk associations. (c) **Table 3** provides an overview of recurrent anticipatory guidance and counseling essential in SSc care.

Psychosocial Experience of Living with Systemic Sclerosis

Screening for aspects psychosocial well-being in systemic sclerosis

Screening for and querying psycho-social well-being upfront can provide an informative entrée into the most pressing biophysical experiences for a patient with SSc. After which, it remains important that clinicians query biophysical aspects that the patient had not yet addressed (see **Fig. 1**). SSc pervasively influences patients' physical,

Box 1
Checklist to support shared decision-making

Shared Decision-Making Checklist

- Restate the patient's items of concern as expressed by the patient and if possible which are of the highest priority to them
- Ascertain patient's thoughts on the potential underlying cause/s of new concerns or symptom changes
- State the items of concern from the clinical perspective including short and long-term concerns (eg, potential progressive damage and associated abrupt complications)
- Respond to patient's perceptions of potential cause to gain further clinical insight, provide support, and clarify any divergence between patient and clinician perceptions.
- Remain transparent in what is known, unknown, yet to be known, and that requires researching by the clinician
- Name available treatment options, including any nonpharmacological options with particular attention to those suggested by the patient
- Discuss safety, side effects, and efficacy (including anticipated onset) of available therapies and those suggested by the patient.
- Assess the patient's expectations, priorities, and desires related to treatment
- Set treatment expectations including prognosis, anticipated degree of symptom/impairments resolution (*ie, cure vs regression vs slowing progression*), and disease activity versus damage

Courtesy of LA Saketkoo, MD, MPH, New Orleans, LA.

Table 1
Red flags in systemic sclerosis that patients should be aware of and report

Organ System	Red Flag	Potential Complication
General	Unexplained weight loss Decreased physical activity Loss of muscle mass	Cancer Infection Active progressive disease Significant GI involvement Deterioration of general health status (Frailty) Depression
Skin	Diffuse skin tenderness, ± pruritus Appearance of active inflammation around calcinotic lesions	Rapidly progressive diffuse cutaneous disease Infected calcinosis cutis Risk of osteolysis or joint infection
Digital vascular	Increased pain, tenderness, pressure, or appearance of tissue inflammation	Digital ulcer occurrence Critical digital ischemia or gangrene Infection ± osteomyelitis
Cardiopulmonary	Reduced performance status Decreased physical activity Inspiratory dry cough Decreased trend in FVC and/or DLCO even if within normal range	Arrhythmia, critical bradycardia Development and/or progression of ILD or PH Ventricular dysfunction
Gastrointestinal	Onset of (severe) anemia Severe swallowing difficulty/ inability Unexplained weight loss Severe abdominal pain Change in bowel habit Elevated serum lactate Low BMI and poor nutritional state	Gastric vascular ectasia (GAVE) Esophageal stricture Pneumatosis Coli (risk of perforation) GI malignancy GI ischemia Intestinal pseudo-obstruction Malnourishment
Sexual health in females	Skin thickening, vaginal dryness, stenosis, ulceration, multiple SSc vascular features, and pain	Sexual dysfunction
Sexual health in males	Multiple SSc vascular features and erectile dysfunction	Sexual dysfunction
Psychological disorders	Anxiety, depression, loneliness, sleeping disorders, and work disability	Poor treatment adherence, deteriorating HRQoL, diminished perceived disease impact regardless of biophysical health status
Musculoskeletal	Presence of synovitis and/or joint tenderness, tendon friction rubs (TFRs), proximal muscle weakness, or atrophy	Joint contractures, arthritis, permanent deterioration of hand function, myopathy, and weakness, myositis
Renal	Sudden onset of hypertension in the early stage of dcSSc	Scleroderma renal crisis: hypertension, azotemia-uremia
Secondary immunodeficiency	Low white blood cell count and neutropenia	Side effects of DMARDs (eg, MTX, MMF, CYC, and tocilizumab)

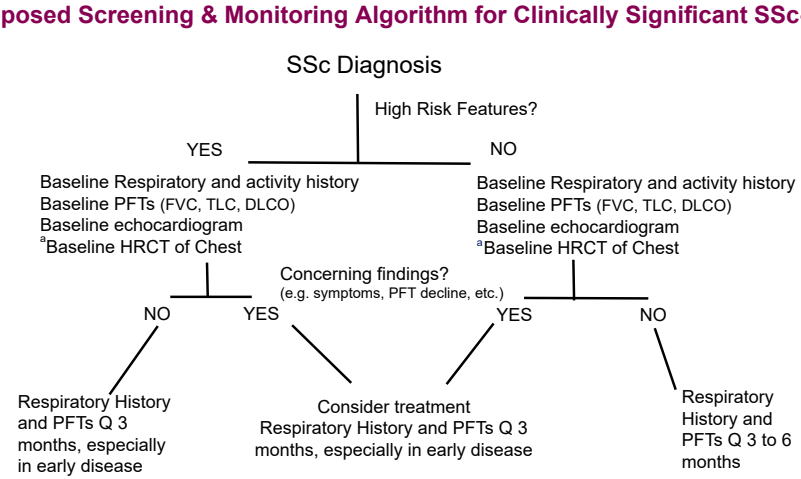

Fig. 1. Proposed screening for ILD in SSc. [a]Currently no absolute consensus on baseline HRCT upon new SSc diagnosis; however there is increasing support. HRCT is not routinely repeated for monitoring, but rather for unexplained or unexpected cardiopulmonary manifestations. (*Courtesy of* LA Saketkoo, MD, MPH, New Orleans, LA.)

psychological, and social well-being. Advances in diagnosis and treatment of SSc, are linked to increased median survival. However, the overall patient-perceived disease impact is influenced to a high degree by the psychological aspects of living with SSc and SSc-related disabilities. These include mood disorders, body image, fatigue, pain, family relations, and disease impact on professional and social life.[3,4] Targeted interventions that improve factors, especially pain and fatigue, can mitigate disease impact[5] (**Table 4**).

Anxiety and/or depression has a prevalence between 17% and 65% in people with SSc, compared with 4% to 10% among the general population.[3–9] Anxiety is associated with the severity of lung involvement, pain, and diminished body image.[6,7]

Appearance changes on visible body areas (eg, face, hands) in SSc are common and distressing. Greater dissatisfaction with appearance, body image, and social discomfort occur more frequently in people of younger age and when unmarried.[3,9–11] People with diffuse cutaneous systemic sclerosis (dcSSc) reported greater body image dissatisfaction than those with limited cutaneous systemic sclerosis, and expressed greater dissatisfaction in appearance with increased finger/hand skin involvement in dcSSc.[7,11]

Symptoms of depression are associated with disease severity, gastrointestinal function, pain, health status, education level, and ability to cope with psychological impact.[10,12–14] Simple self-administrated questionnaires, as an integral part of overall SSc care, support the early recognition and treatment of various psychological distresses (**Table 5**).[10,12–14]

Fatigue and sleeping problems were among the five highest-rated symptoms in terms of severe impact on daily activities reported by 72% and 59% respectively.[15] *Sleeping disorders* have a higher prevalence in SSc patients, with decreased sleep quality further deteriorating fatigue and mental health symptoms that are common characteristics of chronic inflammatory diseases.[15,16]

Poor sleep quality impacts factors important in SSc such as inflammation levels, memory, cognition, anxiety, depression, well-being, wound healing, pain perception, muscle health, and also correlates with a degree of loneliness which in turn influences

Table 2
Risk factors for death, disability, and rapidly progressive disease and for severe organ involvement

