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A Comprehensive Framework for Navigating Patient Care in Systemic Sclerosis: *A Global Response to the Need for Improving the Practice of Diagnostic and Preventive Strategies in SSc*

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Abstract

Systemic sclerosis (SSc), the most lethal of rheumatologic conditions, is the cause of death in >50% of SSc cases, led by pulmonary fibrosis followed by pulmonary hypertension and then scleroderma renal crisis (SRC). Multiple other preventable and treatable SSc-related vascular, cardiac, gastrointestinal, nutritional and musculoskeletal complications can lead to disability and death.

Vascular injury with subsequent inflammation transforming to irreversible fibrosis and permanent damage characterizes SSc. Organ involvement is often present early in the disease course of SSc, but requires careful histories and vigilance in screening to detect. Inflammation is potentially reversible provided that treatment intensity quells inflammation and other immune mechanisms. In any SSc phenotype, opportunities for early treatment are prone to be under-utilized, especially in slowly progressive phenotypes that indolently accrue irreversible organ damage resulting in later-stage life-limiting complications such as pulmonary hypertension, severe ILD, cardiac involvement and malnutrition.

A single SSc patient visit often requires much more physician and staff time, organization, vigilance and direct management for multiple organ systems compared to other rheumatic or pulmonary diseases. Efficiency and efficacy of SSc care enlists *trending* symptoms and bio-data; and can be sustained financially by understanding insurance reimbursement policies. Sharing care between scleroderma centers and local cardiology/pulmonary/rheumatology/gastroenterology

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Conflict of interest:

None of the authors have conflicts of interest to report that are related to the reported content of this paper.

We dedicate this effort to people living with SSc and their grace and valor in the face of devastating disease. We also dedicate this collaborative work to Dr. Nadia Morgan a young, energetic, meticulous, creative and heartful SSc clinical scientist; her loss resounds in the SSc research community.

This work is endorsed by: *Federation of European Scleroderma Associations (FESCA), Scleroderma Australia, Scleroderma Canada, Scleroderma & Raynaud's UK (SRUK), and Scleroderma Foundation USA.*

colleagues may prevent complications and poor outcomes, while providing support to local specialists.

As scleroderma specialists, we offer a practical framework with tools to facilitate an approach to optimal, comprehensive and sustainable care in SSc. We anticipate this framework to remain relevant in the assessment, care and prevention of disease and treatment complications of this complex disease.

Keywords

interstitial lung disease; pulmonary fibrosis; renal crisis; pulmonary hypertension; disability; scleroderma; systemic sclerosis; symptom burden; quality of life; survival; mortality; health systems

I. INTRODUCTION

Systemic sclerosis (SSc), the most lethal of rheumatologic conditions, is the direct cause of death in >50% of SSc cases; led by pulmonary fibrosis, pulmonary hypertension and then scleroderma renal crisis (SRC). Multiple other preventable and treatable SSc-related vascular, cardiac, gastrointestinal, nutritional and musculoskeletal complications also lead to disability and death.

SSc is characterized by vascular injury and disrepair that incites systemic progressive inflammatory transformation to fibrosis at widely variable rates and intensities. Inflammation is a reversible phenomenon provided the intensity of treatment matches that of the inflammation. End-stage fibrosis is permanent and irreversible. Organ involvement is present early in the SSc disease course, requiring ongoing screening and careful patient questioning to detect. Reduction of disability and mortality hinges on prevention of vascular and fibrotic damage which is directly dependent upon early recognition of active disease, even in the indolent disease phenotypes, with initiation of appropriate treatment to prevent fibrotic transformation.

Delayed diagnosis is common in autoimmune diseases and disproportionately frequent in those of African and Hispanic descent, for whom these diseases tend to be more severe and deadly.[1–6] Importantly, slowly progressive phenotypes indolently accruing irreversible structural changes and organ damage are less prone to receive treatment, resulting in end-stage SSc complications such as pulmonary hypertension, cardiac involvement and malnutrition. Diagnostic delays, misdiagnoses and complication oversights are likely underpinned by preferential reliance on laboratory data in a clinical setting that is hurried and where authentic empathetic listening, careful history-taking and physical exam performance may be impaired.