Risk Factor	Clinical Measures	Indication of Rapidly Progressive SSc or Severe Disease
Demographics	Inquiry	African ancestry Asian ancestry Hispanic ancestry Male sex
Diffuse skin involvement	modified Rodnan Skin Score (mRSS)	Increasing diffuse scleroderma skin, mRSS > 29
Tendon friction rub	Palpable presence on examination	Palpable presence on examination
Anti-topoisomerase-1	See measures for ILD, dcSSc, renal crisis, and cardiac fibrosis	
Anti-RNA polymerase III	See measures for SSc renal crisis, dcSSc, GAVE, rapidly development of joint contractures; Malignancies synchronous to SSc onset	
Interstitial lung disease	PFT: spirometry PFT: DLCO HRCT: Extent of ground-glass opacity and honeycombing fibrosis	FVC<70% DLCO<70% >20% extent of disease on HRCT
Pulmonary hypertension (PH)	Echocardiography Right heart catheterization WHO/NYHA Classification	sPAP >40 mm Hg Right atrial or ventricular enlargement Septal flattening mPAP>20 mm Hg PVR > 3 wood units Class III/IV
Cardiac involvement	ECG Echocardiography	ECG arrhythmia Diastolic dysfunction > grade 2 left ventricular ejection fraction <45%
Digital ulcers and gangrene	Nailfold capillaroscopy	Severe capillary loss, fibrotic infiltration
Scleroderma renal Crisis	Hypertension Serum biomarkers	Abnormal or an unusually elevated value for the patient Normotensive if on prednisone Elevated serum creatinine ? Anti-topoisomerase ? Anti-polymerase III
GAVE	Gastric bleeding Anemia	Frank blood on inspection Hb < 9.6 g/dL
Severe malabsorption	Weight loss Muscle atrophy Stool frequency Electrolytes Albumin/prealbumin	

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Table 2
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Risk Factor	Clinical Measures	Indication of Rapidly Progressive SSc or Severe Disease
Polyarthritis	HAQ-DI DAS-28 Cochin Hand Function Scale	Active joint disease: HAQ-DI≥1.0, Cochin Hand Function Scale ≥10 and/or 28-tender joint count ≥6
General health status	Weight loss/BMI Serum biomarkers Loss of muscle mass	Weight loss > 10% Low albumin, low Hb
Comorbidities	Presence of: COPD, malignancy, diabetes mellitus	

Organ Manifestation	Risk Factors
Heart	Pericarditis Arrhythmia Right bundle branch block (RBBB) Left ventricular dysfunction Myopathy Tendon friction rubs
Kidney (renal crisis)	Diffuse cutaneous SSc Rapid skin progression in the first year of the onset Presence of anti-RNA polymerase III autoantibodies Medium or high dose glucocorticoid therapy, that is, >10 mg prednisone daily Significant cardiac manifestation Joint contractures Tendon friction rubs
Interstitial lung disease (ILD)	Male gender High mRSS Diffuse cutaneous SSc Anti-topoisomerase 1 antibody Increased ESR FVC<70%, DLCO<70% Decrease of FVC ≥5% within 6 mo regardless of normal values Increased serum creatinine phosphokinase (CK)
Progressive ILD	Active polyarthritis Increased ESR Disease onset over 55 y High mRSS Reflux (GERD) NYHA III-IV heart disease Decreased SpO_2 during 6MWT
Pulmonary hypertension	Disease onset over 55 y Long disease duration African ancestry for early onset of PH Skin telangiectasias Isolated DLCO decrease in trend—*even with normal values* FVC/DLCO ratio > 1.6 Severe Raynaud's Severe digital ulcers Decreased capillary density by nail fold capillaroscopy

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Table 2
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Organ Manifestation	Risk Factors
	Increased serum uric acid Presence of Th/To, U3 RNP, or RNA Polymerase III autoantibodies
Digital ulcers	Diffuse scleroderma High mRSS Male gender Polyarthritis Early non-Raynaud's first symptom Increased capillary loss by capillary-microscopy
Arthritis, contractures, tendon friction rubs	Early manifestation in diffuse cutaneous SSc Presence of overlap SSc Presence of RNA Polymerase III and Topoisomerase I autoantibodies Lack of early referral to Occupational and Physical Therapy

Abbreviations: 6MWT, 6-min walk test; DLCO, diffusion capacity of the lung for carbon monoxide; ESR, erythrocyte sedimentation rate; FVC, forced vital capacity; GAVE, gastric antral vascular ectasia; GERD, gastroesophageal reflux disorder; HAQ-DI, health assessment questionnaire-disability index; ILD, interstitial lung disease; mRSS, modified Rodnan Skin Score; NYHA, New York Heart Association; PAS, estimated pulmonary artery systolic pressure by Doppler echo; SpO2, blood oxygen saturation; WHO, World Health Organization.

Courtesy of C Varju, MD, PhD, Pécs, Hungary and LA Saketkoo, MD, MPH, New Orleans, LA.

health status and inflammation levels.[17] Screening for and addressing issues related to sleep quality creates opportunities to greatly effect overall perceived disease impact.[10,18–25]

Engagement in remunerative work is greatly impacted by SSc with 18% to 61% of patients discontinuing work.[26] *Work disability* correlates with more severe lung function parameters, less social support, higher fatigue severity scores, and lower education level.[27,28] Awareness of these risk factors, initiation of early appropriate treatment, and nonpharmacological therapy, may mitigate SSc-disease impact on work ability.[29]

Sexual health in people living with systemic sclerosis

Sexual health concerns are common and greatly impact HRQoL *for both women and men* with SSc, with the prevalence of sexual dysfunction (SDF) varying from 46.7% to 86.6% in women and 76.9% to 81.4% in men.[30–38] Yet sexual health is rarely addressed in clinical practice,[30–32] with only 9.6% of patients with SSc ever having discussed sexual problems with their physicians.[31] SDF in SSc is a multifactorial concern influenced by disease-related, treatment-associated, and psychological factors. SDF in SSc may involve any phase of the sexual activity response cycle: desire/libido, arousal/excitement before or during intercourse/activity (such as erectile dysfunction, dyspareunia or vaginismus), orgasm (disorders inhibiting male or female orgasm, premature ejaculation in men) and resolution (physical or psychological dissatisfaction).[30–34,36] Early introduction of pelvic floor muscle exercises may help both men and women to maintain urinary and fecal continence, increase local blood supply, and responsiveness during sexual activity.[39,40]

Sexual health in female patients

The assessment and complex problem-solving regarding female sexual function benefit from collaboration between rheumatology and gynecology. Vaginal dryness, mucosal stenosis, and pain are of the most problematic concerns for women with SSc.[30,31,34] The Female Sexual Function Index Scoring (FSFI) is the most commonly

Table 3
Key elements of recurrent multi-organ system counseling and anticipatory guidance in systemic sclerosis

Category	Subcategory	Item	Advisements for Patients
Vascular	Raynaud	Prevention is key	• Related complications include DUs, calcinosis, osteolysis and core temperature loss • Initiate protective measure in anticipation of and upon noticing a cold atmosphere, before allowing oneself to "feel" cold • Immediate action can result in decreased recovery time, pain and the sequela associated with loss of core warmth (fatigue, headache, incapacity, etc.) • Avoid extreme temperature changes, for example, from cold to warmth • Anticipate cold environments, for example, air conditioning in summer, grocery store freezer aisle, hospitals, etc.
		Core Temperature	• Exercise/movement increases circulation and body heat • Clothes layering and use of insulated vests • Hand warmers, can be placed in pockets, undergarments
		Peripheral	• Gloves/socks always at hand • Should allow for a thin space to trap a warming layer of air • Hand warmers, can be placed in pockets, gloves, socks • Heated gloves/insoles/shoes
	Digital ulcers/calcinosis	Protection	Cushioned bandages for high friction areas Waterproof gloves for washing or handling wet items Bandage and gloves for handling dry household items potentially snagging healing ulcers and to protect from bacteria and chemical irritants Exercise gloves for use of gym equipment as needed
		Pain management	• Protection as above • Topical lidocaine • Wound cleansing routine
		Signs of infection	• Increased pain/tenderness • Redness • Purulence
		Prevention	As much as possible avoid: *Cold exposure* and *Trauma* Use topical antibiotics with signs of infection

	Additional calcinosis	Advisement	• Avoid digging to prevent infection • If pain intolerable can try repeated soaking in warm Epsom salt water • Topical antibiotics • Seek help if seems infected or ulceration occurs
	Erectile dysfunction		• Increased physical activity helps protect circulatory and neuronal function • *RP* and *Core Temperature* preventive measures may have a protective effect
Nutrition	Calorie intake	Nutritious	• Avocado • Nuts, nut butters, sprinkling nut and protein powders • Adding cheeses (soft or hard as tolerated), butter, creams • Potatoes, rice • Olive and other oils • Plant-based high calorie formulas eg, *Kate Farms*
	Food tolerance	Nutritious	• Thoroughly chewing/macerating food to liquid/paste • Pureed foods (soups, dips, stews) • Smaller amounts of a food type • Variation of food type, for example, sliced, pureed, grated, cooked, etc. • Foods softened (marinated) with small amounts of citrus or vinegar • Mobility after eating to increase motility
Heent	Oro-facial		Facial Exercises and Massage for skin tightness, mobility and circulation
	Oral		High risk for dental complications: • Essential follow-up with a dental clinician sensitive to SSc care or perhaps pediatric dentist • Proactive dental care • Topical Fluoride Rinse to protect against dental caries • Keeping mouth moist • Adapted and powered devices for teeth and oral care
	SICCA		Wetting and pro-salivation products Singing, humming, chanting and exercise to increase salivation and oral, facial and diaphragmatic muscle mass