Efficiency and efficacy of SSc care that meets the health-related quality of life (HRQoL) and survival needs of patients requires *trending symptoms and bio-data over time*; it also requires multiple streams of management that are sustained by understanding visit reimbursement policies. A single SSc patient visit commonly involves extensive investigation, coordination and direct management for multiple organ systems, exacting

physician and staff time and effort beyond other diseases. Sharing care between scleroderma centers and local specialists provides robust patient-centered management and patient skill-building for self-management of this complex disorder.

As scleroderma specialists, we offer an abbreviated reference manual and practical framework, that we hope supports clinicians and patients, with informational summaries on symptoms, manifestations and complications with tools and templates for screening, assessment, documentation, risk stratification, counselling and anticipatory guidance, and discussions surrounding clinician sustainability.

II. PATHOLOGIC DRIVERS IN SSC THAT IMPACT TREATMENT DECISIONS

A. Inflammation-Fibrosis Axis: From Preventable to Irreversible Damage

Beyond the widely heterogeneous nature of SSc presentation, progression and potential organ involvement, a major challenge impeding SSc care is the ability to distinguish between states of active progressive disease and its subsequent fibrotic damage. Inflammation-fibrosis transformation is a progressive process with an advancing front of potentially reversible inflammatory assault. Inflammatory tissue left untreated is damaged with increasing expanses of fibrosis. Inflammation and fibrosis are often coexistent, but with increasing fibrotic expanse leads to worsening irreversible disability and, possibly, death over time. Though currently difficult to distinguish with certainty, *even in the absence of ESR or CRP elevation* and regardless of coexistent fibrosis, concern for any degree of inflammation i.e. progression, should prompt consideration to initiate systemic immunomodulatory therapy.

Symptoms and impairment burden dynamically relate to the extent of either inflammation, fibrosis or a combination thereof (Figure 1). Symptoms worsen with extent of involvement; but potential symptom reduction or reversal with systemic treatment requires some degree of active tissue inflammation to be present. For example, progressive ILD, can manifest by dropping forced vital capacity (FVC), dry inspiratory cough, and breathlessness that improves after systemic treatment.[7–10] Whereas, residual inactive fibrotic damage resulting from prior inflammation is now unresponsive to immunosuppression.

B. Circulation and Mechanisms of Disease

Vasculopathy, vascular injury with tissue hypoxia and pathologic circulation interplay with and are drivers of inflammation and fibrosis. The earliest hallmark of SSc disease is vascular injury, dysfunction and disrepair, without evidence of inflammatory infiltration i.e. not vasculitis.[11,12] Vascular dysfunction and Raynaud's phenomenon (RP) symptoms predominantly predate non-RP symptoms by several years. In the genetically predisposed host, vascular injury may incite immune system activation through upregulation of adhesion cells and perivascular migration of immune cells, including macrophages, which may have a direct role in fibroblast stimulation.

The presence of *abnormal capillaroscopy* predicts the development of connective tissue disease (CTD) in patients with RP; and ANA positivity heightens that predictive power.[13] SSc nailfold capillaroscopy patterns are well-described reflecting the vasculature struggling

against the pathologic progression of the disease. [14](Figure 2). The presence of abnormal nailfold capillaries contributes >20% toward SSc classification criteria[15] and predicts[16] the development of a CTD [17]and SSc;[13,16,18,19] making capillaroscopy, with at least a handheld device, an essential assessment tool in rheumatologic care (Figure 3).

A normal nailfold bed demonstrates long thin hairpin loops resembling the abundance of wheat fields. In the 'early' and 'active' SSc patterns, the capillaries dilate and giant loops occur, as well as microhemorrhages, ballooning above the injured vessels. Later in the course of SSc, capillaries 'drop-out' leading to a rarefaction of the capillary network. Edematous 'puffy fingers' or diffuse infiltrative fibrosis sometimes make nailfold capillaries difficult to visualize. [19–25] The 'late' pattern is characterized by marked rarefaction and often reflects the vasculature's struggles to repair itself, albeit ineffectively despite high levels of circulating pro-angiogenic factors, creating a network of thin, matted vessels inefficient for supporting healthy tissue. This can be seen also in GI and skin i.e. GAVE and telangiectasias.

Lethal vascular complications such as PH and cardiac involvement correlate with other circulatory phenomena e.g. digital ulcers (DU), telangiectasias,[20,21] osseous vascular complications e.g. radiographic calcinosis, and acro-osteolysis,[22] and with inflammation-predominant complications e.g. arthritis and muscle involvement. These associations suggest a deep-rooted interplay between systemic inflammation, autoimmunity, fibrosis and vasculopathy.

Systemic autoimmune, inflammatory drivers influencing SSc vascular complications is a major current consideration in research and patient care.[23–27] SSc-specific autoantibodies help predict the potential clinical course and phenotypes in SSc patients, however, only functional antibodies not specific to SSc, such as the anti-endothelial cell antibody, demonstrate a direct pathogenic role; although reports are conflicting.[28,29] Healing of non-friction DUs upon initiation of systemic treatment e.g. mycophenolate mofetil (MMF), and subsequent DU re-emergence upon immunosuppression discontinuation, are anecdotally noted by SSc experts. Potential influence of immunosuppressants on improved outcomes in SSc-PH are increasingly being investigated.[23–27]

III. CONSIDERATIONS THAT DRIVE MANAGEMENT IN SSC

A. Goals of SSc Management

Preventing death and permanent disability in SSc is accomplished with early and appropriate treatment.—SSc is an extensively complex disease often with delayed diagnosis. By the time patients receive expert management, most will have permanently lost some degree of physical function and have diminished well-being, eroding one's ability to sustain the crucial life areas and personal satisfactions of family, intimate and social interactions including financial solvency. Recent data suggest initiating early treatment may prevent development of complications such as ILD.[30]

SSc is associated with significant unemployment, worker absenteeism, decreased worker productivity.[31] Preventable SSc-related work impairment results in substantial economic

burden and diminished HRQoL[32] with loss of work, lost income, and loss of health insurance and healthcare. Working closely with patients and their employers to attain appropriate modifications to their work environment and situation may improve functioning and improve productivity.[31–36]

B. Risk Awareness in SSc

The risk for and the actual rate of disease progression, guides the level of systemic treatment intended to quell inflammation and prevent further organ damage. They also identify patients with rapidly progressive disease potentially benefitting from hematopoietic stem cell transplantation (HSCT) before end-organ damage occurs. While there is no formal SSc risk stratification tool, certain factors put patients with SSc at even greater risk of death, disability and rapidly progressive disease (Table 1, 2). Sensitizing clinicians to these risk factors heightens vigilance for treatable lethal and/or permanently disabling disease.

It should be clarified that both limited cutaneous SSc (lcSSc) and diffuse cutaneous SSc (dcSSc) carry an increased risk of death. The terms *diffuse* and *limited* cutaneous are descriptors of skin thickness distribution only; and provide crude sub-typing of an extremely complex disease. However, limited sub-type may carry a higher risk of PAH, dcSSc carries higher risk for progressive ILD; and early dcSSc with rapid increases in skin thickening is associated new internal organ involvement.[37,38], [19,39–49] Both sub-types can develop ILD and PH, and malnutrition from severe GI involvement.

Autoantibodies are also helpful for predicting outcome, particularly anti-centromere predicting PAH, Scl-70 predicting ILD and RNA polymerase III predicting renal crisis (Figure 4). Race and ethnicity are also associated with increased risk of severe disease. Black race, compared to whites, independently predicts more rapid progression and higher mortality, more severe disease at a younger age of onset, and with higher risk of early and *concomitant* ILD and PH. These racial differences may be associated with distinct antibody and genetic profiles supporting that early aggressive intervention in blacks with ILD may offset mortality.[5,32] Hispanic and Asian ancestry also portends higher severity than whites.[50–52] Male sex, early diffuse cutaneous disease or presence of tendon friction rubs also confer increased risk of mortality.

C. Tracking Symptoms and Metrics for Recognition and Intervention

Any type of organized framework containing SSc domains and sub-domains that tracks changes in clinical features, symptomatology, complications and bio-data of multiple manifestations over time, facilitates a comprehensive and efficient care continuum. This also enables communication of important details across specialties. Such documentation captures SSc manifestations as they newly emerge, improve, resolve, stabilize or worsen, and creates an overview that depicts treatment responsiveness, potentially sparking consideration for new, additive or change in treatment approach. Tables 3–6 and the resource list provide example tools.

IV. MULTI-FACTORIAL SYMPTOMATOLOGY

This section addresses common SSc symptoms that have multiple or combined causes, approaches to distinguishing cause(s), and where applicable, therapeutic intervention. SSc being a disease of inciting vascular injury, special attention is given to RP in this section, though not a multi-factorial symptom, as it is pervasive and often not straightforward to diagnosis.