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Table 3
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Category	Subcategory	Item	Advisements for Patients
Cardiopulmonary			Graded exercise essential to health Control of GERD and PND to avoid lung injury from micro-aspiration Vaccination for prevention of infection (see Table 7)
	PH and cardiac		Daily weights as needed Alert MD of new-onset lower extremity edema
Gastrointestinal	GERD	Esophageal injury and lung risks	Reflux in SSc is a serious issue of which related injury can lead to multiple complications that impact mortality. • Often exists without pain • Pain does not equate severity • Esophagitis • Esophageal cancer • Dysphagia and potential loss of swallow function • Strictures & Webbing • Need for esophageal stretching • Acid aggravates lung disease • CPAP use can inhibit reflux
		Medications	• PPI daily or twice daily, especially with esophagitis or esophageal ulcer • it is perceived that in SSc the benefits of PPIs greatly outweigh associated risks • Adding PRN or OTC agents (eg, sucralfate, H2 blockade) • Advise on the timing of administration to avoid drug-drug interactions
		Sleep essentials	• Head of Bed Elevation (wedge pillow, leveraging mattress, bricks/books under bed legs) • Avoid right-side lying
		Reflux hygiene	• Smaller, more frequent meals

	Gastroparesis		• Avoid meals 2 to 3 h before lying down • Avoid sphincter relaxants at end of day, for example, alcohol, chocolate, caffeine, mint, etc. • Sleep and hygiene as for GERD • Exercise/walking may help • Gravity strategies for passive digestion • Upright position • Attention to food consistency, for example, thinner foods • Gastroparesis dietary suggestions for food tolerance
	Bloating		• Exercise for motility • Small frequent meals • Simethicone or *IBGard* are safe over-the-counter options for possible relief
	Nausea	SSc or medication related	• Mobility/exercise to decrease nausea • Ginger-based sweets, tea, and drinks • Sucking candies • Cold pops • Instruction on PRN anti-emetics
	Diarrhea	SSc or medication related	Logistics until controlled: change of clothes, time planning Medication use, for example, anti-motility agents: risks/benefits/when to use/limited use
Exercise	Key element to SSc care	Counseling at each visit for support, guidance, and consideration for therapeutic referral Early OT/PT referral can have a critical impact on function and disability prevention	Improves: • Circulation and vascular responsiveness • Body warmth • Sleep • Energy • Self-esteem • Breathlessness • Hand function • Joint mobility stiffness and lubrication • Skin function and health • GI function and microbiome diversity • Nausea • Salivation

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Table 3
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Category	Subcategory	Item	Advisements for Patients
			• Respiratory performance • Cognitive clarity Decreases: • inflammation • Pain (anywhere) • Joint stiffness • Possibly contractures • Possibly skin tightness • Depression • Stress • Fatigue • Cancer risk
Women of Child-Bearing Age	Medication toxicity		• Use of contraception essential with specific IS and PAH medications • Discontinuation of specific IS or PAH medications before conception
	Conception		• Should be a planned event • Medication washout pre-conception • Discuss assessing the extent of ILD, PH, cardiac or renal involvement in light of safe pregnancy
	Care of children		• Adaptations for childcare • Strategies to manage fatigue
Psychological			Advocacy/education groups Local support groups Online self-management program eg, *Dr. Janet Poole* Referral for professional psychological support

Courtesy of LA Saketkoo, MD, MPH, New Orleans, LA.

Table 4
Modifiable causes and treatment of fatigue and pain in systemic sclerosis

Symptom	System/Origin	Potential Causes	Team Involvement/Interventions
Fatigue	Anemia	GI loss, chronic inflammatory disease	
	Cardiac	PH, diastolic HF, CAD, and physical deconditioning	PT and PR teach adapted aerobic and muscular exercises and breath pattern training OT teaches energy conservation strategies such as pacing, prioritizing, and accommodating devices
	Respiratory	PH, ILD, and OSA	OT, PT, PR, as for cardiac above
	Muscular	Low muscle endurance, muscle strength, or reduced aerobic capacity	MT, MMM, PR-PTr, PT for Aerobic exercises, muscle strengthening and endurance exercises, and education
	Systemic inflammation	Effects on hypothalamic axis, causing systemic malaise, effects on muscle	Immunosuppression, exercise
	Psychological	Anxiety, depression, fear, impact of reduced self-esteem, and self-image	MT, MMM, PR-PTr, PT, OT, Breath pattern training, Psychologist, Social Worker
	Neurologic	Pain: ischemic, edematous skin, articular, restless leg syndrome	Assess treatable causes, MT MMM, and PR
	Malnutrition	Weight loss, and malabsorption	
	Sleep-related	OSA, nocturnal pain, pruritus, GI symptoms, depression, anxiety, steroid, or opioid use	SH, RSS, MMM, and MT
	Medication-related	Methotrexate, MMF, nintedanib, etc.	
Pain/dysesthesia	Vascular	Raynaud	EC preventive strategies, MT, vasodilators, sympathectomy, PT for aerobic exercise to improve blood flow
		Digital ulcers	EC wound care, protective dressing, anesthetics, OT for daily activities, MT, PT as for RP
		Calcinosis	As above, UTPRM: soaking for relief
		Infected digital ulcers/calcinosis	EC red flags, Aerobic exercise to improve circulation
	Dermal	Skin tightening	PT, ST, and OT for stretching and manipulation
		Subcutaneous edema and pressure	MT, ST, OT as above
		Pruritus	MT, SH, ST, opioid receptor blocker, and phototherapy

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Table 4
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Symptom	System/Origin	Potential Causes	Team Involvement/Interventions
	Musculoskeletal	Myopathy/myalgias	MMM, OT, PT, PR-PTr, for strength, endurance, and anti-inflammatory effects of exercise
		Fibrous tendinopathy	MMM, OT, PT, THE as above
		Inflammatory arthropathy/tendinopathy	MMM, OT, PT, ST, and local injections, muscle strengthening, stretching, and targeted hand exercises
		Secondary fibromyalgia	MMM, PR-PTr, SH, and education
	Gastrointestinal	Heartburn	EC, RH, NH, and anti-acid and PPI
		Abdominal cramping Abdominal bloating	Assessment with Giessen GI Questionnaire or UCLA GIT[106,107]
	Genitourinary	Dyspareunia	Pelvic floor therapies and sometimes systemic treatment
		Vaginal dryness	Lubricants, topical estrogen
		Erectile dysfunction	Vasodilators, PT for aerobic exercise, and specialist referral

Abbreviations: AG, anticipatory guidance; ATT, assessment with targeted treatment; DHS, dental hygiene strategies; EC, education/counseling; ILD, interstitial lung disease; MMM, mindful movement modalities (e; g, gentle yoga; tai chi etc.); MT, mindfulness training strategies; NH, nutrition hygiene (EC on attention to selection, volume; texture, preparation; combination strategies of foods); OSA, obstructive sleep apnea; OT, occupational therapy; PAH, pulmonary arterial hypertension; POS, practical organizational strategies; PPI, proton pump inhibitors; PR, pulmonary rehabilitation; PR-EC, pulmonary rehabilitation educational component; PR-PTr, PR physical training component; PT, physiotherapy; RH, reflux hygiene (including head of bed elevation); RHS, refer to hand specialist; RME, refer to motility expert; RSS, refer to sleep specialist; SH, sleep hygiene; SR, specialist referral; ST, systemic treatment; THE, targeted home exercises; UTPRM, untested patient-reported management.[2]

Courtesy of LA Saketkoo, MD, MPH, New Orleans, LA.