A. Cold in SSc, and Raynaud's Phenomenon specifically, is the most common symptom and highest ranked SSc-specific symptom diminishing HRQoL. Without preventive and palliative intervention, RP can lead to other vascular complications such as DUs, acro-osteolysis and calcinosis.[20,53–56] (Table 7) RP affects glabrous skin regions (fingers, toes, nipples, ears, toes). Glabrous skin's unique vascular structure contains large numbers of cutaneous arteriovenous connections. RP in SSc, triggered by stress or cold has variable duration and severity, generally lasts <20 minutes upon trigger removal, but can endure hours or days, or establish a new baseline severity upon which exacerbations occur.

The classic tri-phasic episodes of RP, more noticeable in lesser pigmented populations, demonstrates discoloration with distinct demarcation lines of *blanching* (white), *cyanosis* (blue/purple) and then *erythematous* (red) phase with rewarming, which can be the most painful phase. Not all individuals experience tri-phasic attacks, but some degree of blanching which may be difficult to notice in highly pigmented patients, supports a RP diagnosis.

While *Primary RP* may affect healthy individuals or be familial, SSc-RP vascular patterns are uniquely associated with vascular injury and vasculopathy. As previously mentioned, ANA presence with abnormal capillaroscopy predict CTD occurrence.[13] Similarly, puffy fingers, SSc-specific antibodies and abnormal capillaroscopy are highly predictive for development of SSc[57]

The impact of RP events on vital organ vasculature or hastening PAH, is lesser known, but patients report that episodes can result in systemic symptoms of whole-body heat loss, debilitating fatigue, headache in addition to worsening pain of DUs and calcinosis.[55,56,58] Thus, RP worsens diffuse, diverse disability, making recurrent preventive counselling imperative, with non-pharmacological therapy, e.g. electrical heated gloves and treat-to-target pharmacological therapy often required.[54,56,58–60]

B. Pain in SSc is often multi-factorial requiring careful discernment to address coinciding diverse, modifiable causes. SSc-pain can be an overwhelming prospect for the clinician resulting in inaccurate 'fibromyalgia' diagnoses.[61] Careful characterization of each pain type the patient is experiencing is critical towards determining the most appropriate treatment (Table 8). For example, inflammatory pain can manifest as either diffuse subcutaneous edematous tenderness, or skin-tightening, often with accompanying pruritus, neuropathic pain from small nerve fiber disruption, or as joint tenderness, stiffness or aching, or even myalgias possibly requiring systemic treatment(x).[56,62] While fibrous shoulder tendinopathy might require targeted physical therapy.

The presence of tendon friction rubs (TFRs), another source of pain from inflammation and tendon sheath irritation, indicates active cutaneous or inflammatory disease that without appropriate treatment, portends a poor prognosis including worsening skin and risk for SRC.[38,62,63] Thus, careful tendon examination is necessary; and ultrasound can helpful to assess for active joint inflammation and risk for disability.[63]

Vascular complications such as ischemic RP, ischemic digital ulcers and calcinosis cause significant, and sometimes constant, pain even at rest.[55] Increased intensity of pain and local tenderness may also signal concomitant infection, however, calcinotic lesions are frequently painful in the absence of infection depending on location. Large lesions can occasionally lead to nerve impingement resulting in neuropathic pain symptoms. Pain and discomfort related to the GI system in SSc is diverse. Dry mouth, oral thrush, odynophagia from esophageal candidiasis, abdominal pain and cramping from obstipation or distention are common pain sources that patients experience. Opioid analgesics requires careful consideration for worsening SSc-symptoms e.g. sicca, GI motility; with initiation of preventive regimens being important.

C. Fatigue in SSc, another potentially overwhelming clinical consideration, impacts all areas of daily living, work, parenting, and social participation. There are many types of fatigue: mental/cognitive, motivational, physical, muscular, general, etc. Although non-specific symptom, fatigue can be evidence of several serious SSc complications such as GI bleeding, ILD or PH. Fatigue may also reflect worsening inflammatory disease, malnutrition, poor sleep quality, gastroesophageal reflux (GERD) or the burden of decreased physical function. Further, dyspnea and cough episodes with longer recovery times are exhausting symptoms with high calorie demand and psychological burden. An organized approach to assessing and addressing fatigue can guide investigation.

Sleep disordered breathing is significantly elevated in SSc and beyond fatigue likely impacts cardiopulmonary health(ref).[64,65] Epworth Sleepiness Scale and the STOP-BANG questionnaire help identify those patients at risk for OSA and qualify for a sleep study. If warranted, CPAP use improves fatigue and potentially prevents SSc cardiopulmonary and esophageal complications.[66] However, as with breathlessness, fatigue in SSc can result from commonplace co-morbidities requiring investigation, such as hypothyroidism and coronary artery disease.

D. Breathlessness and Exercise Intolerance in SSc is often multi-factorial and can be related to myriad, sometimes severe, complications beyond cardiopulmonary involvement, and like fatigue requires thorough investigation. Breathlessness is the most common symptom of ILD, PH and myocardial disease. However, its development is often quite subtle, and patients may not recognize or explicitly complain of dyspnea. Careful questioning of patients' activity and changes in activity over time is necessary to determine if there has been a significant change (Table 9). Careful historical probing may reveal a history of decreased exercise tolerance, changes in the intensity and duration of daily activities and an unconscious slowing of movement. Further these changes may be apparent to patients' loved ones when not overtly apparent to the patient themselves. Therefore, screening requires physicians asking appropriate questions and patients recognizing

changes to determine if dyspnea is present. Dyspnea or coughing with deep inspiration or activities that engage deeper inspiration such as laughing, sneezing walking-talking suggest a restrictive process like ILD.[67–70] ILD, PH, anemia, heart involvement, physical deconditioning and anxiety are each common causes of dyspnea in SSc and are not mutually exclusive. (Table 10)

E. Cough in SSc, the second most common symptom of ILD, is associated with increased ILD severity and worse health-related quality of life (HRQoL).[7,8] Cough, though, is often multi-factorial and requires careful historical assessment to differentiate the causes e.g. ILD, reflux, post-nasal drip (PND) or sinus problems. A dry, inspiratory cough limiting inspiratory depth is often ILD-related; and can trigger frightening, embarrassing, exhausting and inconvenient episodes dyspneic coughing that usually have prolonged recovery phases.[67–70] Patients often restrict inspiration to prevent this from happening.[67–70] The quality of cough varies in patients with SSc-ILD with >50% of patients reporting a cough productive of sputum.[8,71]

Dysphagia and GERD with micro- or macro-aspiration may produce a wet, post-prandial or early morning cough that often clears or lessens during the day, but recurs at night. However, a dry cough related to GERD can also occur from pulmonary irritation. SSc-ILD patients with GERD reported cough significantly more frequently than SSc-ILD patients without GERD.[8] PND can also cause a wet or throat-irritating cough. *Cylindrical* bronchiectasis, weakening of bronchiole walls creating mucous stasis and sub-acute infection (as opposed to *traction* bronchiectasis, an extrinsic force causing bronchial distortion often seen on HRCT in ILD) is not uncommon in CTDs often occurring with productive cough that comes and goes, and often improves with antibiotic therapy.

V. SYSTEM-BASED SYMPTOMATOLOGY AND MANAGEMENT

A. Gastrointestinal System manifestations occur in virtually all SSc patients from the oral cavity through the lower GI tract and anus (Fig. 5). Gastrointestinal symptoms are associated with higher patient-perceived disease severity and lower HRQoL, when compared to traditional SSc severity measures (PH, ILD, renal and cardiac).[54,56] Multiple and diffuse morphological and functional GI abnormalities result in high degrees of symptom distress, life disruption and diminished HRQoL. These destructive changes are hypothesized to result from progressive sub-/mucosal inflammatory-fibrotic infiltration and vascular insufficiency, leading to neuronal dysfunction, and subsequently to dys-/non-motility.

Oro-maxillary and pharyngeal structural changes with painful or difficult mastication and swallowing; esophageal dysmotility with dysphagia; malnutrition from malabsorption or decreased intake; gastroparesis with bloating, nausea/emesis; colonic inertia with constipation; bacterial overgrowth with bloating, abdominal distension and diarrhea; and loss of anal sphincter tone resulting in fecal incontinence. Dysmorphic surface vessels, vulnerable to abrasion, such as arteriovenous malformations and gastric antral vascular ectasia (GAVE), may cause symptomatic anemia with dyspnea/fatigue due to slow or rapid blood loss.