Table 5
Selected questionnaires for psychosocial status in patients with systemic sclerosis

Instrument	Item Breakdown Qualities	Demonstrated Use in SSc
Psychological Impact		
Beck Depression Inventory[14,15,17]	A simple 13-items self-report questionnaire	Reliably Discriminates Between Depressed and Nondepressed Medical patients
The Hospital Anxiety and Depression Scale (HADS)[10,11]	A simple 14-item self-administered questionnaire, with 7 anxiety items and 7 depression items, on a 4-point (0 to 3) scale	Feasibility, validity, and responsiveness in SSc
Patient-Reported Outcomes Measurement Information System PROMIS-29[19,99,129]	https://www.promishealth.org Assesses 8 HRQoL domains: physical function, anxiety, depression, ability to participate in social roles, sleep disturbances, pain interference, pain intensity, fatigue	Internal consistency, reliability, and construct validity in SSc-ILD; uncertain discrimination and change over time
Center for Epidemiologic Studies-Depression scale (CES-D)[4,5,20]	CES-D is a 20-item questionnaire that measures depressive symptomatology using Likert scales of 0 to 3, and the total score ranges from 0 to 60. Scoring above 16 denotes possible depression	CES-D is a reliable and valid instrument for measuring depressive symptoms in SSc. Specific cut-off scores need to be established.
Ten-Item Personality Inventory (TIPI)[6,21]	TIPI is assessing five major personality dimensions on a 7-point scale	Not specifically tested in SSc
UCLA—Loneliness Scale[22]	20-item questionnaire, a commonly used measure of loneliness. There are shorter versions, for example,.ULS-8 (8-item version)	Not specifically tested in SSc
Body Image		
The Brief-Satisfaction with Appearance Scale (Brief SWAP)[11,16]	Easy 6-item self-administered questionnaire Items are scored on a seven-point scale ranging from 0 to 7. Higher scores indicate greater dissatisfaction or social discomfort.	Internal consistency, reliability, and construct validity in SSc; Sensitivity to change has not been studied.
Derriford Appearance Scale short-form[7]	DAS-24 is a 24-item questionnaire that measures distress and dysfunction related to physical appearance	Internal consistency, reliability, and construct validity in SSc

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Table 5
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Instrument	Item Breakdown Qualities	Demonstrated Use in SSc
Sexual Dysfunction		
The International Index of Erectile Function (IIEF)—for male patients[45]	The IIEF includes five questions on erectile function, orgasmic function, sexual desire, intercourse satisfaction, and overall sexual satisfaction with each item being scored from 1 to 5. A scoring <22 denotes possible erectile dysfunction (ED)	IIEF is a fully validated measure of ED in the general population. IIEF has been used in some clinical studies with SSc patients; uncertain discrimination and change over time
Female Sexual Function Index Scoring (FSFI)[32,41]	19 items that easily assess desire, arousal, satisfaction, lubrication, orgasm, and pain on vaginal penetration	Fully validated instrument of sexual function in the general population. In some clinical studies with SSc patients, FSFI has been used.
Qualisex[35,130]	10-item questionnaire with less intimate questions on the influence of the respective disease on sexual function. The score ranges from 0 to 10 with higher scores indicating more sexual impairment.	No validation process has been performed in patients with SSc. In one clinical study, Qualisex has been used in patients with SSc.[130]
Pelvic Floor Impact Questionnaire Short Form 7 (PFIQ-7)[34,43]	7-item self-administered questionnaire to evaluate sexual function in women	No validation process has been performed in patients with SSc. In one clinical study with SSc patients, PFIQ-7 has been used.
Pelvic Organ Prolapse/Urinary Incontinence Sexual Questionnaire Short Form (PISQ-12)[34,42]	12-item self-administered questionnaire to evaluate sexual function and urinary incontinence in women	Validated measure in the general population. In some clinical studies with SSc patients, PISQ-12 has been used
Fatigue, Sleeping Disorders		
Functional Assessment of Chronic Illness Therapy Fatigue Scale (FACIT-F)[16,17]	FACIT-F is a 13-item measure designed to assess tiredness, weakness, and difficulty managing daily activities due to fatigue in the past 7 d. Items are scored on a 5-point Likert-type scale Total scores range from 0 to 52, with higher scores indicating less fatigue.	Internal consistency, reliability, and construct validity in SSc; Sensitivity to change has not been studied.

Multidimensional Assessment of Fatigue (MAF)[168]	MAF, with 16 items, is used to evaluate fatigue. The score ranges from 1 to 50 and higher scores signify greater fatigue.	The MAF in Swedish has been validated in SSc (internal consistency, reliability, and construct validity).
Pittsburgh Sleep Quality Index (PSQI)[15,169]	PSQI has 19 items and measures 7 components of sleep quality: subjective sleep quality, sleep latency, duration, habitual sleep efficiency, sleep disturbances, use of sleeping medication, and daytime dysfunction (each domain score ranges between 0 and 3).	No validation process has been performed in patients with SSc. In some clinical studies with SSc patients, PSQI has been used.
Family relations, social functioning, Disease impact on professional and social life		
PROMIS-29[19,129]	See above	See above
Scleroderma Health Assessment Questionnaire (SHAQ)	A 30-item questionnaire that assesses the global impact of SSc addressing overall perceived disease severity, pain, fatigue, organ-based physical impairment, and SSc-specific symptom interference in daily life and self-care as well as need for assistance.	Widely validated in SSc. Routinely used in SSc centers and in SSc clinical trials. The most global and specific PROM in SSc.
Short Form 36	HRQoL generic measure with 36 items evaluating the physical function, energy, pain, mental health, social participation, and perceived health status,	Widely used to assess HRQoL in SSc
Short Form of Social Support (SSq)[5,23]	A 6-item questionnaire, which consists of two parts: the number of persons that provide support to each participant (min. 0, max. 9) and the level of satisfaction from that support, measured on a 6-point scale (1 to 6).	Clinical studies with SSc patients have used SSq.
The Ways of Coping Checklist—Revised (WCCL-R)[24,25]	WCCL-R is a 57-item self-report measure, it yields 8 coping subscales: problem-focused, wishful thinking, seeking social support, avoidance, self-blame, blaming others, counting one's blessings, and religiosity.	WCCL-R has been used in one clinical study of patients with SSc.

used self-administrated questionnaire in clinical practice and studies.[41] The association of impaired sexual function and pelvic floor function in women with SSc has been recently shown.[42] The Pelvic Floor Impact Questionnaire (PFIQ-7) and Pelvic Organ Prolapse/Urinary Incontinence Sexual Questionnaire (PISQ-12)[43] easily assess the severity and impact of pelvic floor muscle impairment. Clitoral circulation as assessed by resistive index (RI) and the systolic/diastolic (S/D) ratio of clitoral blood defined by color Doppler ultrasound have uncertain clinical significance.[37,38]

Sexual health in male patients

SDF in men with SSc, especially ED, is highly prevalent (~80%) and an early occurring symptom within 4 years of SSc onset.[30,32,39,44,45] Impairment of endothelial-dependent smooth muscle relaxation (functional vascular ED, initial stages), the occlusion of the corpus cavernosa arteries by fibrotic lesions (structural vascular ED, late stages) or a combination of these processes contribute to SSc-related ED.[45,46] Complex interactions between subclinical autoimmune inflammation, myo-intimal proliferation of the small penile arteries and corporal fibrosis underlie SSc-related ED pathophysiology.[32,39] Common risk factors for ED include hypertension, diabetes mellitus, obesity, and smoking, whereby endothelial dysfunction and low level of inflammation has been identified.[32,39,45] However, progressive SSc vascular disease is associated with rapidly developing ED, underscoring the importance of routine screening in the "very early" phase of SSc.[32,39,45] The International Index of Erectile Function (IIEF), a widely used, easily self-administered assessment tool[46] that investigates erectile function, orgasmic function, sexual desire, intercourse satisfaction, and overall sexual satisfaction.[47] A lower IIEF score is associated with higher scores on the Beck Depression Inventory.[44,48] Early urologic referral and initiation of ED treatment may prevent progression to arterial occlusion. Penile color Doppler ultrasound and hormone panel comprise the routine workup.[32,39,46,47]

Vascular Experience in Systemic Sclerosis

Raynaud's phenomenon

Raynaud's phenomenon (RP), being a hallmark SSc feature, its absence prompts consideration of 'scleroderma mimics'.[49] The sub-absolute reporting of RP prevalence of ~96% in SSc likely reflects either strict adherence to a report of bi-phasic color changes which are not present in all patients with SSc-RP, or non-standardized history-taking, especially for non-whites.[50,51]