Patients express frustration that despite extent and severity of GI manifestations in SSc, rheumatologists generally avoid GI-related discussion. Anecdotal clinical evidence and patient discussions support that systemic treatment in early SSc disease – as with ILD - may prevent or reverse GI symptom progression.

While esophageal involvement is the most common aspect of GI involvement, weight loss, diarrhea, and fecal soilage can indicate the presence of small bacterial overgrowth requiring treatment.[72] Additionally, micronutrient deficiency and malnutrition is a concern in SSc and patients' appetite and dietary intake should be assessed.[43] Working closely with a dietician and gastroenterologist to help guide diagnostic and therapeutic interventions can help with the management of SSc GI involvement.[73]

Gastroesophageal Reflux Disorder (GERD), a manifestation with far-reaching detrimental effects on the esophagus and the lung, demands dedicated robust attention. The ongoing injury caused to the esophageal mucosa puts patients with SSc at higher risk of pre-malignant and malignant injury, as well as structural abnormalities such as webbing, scarring and the development of strictures. The injury to associated neuromuscular complexes results in dysphasia and poor acid clearance. The absence of heartburn or regurgitation are often discordant with endoscopic findings of esophageal injury and pH testing. Prior to proton pump inhibitor (PPI) introduction, inability to eat from severe esophageal dysfunction, was a major cause of malnutrition and mortality. The advent of PPI use, effected a significant decrease in esophageal strictures. Further, extent of ILD and lung parenchymal inflammation is associated with degree of GERD and uncontrolled GERD, and hypothetically PND poses a similar concern. Chronic GERD or PND can cause hoarse voice or dysphonia. Guideline-based care highlights the value of a multidisciplinary approach and the role for diagnostic testing.[74]

Severe GERD may not be symptomatic, as early stages require significant neuronal recruitment and in later stages nerves may be dysfunctional to pain perception – but ongoing injury will still occur. The SSc specialist community is largely of the opinion that benefit of empiric PPI use in SSc-GERD outweighs the risks. Often, standard dosing of PPIs may require increased frequency and possibly addition of other agents such as histamine-2-blockers (H2-blockers) e.g. famotidine, or coating agents such as sucralfate. Use of these therapies may require attention to timing of administration to avoid drug-drug interactions.[75]

However, it is essential that anti-reflux measures are thoroughly explained and strictly practiced. This includes: elevation of the head of the bed to 60 degrees by wedge pillow, mattress elevation, bricked bed legs or automatic adjustable bed; and avoidance of right-side sleeping as gastric contents will spill back toward esophagus. For patients using CPAPs, we underscore that adherence can help to suppress reflux.[66]

B. Cardiopulmonary Involvement

Pulmonary Involvement in SSc—ILD and PH are the leading causes of SSc-related death. Identifying these entities early and initiating early appropriate treatment prolongs survival.[2,9,10] Initial screening in all SSc patients with pulmonary function testing (PFTs) including diffusion capacity of lung for carbon monoxide (DLCO) and high resolution CT

scan (HRCT), exercise tolerance and PFTs are key to detecting important changes reflecting developing cardiopulmonary involvement (Diagram 1).

It is essential in SSc care to recognize that: 1. ILD behavior is variable across patients (e.g. stable, slowly progressive, rapidly progressive), can change over time and requires individualized and vigilant approach, 2. ILD and PH *often coexist,* combined PH/ILD occurs much earlier in patients of African descent, 3. Patients with SSc are vulnerable to developing: a) either PH WHO Group 1, 2, 3 or 4, each requiring different therapeutic approaches b). coexistent PH group types (e.*g. combined WHO Groups 1 PAH and 2 diastolic dysfunction, combined WHO Groups 1 PAH and 3 ILD*), 4. Screening, detection, characterization of PH Group type, and initiation of appropriate treatment demands adherence to clinical diagnostic algorithms and tracking of patient symptoms (Table 11).

Though, without formal consensus amongst SSc specialists, HRCT is the gold standard for screening for ILD in SSc. Numerous studies demonstrate that PFTs are inadequate in detecting ILD in this population, particularly early in the stages.[71] However, insurance constraints may limit the ability to obtain this study in a limited cutaneous, asymptomatic patient with normal PFTs. Follow-up PFTs with careful trending are crucial. *Repeat HRCT* is indicated for unexplained symptom changes (dyspnea, cough), PFT worsening (drop ≥10% in FVC or 5–10% fall in FVC with ≥15% decrease in DLCO) to investigate co-existent infection or malignancy versus progressive ILD. Bronchoscopy is reserved for co-existent concern of infection or malignancy. Lung biopsy is *not* warranted for diagnosing SSc-ILD in patients with SSc with a typical HRCT pattern i.e. usual or non-specific interstitial pneumonitis (UIP or NSIP).

Documenting serial PFT data along with temporally coincident medication dosing and any contextual factors that might explain an aberrant PFT performance on that day (e.g. sinusitis, allergies etc) is an *essential investment in the care of SSc patients*. Charting the trajectory beginning from first available PFTs affords insights into disease behavior, e.g. rapidly progressive vs. stable vs. slowly progressing ILD.[76] Furthermore, it protects the clinician from overlooking progressing disease in the context of normal range values, as a 5% decrease in FVC over 6 months (or 10% annually) *despite normal values* warrants investigation and possible changes to or additions to treatment.

Though serial FVC is considered a reliable reflection of restrictive lung disease, DLCO can be a key differentiator between parenchymal versus vascular lung disease, and provide an early detection mechanism for pulmonary hypertension. While FVC reflects restriction related to parenchymal lung disease, DLCO reflects the ability of gas to cross from airspace to bloodstream which requires gas to diffuse across two barriers: the lung parenchyma and also the blood vessel wall (Figure 6). If either or both are resistant to permeable gas, as can occur in SSc-ILD or SSc-PH this will cause reduction in DLCO. In parenchymal disease the FVC and DLCO commonly trend downward in parallel; while in vascular disease the DLCO has a much steeper decline than FVC (Figure 7). However, early in the course of SSc-ILD, the FVC may be normal, while the DLCO is often decreased. Over the course of SSc, the FVC:DLCO ratio may help distinguish pulmonary vascular disease from progression of SSc-ILD with a higher ratio suggesting a predominant pulmonary vascular process(x).[77,78]

Therefore, in addition to yearly screening echocardiogram at rest and with exercise, DLCO is an important indicator of pulmonary vascular involvement.

Cardiac Involvement in SSc may result from microvascular insufficiency, or inflammatory-fibrotic infiltration of the myocardium, causing arrhythmias, diastolic or systolic dysfunction, pericarditis, or myocarditis which are managed similarly to non-SSc cardiac complications. SSc-specific treatment is yet unclear, and likely depends on suspected disease activity. Baseline/annual echocardiogram serves as a comparison should cardiac problems or PH develop later. Non-contrast cardiovascular magnetic resonance (CMR) demonstrates 45% prevalence of myocardial fibrosis unexplained by other causes and often associated with diffuse skin involvement and elevated ultra-sensitive CRP; CMR may play a role in early diagnosis. [79–81] Additional serum biomarkers that are commonly followed as predictors of onset and worsening are NT-Pro-BNP and uric acid, of which NT-Pro-BNP has demonstrated reliably properties.

Routine cardiovascular risk reduction with blood pressure monitoring and lipid screening is encouraged in SSc patients. Cardiac involvement was often found to be associated with SSc-myopathy in several studies.[79,82–85]

When to Consider Transplantation: Despite prior misconceptions of worse outcomes for patients with SSc (for ILD, PH, or both) compared to those with non-SSc lung disease, lung transplantation in SSc is safe, with similar survival outcomes. Lung transplantation is reserved for patients whose lung disease progresses despite maximal systemic therapy. (Table 12). Early referral for transplant evaluation permits time for patients and caregivers to become familiar with the transplant process, make informed unhurried decisions, and adjust to psychosocial and financial pressures related to transplant.

Most common barriers to lung transplant in patients with SSc can be overcome (Table 13). Physical conditioning is an important factor in transplant selection and successful post-transplant recovery. Early referral gives patients who are deconditioned an opportunity to engage in healthy lifestyle changes and home fitness practices supported by pulmonary rehabilitation.

Potential transplant candidates with SSc undergo extensive testing to identify needed interventions for SSc manifestations that might overtime injure the allograft, e.g., Nissen fundoplication for severe GERD or heart-lung transplantation with coexistent irreversible myocardial disease. Severe esophageal dysmotility or GERD (lower esophageal sphincter incompetency) lead to chronic aspiration which poses significant risk for acute and chronic allograft rejection, may also warrant GI tube for nutrition posttransplantation.