Preserving core temperature facilitates maximal digital vasodilatation of thermoregulatory arteriovenous anastomoses.[52,53] SSc-RP symptom burden doubles over winter,[54,55] and exposure to drastic temperature changes such as air-conditioning or during grocery-shopping. Counseling on the importance of vigilance for cold situations, carrying hand warmers, gloves, and extra layers of clothing and, if needed, smoking cessation can help avoid and/or ameliorate SSc-RP symptoms.[50,53,56,57]

Digital ulceration and calcinosis cutis

Digital ulcers (DUs) occur in over half of SSc patients and contributes largely to SSc disease-related morbidity.[58] Previous DU, dcSSc sub-type, elevated inflammatory response, early-onset RP and anti-topoisomerase antibody presence increase DU occurrence risk.[59,60] Categorizations of DU etiopathogenesis have been attempted without consensus that includes purely/true ischemic (typically digital tip), mechanical or friction (typically over extensor aspects held in fixed flexion) and mixed etiology (eg, those overlying calcinotic deposits).[61] Patterns of DU occurrence, with or without calcinosis present, show ~50% of patients with recurrence, 1/3 solitary DU, ~10% infrequent episodic DU, and ~10% "chronic" refractory DU.[62]

SSc-DUs are scleroderma emergencies. Digital ischemic lesions and calcinosis warrant documentation at routine clinic visits, with vasodilator and other approaches optimized to reduce DU and pain burden.[53] DU emergence and healing are often influenced by modifiable exposures such as cold exposure, local trauma, or soft tissue (or deep) infection.[58,63–66] Calcinosis cutis forms at the foci of ischemic injury, often at sites overlying the extensor aspects of joints that are regularly subject to local pressure or the blanching effects of taught skin.[67,68]

Anticipatory guidance and early intervention with hand therapy, counseling on RP management and skin care, and protection against trauma and microtraumas by joint cushioning or work glove use (especially in people with known flexion contractures or evidence of tissue vulnerability by visible blanching of sclerotic skin). Smoking, being an independent risk factor for DU occurrence, makes smoking cessation an imperative.[52,53,66,69,70]

Prodromal symptoms of ischemic pain, "pressure" and local inflammatory symptoms help patients predict DU emergence.[64] Counseling patients on red flag symptoms and complications such as infection or calcinosis[71] along with contact details for prompt reporting and assessment of new lesions is critical. Patient education in infection prevention, wound care, and dressing strategies are crucial to healing, that is, wet ulcers managed with alginates and antimicrobial dressing to promote drying, and dry ulcers kept moistened with local application of hydrogel or hydrocolloid dressings.[53,71]

Cutaneous Experience in Systemic Sclerosis

Skin thickening

Skin thickening or subcutaneous edema reflecting the inflammatory transformation to fibrosis is a classic consideration in SSc that is *not always present*. The *pattern* of skin thickening provides the basis for SSc disease subsets.[72] All subsets including *sine scleroderma* are serious life-threatening illnesses. However, documenting changes in the extent and severity of skin involvement (eg, telangiectasias, skin score), especially in early disease, can guide prognostication and aggressivity of investigation and systemic treatment.

Skin thickening in early phases often gives rise to subcutaneous inflammation and edema resulting in diffuse pain/tenderness (often mistaken for fibromyalgia) and pruritus. In addition to counseling on general skincare (eg, moisturizing, sun-protection), anti-pruritus strategies, early referral to occupational and physical therapy for face/mouth and joint exercises to prevent/mitigate contracture formation and microstomia[66,73] may be pivotal to HRQoL.

Soft tissue vulnerability, pigment, and vascular changes

SSc results in vulnerability to soft tissue injury, ulceration, and infection; warranting guidance on skin protection, for example, wearing gloves when gardening, handling chemicals, or activities prone to microtrauma. Pigmentary changes and telangiectasia are associated with body image dissatisfaction and emotional distress. If dissatisfaction is detected, counseling on laser treatments, camouflage cosmetics, and other mitigating strategies might be introduced.[66,74,75]

Musculoskeletal Experience in Systemic Sclerosis

Most patients with SSc develop disabling musculoskeletal (MSK) symptoms with joint, tendon and muscle involvement. Early referral of and maintaining intermittent care from occupational and physical therapy can preserve function and mitigate progression.

Articular involvement

Extent of synovitis, chronic tendinitis and tendon friction rubs (TFRs) are independent predictors for overall disease progression, development of new DUs, and decreased left ventricular ejection fraction in early-phase SSc.[76] Arthritis-related disability and diminished HRQoL is most strongly experienced in the hands resulting in pain, stiffness, contractures, and extensive disability. Progressive articular involvement is a marker of active disease—*even if slowly progressive*—and without early intervention can become irreversible regardless of antibody presence/specification.[77]

The Health Assessment Questionnaire Disability Index (HAQ-DI), the Cochin Hand Function Scale[78] are validated simple instruments for measuring hand function and disability in SSc.[79,80] Similarly in RA, inflammatory articular involvement is easily monitored using the Disease Activity Scores of 28 joints (DAS28),[81] except that in SSc the number of tender and swollen joints is expectedly less. Interestingly, on ultrasound, joint effusions do not appear to differ between SSc and RA patients, but SSc patients show lower prevalence of synovial proliferation.[82] Progressive and, in many cases, irreversible joint erosions and other MSK involvement often occur sub-clinically, making color Doppler ultrasonography, MRI, and MR angiography (MRA) useful techniques to evaluate joint, muscle and synovial vascularity, thus the active MSK inflammation.[83]

Muscle involvement

Myopathy in SSc is frequently under-recognized with prevalence varying from 5% to 96%[84] SSc-myopathy can reflect atrophy, inflammatory, vasculopathic, fibrotic, or necrotic pathology. Both muscle strength and endurance in proximal muscles are commonly reduced[85] especially in patients with significant lung disease and predicts SSc-related cardiac involvement.[85–92]

Several auto-antibodies are predictive of SSc-myopathy: anti-PM-Scl, anti-topoisomerase-1, anti-Ku, anti-U1-RNP, anti-U3-RNP, anti-Jo, and anti-RuvBL1/2.[93] Basic diagnostic testing includes serum creatine kinase (CK), aldolase, inflammatory markers, and transaminases. However, a normal CK value does not exclude the presence of inflammatory myopathy.[84,93] Supportive investigations include electromyography (EMG), imaging modalities (US, MRI), and muscle biopsy.

Although the Manual Muscle Test (MMT-8) assesses moment muscle strength (on a 0 to 10 scale) of eight muscle groups commonly affected in idiopathic inflammatory myopathies (IIMs),[93] the Functional Index-2 (FI-2) and FI-3 evaluates muscle weakness and endurance in IIMs. Muscle endurance is the more sensitive performance outcome in IIM. FI-2 uses time-controlled repetitive movements such as shoulder flexion, shoulder abduction, head lift, and hip flexion, whereas FI-3 is equally validated and focuses on three muscle groups requiring 3 minutes to administer.[93]

Maintaining muscle mass, strength, and physical activity are key predictors of frailty and mortality across health conditions including SSc.[94–96] During muscle contraction hundreds of pro- or anti-inflammatory and metabolic cytokines (myokines) are synthetized, for example, interleukin-6, Irisin, and Meteorin-like adipomyokine.[97] Optimally dosed aerobic and strengthening exercises have positive effects on the whole organism through myokine production and maintenance of physical capacity in many chronic diseases.

Gastrointestinal Experience in Systemic Sclerosis

Oral and gastrointestinal involvement occurs in virtually all SSc patients from the oral cavity through the upper and lower GI tract and anus and remains a leading cause of SSc death with the most common causes being malabsorption, malnutrition, hyperalimentation, hemorrhage from ectasias along the GI tract, or obstruction[98,99] (**Fig. 2**). GI

involvement correlates with patient-perceived disease severity, distress, and lower HRQoL that is worse even than that associated with severe PH, ILD, renal and cardiac involvement.[100,101] Reduced esophageal motility with lower esophageal sphincter relaxation (LES), gastroesophageal reflux disorder (GERD), lower intestinal dysmotility leading to bloating, diarrhea, and/or constipation, small intestinal bacterial overgrowth (SIBO) and malabsorption, and fecal incontinence are frequently reported SSc-GI manifestations.[102] GI symptoms often progress over the disease course.[103] Patients express frustration that despite the extent and severity of their GI manifestations, they often lack support from rheumatologists generally avoiding GI-related discussion.[1] Diagnostic and therapeutic interventions can be guided by a dietician, speech therapist, and gastroenterologist.[104]

Of note, GERD has far-reaching detrimental impacts on the esophagus and the lung. Premalignant and malignant injury, structural abnormalities such as webbing, scarring, strictures, and esophageal dysmotility were more common before proton pump inhibitor (PPI) use; with severe esophageal dysfunction, being a major cause of malnutrition and mortality. Endoscopic findings of esophageal injury can occur in the absence of heartburn or regurgitation. Further, GERD plays an inciting role in the extent of ILD, as may post-nasal drip.[105] **Table 3** provides essential SSc-GI and oral health counseling points, the Giessen GI Questionnaire is a direct and simple GI assessment for the detection and severity of symptoms clinical use[106]; however, the UCLA GIT is more elaborate and helpful to monitor the frequency of symptoms.[107]

Cardiopulmonary Experience in Systemic Sclerosis

Respiratory-type symptoms

Breathlessness, exercise intolerance, and cough in SSc is often multifactorial and can be related to diverse, severe complications other than the onset or worsening ILD or PH; and require careful consideration as to cause (**Table 6**). ILD, PH, anemia, heart

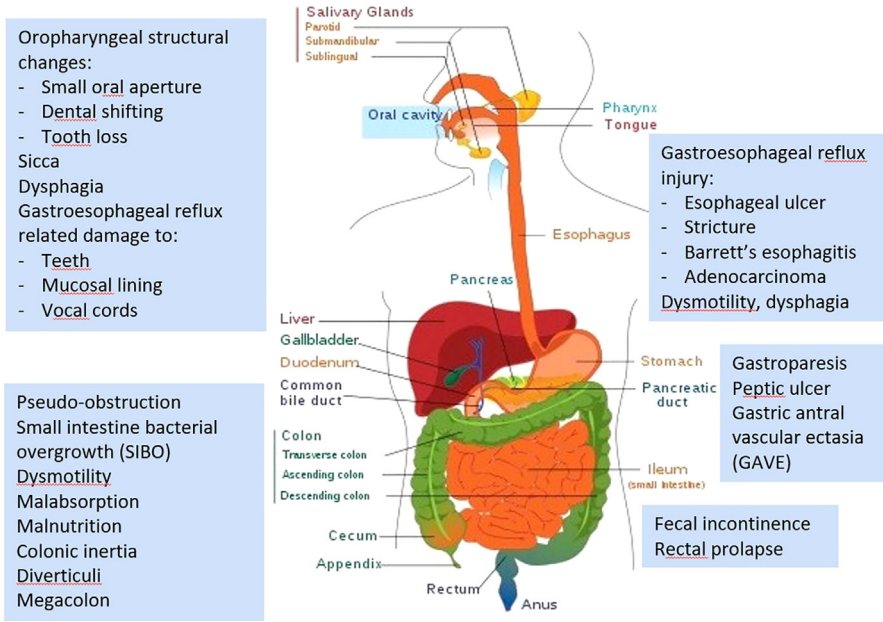

Fig. 2. Depiction of the diffuse nature of gastrointestinal involvement in SSc. (*Courtesy of* T Frech, MD, MS, Nashville, TN.)

involvement, physical deconditioning, GERD, and anxiety are common causes of SSc respiratory symptoms and are not mutually exclusive. Cylindrical bronchiectasis, bronchiole wall weakening resulting in mucous stasis and sub-acute infection, as well as pneumonia, occurs not uncommonly in SSc.

Symptom development is often quite subtle. When symptoms become apparent to the patient, lung involvement is usually significantly progressed. Patients may not recognize or explicitly complain of breathlessness; instead, they unwittingly modify pace, intensity, and types of activities to avoid the biophysical stress creating the symptoms. Careful historical probing may reveal experiences of decreased exercise tolerance, intensity, speed and/or duration of daily activities, and an unconscious slowing of movement (**Table 7**). Queries on "change over time" of these parameters are necessary to facilitate patient (and their loved ones) recall.

Queries more specific to ILD include breathlessness and coughing with deep inspiration or activities requiring deeper inspiration such as laughing, sneezing, walking-talking, or a catching sensation with inspiration which suggest a restrictive process like ILD.[108–111]Patients often restrict inspiration to avoid symptoms, which often results in incomplete inspiration during the physical examination and therefore ILD physical examination findings (ie, basilar crackles) and tell-tale inspiratory cough[108–111] are missed on clinical assessment.

Cough in SSc is associated with increased ILD severity and worse HRQoL.[112,113] Exertion and/or inspiration can trigger frightening, embarrassing, exhausting, and inconvenient episodes of dyspneic coughing with prolonged recovery phases.[108–111]

Table 6
Common causes of dyspnea and cough in systemic sclerosis

ILD	ILD—Dry Inspiratory
Pulmonary hypertension—any or any combination of the following: Groups I, II, III, and IV	
Heart failure	Heart failure
Bronchiectasis[a]	Bronchiectasis[a]
Pneumonia	Pneumonia
Cardiac dysfunction or arrhythmia	
Anemia—*GAVE* or chronic inflammatory disease	
Physical deconditioning/Lack of Physical Activity	
	GERD—can be "wet" cough/gastroparesis
	PND—possible drip sensation, often in the morning, sore throat
Disordered breathing patterns/dysfunctional breathing	
Depression/fear of physical activity	
CAD, COPD/history of Smoking	

Abbreviations: GAVE, gastric antral vascular ectasia; GERD, gastroesophageal reflux disorder; ILD, interstitial lung disease; PND, post-nasal drip.

[a] *Bronchiectasis* can be either *traction* (extrinsic pulling and distortion of the bronchioles often seen in pulmonary fibrosis on HRCT) or *cylindrical* (laxity of the bronchiole wall either due to infection or perhaps CTD itself, creating a stasis environment for bacteria cough is often productive).

Courtesy of LA Saketkoo, MD, MPH, New Orleans, LA.

Table 7
Screening questions to help patients reflect on potential onset and changes in dyspnea and cough

DYSPNEA Screening	COUGH Screening for ILD
Do you notice being more short-winded now than 1 mo ago? 3 mo ago? 6 mo ago? last year? while doing activities (consider activities likely for the patient)?	Have you been coughing? Do you feel it's been the same or worse in the past 3 mo? 6 mo?
Do you notice you are becoming shorter of breath when vacuuming, making the bed, or mowing the lawn?	Are you coughing anything up? Is your cough dry?
Do you notice it takes you longer to, for example, vacuum, mop, make the bed, and mowing the lawn?	Do you cough when taking a deep breath in?
Do you notice that you need to take more breaks when going upstairs, walking, vacuuming, mopping, making the bed, and mowing the lawn?	Do you cough with laughing or sneezing?
Are you able to keep up with family members/ peers when walking? Do you feel they slow their pace for you? Do you find it difficult to walk and talk at the same time?	Do you cough while talking?
Do you feel that bending over takes your breath away?	Does coughing make you feel short-winded?
Do you notice a "catching" sensation when taking a deep breath in?	

See Table 5 for potential causes of respiratory symptoms in systemic sclerosis.
Courtesy of LA Saketkoo, MD, MPH, New Orleans, LA.

Lung involvement in systemic sclerosis

Cardio-respiratory manifestations are associated with deterioration of the physical condition and early mortality in SSc.[114–116] ILD and PH are the leading causes of SSc-related death. Early identification and initiation of early appropriate treatment prolongs survival.[117–119] Careful history, pulmonary function testing (PFTs) including diffusion capacity of the lung for carbon monoxide (DLCO), high-resolution CT scan (HRCT), echocardiogram and exercise tolerance testing (6-min walk test (6MWT)) for distance and oxygen saturation (preferentially by forehead oximeter[115,120]) are key assessments (**Figs. 3** and **4**).

HRCT is the gold standard to screen for and diagnose SSc-ILD and with a typical pattern that is, usual or nonspecific interstitial pneumonitis (UIP or NSIP) makes lung biopsy unnecessary. PFTs, though crucial for trending baseline and follow-up studies, are inadequate in detecting ILD particularly in the early stages.[121] Repeat HRCT is reserved to investigate unexplained symptoms or PFT worsening to ascertain other possible causes versus progressive ILD. Bronchoscopy helps investigate co-existent concerns of infection or malignancy.

ILD behavior is highly variable and requires a vigilant individualized approach. Maintaining a chart trajectory from the first available studies affords insights into behavior patterns that is, rapidly progressive versus stable versus slowly progressing ILD.[122] Trajectory charting prevents ignoring progressing disease as any $\geq$5% decrease in FVC or DLCO over 6 months despite normal range values warrants investigation and likely treatment.

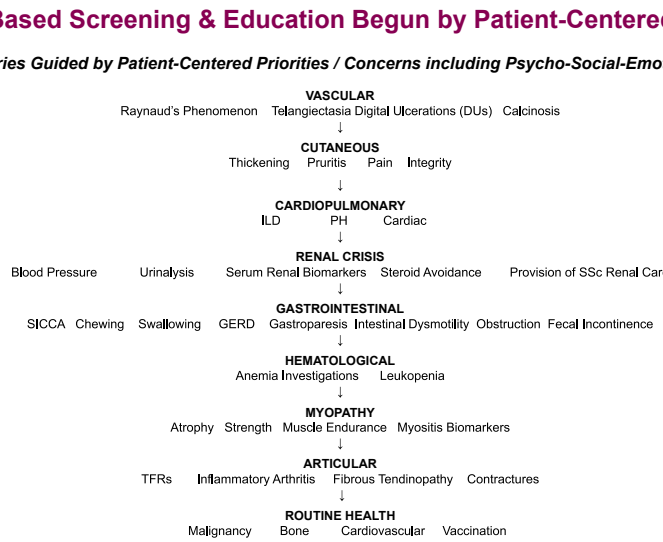

Fig. 3. Overall framework to approach biophysical assessment.

ILD and PH often coexist, and can be temporally coincident in early SSc, especially in patients of African descent. PH in SSc can be of either WHO Group 1, 2, 3, or 4; and more commonly PH group types coexist together. Right heart catheterization is required to diagnose PH. However, annual echocardiogram without following trends of patient symptoms (*dyspnea, fatigue, exercise tolerance*), serum NT-pro-BNP, 6MWT *distance,* and *oxygen saturation levels*, is unreliable missing up to 40% of RHC-confirmed SSc-PH cases.[123]

DLCO provides an early detection mechanism for PH and when compared with FVC or TLC can differentiate parenchymal from vascular lung disease. DLCO reflects gas

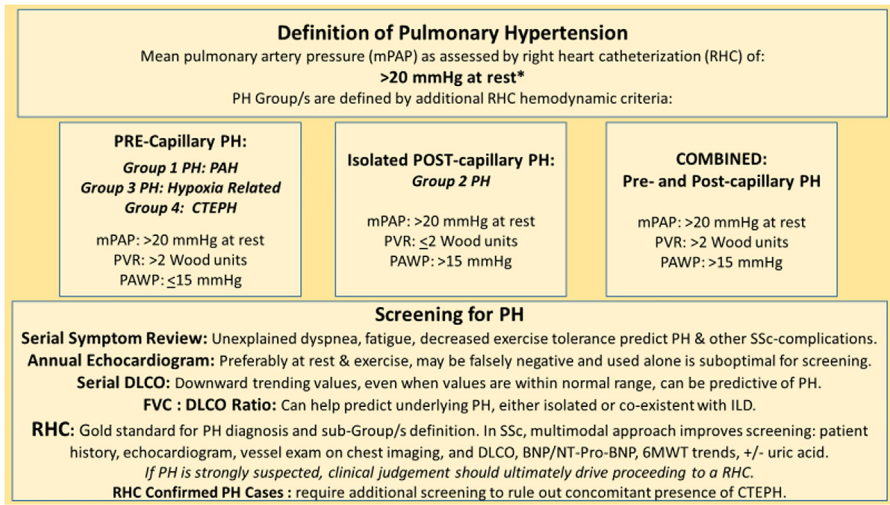

Fig. 4. Screening and characterization of pulmonary hypertension in SSc. (*Courtesy of* LA Saketkoo, MD, MPH, New Orleans, LA.) *'Exercise Induced PH' is defined by mPAP/Cardiac Output slope between rest and exercise; 'Unclassified PH' is defined as mPAP >20mmHg but low PVR (≤2 Wood units) and low PAWP (≤15mmHg); >3mmHg/L/min. Humbert, M., Kovacs, G., Hoeper, M. M., et al. ESC/ERS Scientific Document Group (2022). 2022 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension. European heart journal, 43(38), 3618–3731.

transfer from airspace to the bloodstream which requires gas to diffuse across *two barriers*: the *lung parenchyma* and the *vascular wall*. Resistance to permeable gas of either or both barriers causes reduction in DLCO. In ILD the FVC and DLCO trend downward in parallel; however, in PH the DLCO declines more steeply than FVC. However, in early SSc-ILD, the FVC may be stable, whereas the DLCO decreases, but generally FVC:DLCO ratio helps distinguish between the presence/predominance of PH from ILD.[124,125]

Lung transplantation in SSc is safe, for patients with progressive lung disease despite maximal therapy. Early discussions on transplant evaluation permits time for familiarization with the transplant process, make informed unhurried decisions, and adjust to psychosocial and financial pressures related to transplant. It also provides lead time for habituation of healthy life practices including optimizing fitness supported by pulmonary rehabilitation.[116]

Cardiac involvement in systemic sclerosis

Microvascular insufficiency, or inflammatory-fibrotic infiltration of the myocardium, may underlie SSc-cardiac involvement causing arrhythmias, diastolic or systolic dysfunction, pericarditis, or myocarditis. Cardiac involvement is often associated with SSc-myopathy.[89–91] Noncontrast cardiovascular magnetic resonance (CMR) may play a role in early diagnosis and has shown a 45% prevalence of myocardial fibrosis unexplained by other causes. Cardiac involvement is often associated with diffuse skin involvement, elevated CRP, and upward-trending NT-Pro-BNP.[126,127]

Renal Experience in Systemic Sclerosis

Before the recognition of risk factors and *early* effective intervention with angiotensin-converting-enzyme inhibition (ACEi), scleroderma renal crisis (SRC) was the leading cause of SSc-related mortality.[99,128–130] Delayed ACEi continues to lead to poorer outcomes.[130] However, the prophylactic role of ACEi has been associated with increased incidence of SRC and with poorer outcomes.[131,132]

Clinical and serologic risk factors for SRC[130] can be nonmodifiable such as dcSSc subset, early rapidly progressing skin disease and the presence of anti-RNA-polymerase III antibodies[133]; or modifiable such as corticosteroid exposure (prednisolone >10 to 15 mg daily).[133–135]

Notwithstanding the lack of clear SRC screening standards, educating high-risk patients about SRC and the provision of the SRC prevention card (**Fig. 5**) can help patients and other health care professionals, especially emergency and primary care physicians, recognize SRC.[136] Despite the apparent rapidity of presentation, SRC likely has a protracted asymptomatic prodromal period, providing an opportunity to avert renal injury. Monitoring trends in routine simple point-of-care assessments such as blood pressure (BP) and urine-dipstick, and at-home blood pressure recording 2 to 3 times weekly can help identify SRC in the absence of symptoms. Red flags such as increased systolic BP 20 mm Hg above usual values, and features of malignant hypertension such as headaches or visual disturbance[137] are prompts to seek medical attention.

Additional Health Maintenance in Systemic Sclerosis

Vaccination

Dysregulated immune responses and widespread use of immunomodulatory drugs predispose to serious infection in SSc, thrusting rheumatologists into the pivotal role of advocating for vaccine adherence in SSc[138,139] (**Table 8**). However, lack of specialist recommendation (36.1%) topped the list, along with fear of side effects (23.1%) or of inefficacy (4%), in reported reasons for influenza vaccine noncompliance in SSc.[140] Similarly, poor vaccine compliance with pneumococcal vaccine[140]; occurs

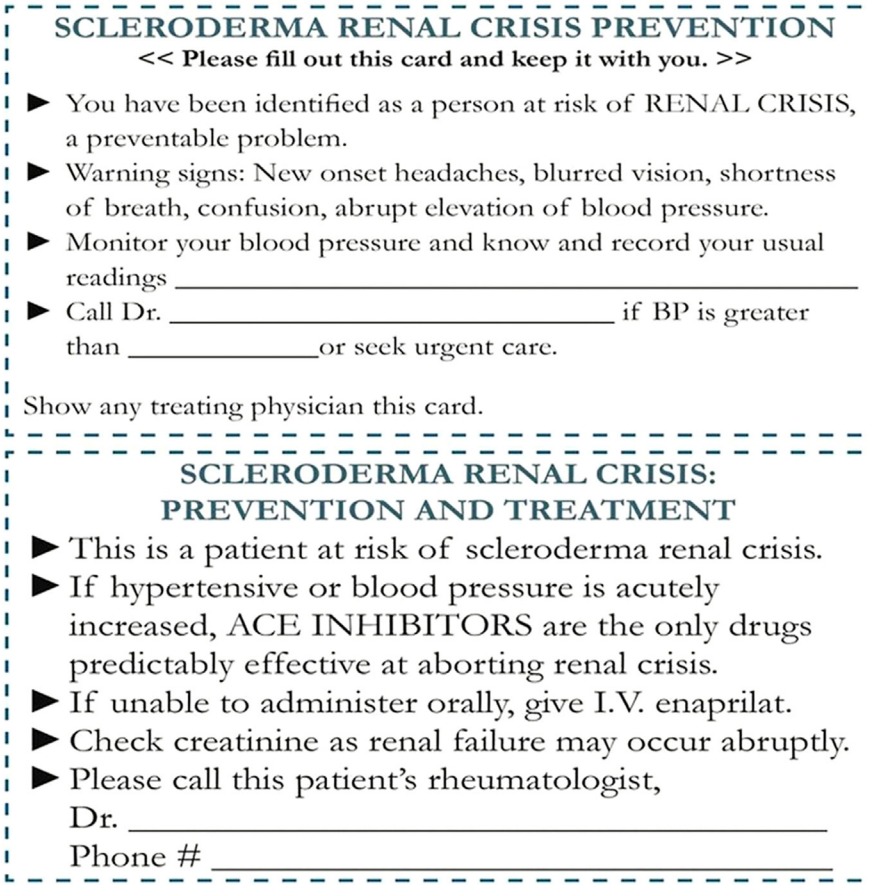

Fig. 5. Renal crisis prevention card may help patients direct emergency health care providers to abort a crisis and avoid adverse outcomes.[136] (*From* Shapiro, L, Saketkoo, L, Farrell, J et al AB0712 Development of a "Renal Crisis Prevention Card" as an Education Tool to Improve Outcomes in High Risk Patients with Systemic Sclerosis (SSC). Annals of the Rheumatic Diseases 2015: 74: 1136.)

despite a higher rate ratio of pneumococcal-related hospitalization in SSc (4.2 vs 3.7 for diabetes).[141]

SSc immunomodulatory treatments create concern for vaccine efficacy, but regardless whenever possible adherence to vaccination schedules is essential to SSc care vaccination timing (eg, around rituximab therapy use) informed by most current approaches.[142–146] Hematopoietic stem cell transplant (HSCT) requires re-vaccination as immunologic memory to vaccines is often lost (>24 months for live vaccines).[147–149] Administration of "killed" (pneumococcal, influenza, hepatitis B, and zoster) vaccinations, including for SARS-CoV-2, are key in patients receiving immunosuppressants.[150,151] The malignancy risk associated with SSc, makes the recombinant (human papillomavirus, HPV) vaccination an important consideration.[152]

Cancer screening

A close temporal relationship exists between cancer and SSc. SSc confers relative risks (RR) ranging from 1.55 to 1.81[153,154] with 7.1% to 14.2% of patients having a history of cancer. Cancer accounts for ~16% of deaths in SSc[155]; with breast,

Table 8
Health maintenance screening in systemic sclerosis

Immunizations	Inactive formulations of vaccines: Influenza (annually) COVID-19 according to guidelines for vulnerable/immunocompromised Hepatitis B series Pneumococcal series Diphtheria/tetanus/pertussis Varicella Zoster vaccine/Shingles (Shingrix) HPV series for females
Age-appropriate malignancy screening	Gynecologic Breast Prostate Colon Annual skin cancer screening Smoking history with cognizance of lung and oral malignancy potential Lung cancer screening
Cardiovascular	Appropriate assessment and treatment to target hypertension, diabetes, and high cholesterol Routine screening for pulmonary hypertension and heart failure Consider screening for OSA Weight trends especially in those with pulmonary hypertension or heart failure Regular assessments of volume status
Bone health	Risk factors for DEXA screening earlier than 65 years old: Osteopenia on radiographs History of fracture History of malabsorption Corticosteroid use Low serum testosterone Prolonged use of proton pump inhibitors
Ophthalmologic health	Evaluation and management of SICCA-type symptoms Hydroxychloroquine toxicity screening, as applicable Visual acuity
Dental health	Twice-yearly routine dental visits are advised Evaluation and management of SICCA-type symptoms Evaluate for impact on nutritional intake

Courtesy of LA Saketkoo, MD, MPH, New Orleans, LA.

hematological, skin, and lung cancers being most prevalent,[156,157] particularly with anti-RNA-polymerase III and anti-topoisomerase antibody positivity.[153,156,158–160] Though formal guidelines are not yet established, age-appropriate malignancy screening should be rigorously adhered to, and symptoms suggestive of possible malignancy should be met with a low threshold for investigative imaging.

Cardiovascular disease

Vasculopathy, having an indisputable central role in SSc pathology, provides a strong rationale for screening and modification of traditional cardiovascular risk factors (such as prioritizing smoking cessation) to avert additive damage to already vulnerable vasculature.[53] Beyond this, enhanced cardiovascular risk in SSc[161] is suggested by increased carotid intima-medial thickness with reduced flow-mediated dilatation,[162] increased coronary calcifications,[163] and the risks of MI and stroke being approximately 2-fold in SSc compared with controls.[164]

Bone health in systemic sclerosis

Patients with SSc seems to be at greater risk of low bone mineral density and fracture, with risk highest amongst patients with known risk factors for reduced bone density for example, corticosteroid use, and fracture history.[165,166] No formal guidance exists for osteoporosis screening in SSc. Thus prevention rests on the recognition and modification of risk factors such as nutritional impairment, immobility, sedentary indoor lifestyle, corticosteroid exposure, and smoking cessation counseling.[166] Long-term proton pump inhibitor use in SSc also increases concerns around fracture risk.[167]

SUMMARY

Presented here is a paradigm of philosophic approach to prioritize HRQoL with biophysical elements being a crucial pillar in attaining this priority. Though the clinician's level of care and vigilance of the biophysical aspect may not alter, this patient-centered approach may sensitize us to the importance of SDM, empowering patients with anticipatory guidance and counseling, and the value of more readily and proactively integrate the experience of living with SSc into clinical decision-making.

CLINICS CARE POINTS

- Routine assessment of HRQoL in SSc may provide clinical guidance to pressing and treatable patient concerns.
- Screening for depression, anxiety, sleep, fatigue and sexual dysfunction in people with SSc may reveal treatable conditions that markedly improve HRQoL in SSc.
- Pain and Fatigue are each multi-factorial experiences in SSc and require careful assessment to identify and treat their cause/s.
- Raynauds, digital vascular complications and hand impairment are key sources of disability in people with SSc. Proactive history, assessment, counselling and early referral to occupational therapy are key to controlling symptoms and preserving function.
- Gastrointestinal impairment and dysfunction is a leading cause of poor HRQoL in people living with SSc. Routine assessment of symptoms, proactive management and counselling may markedly improve HRQoL in SSc.
- Screening for ILD and PH requires a vigilant multi-modal approach that combines history, pulmonary function, exercise testing and imaging for all SSc sub-types.
- DLCO trend is an important predictor of ILD and/or PH in people with SSc.
- RHC is the gold standard for diagnosis and classification of PH. Though multiple diagnostic variables should be considered, the decision to perform a RHC relies heavily upon a clinician's judgement.
- Multiple types of PH can co-exist in a person with SSc.
- A wallet card, anticipatory counselling and home blood pressure monitoring may help prevent death and disability for people with SSc who are at higher risk for Scleroderma Renal Crisis (SRC).

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