C. Muscle Involvement in SSc is under-recognized and multi-factorial and ranging from atrophy, inflammatory, vasculopathic, fibrotic to necrotic pathology. Both muscle strength and endurance in proximal muscles are commonly reduced, especially in patients with significant lung disease.[86] Systemic treatment and exercise can improve SSc myopathy, with physical therapy targeting strengthening and prevention of large joint contracture, particularly in the shoulders. (Table 14)

Consideration of medication-related myopathy culprits, such as statins, steroids and hydroxychloroquine, is a mainstay of investigation. SSc-myopathy predicts SS-related cardiac involvement.[79,82–85]

D. Hands in SSc are especially subject to diffuse morphological changes, impairment and pain due to inflammation, vasculopathy and fibrosis. These pathological processes result in bony, periarticular and cutaneous destruction with infection, ulceration, calcinosis, acro-osteolysis, flexion contractures, synovitis, tendinopathy and amputation. Arthritis, contractures, tendon friction rubs come early during the disease course, therefore require early intervention. The role of hand exercises in SSc is critically important. Exercise improves circulation, healthy vascular and skin repair, increases warmth, reduces local inflammation and stiffness, and very importantly, increases muscle strength and hand function. Preventive strategies to maintain hand warmth may help to prevent further vascular injury (Table 14).

E. Renal Involvement in SSc: prior to the availability of Angiotensin Converting Enzyme (ACE) inhibitors renal crisis was the leading cause of death in SSc. Early intervention with ACE inhibitor therapy and rapid control of blood pressure may abort a “crisis” and minimize renal damage. However, with close monitoring of high risk patients including prednisone use >10 mg/day, abrupt and severe BP elevation, presence of anti-RNA polymerase III, we can identify and aggressively treat SRC. Late recognition, delayed or inappropriate therapy persist and result in renal failure and other complications of malignant hypertension. Despite progression to end-stage disease, with continued treatment with ACE inhibitors, renal function may return months after initiating dialysis. Educating patients at higher SRC risk on warning signs and plan of action is crucial to improving outcomes, including consideration of home blood pressure monitoring, and providing the “renal crisis prevention card” (Fig 9) on a patient’s first visit for use in emergent situations.[87]

VI. IMPORTANT NON-PHARMACOLOGICAL THERAPEUTIC CONSIDERATIONS

A. Exercise as an Essential Multi-Modal Disease-Modifying Medicine

Physical function and activity are key predictors of HRQoL and survival. Available evidence on exercise strongly supports diverse and diffuse benefits of physical activity as a potential cornerstone to SSc management[88]. (Table 15) Exercise reduces inflammation and increases circulation (and body heat), which are essential drivers of SSc symptoms, in addition to enhancing mobility through improving strength, stiffness, endurance and aerobic capacity. Physical activity is critical for all levels of ability and for modulating the biochemical impact of depression/anxiety, stress and physical pain – while improving self-esteem in a disease notorious for diminished self-image. Exercise’s muscle and vascular benefits likely contribute to its beneficial impact on sleep and fatigue.[89] Increasing physical activity and reduction of a sedentary lifestyle in SSc is crucial to self-management, even in mild pulmonary involvement.[90] Patients with SSc desire physician counselling and augment their physical activity accordingly. A routine visit should document patients physical activity, counsel on the medicinal effects of exercise and advise that exercise be pleasurable, working

up to ≥*30-minutes/day, 5 days weekly*; with hand, face and feet exercises to increase circulation, mobility and anti-inflammatory profiles regularly reviewed. (See resource list) Further, a long-term physically active lifestyle improves GI motility, and favorable enhancement of gut flora.[91]

B. Anticipatory and Preventive Education

Keys to Patient-Centered Outcomes—Counselling and education (Table 16) on a model of shared decision-making (SDM) (Box. 1) provide patients with insight into this complex disease as pertains to their circumstances, cultivates clinician-patient partnership, and increases patient trust, adherence, self-efficacy, and mental health – all essential to patient outcomes. SDM is an ongoing process requiring time to ensure clinicians understand and address the patient's perceptions, priorities and self-management activities of their disease experience. SDM enables effective palliation and protection against disease progression and complications. Patients with SSc often feel fearful, scared and isolated especially as families, friends, and other health care providers are not familiar with SSc. SDM and providing resources on self-management strategies and support groups are imperative.[92,93]

Routine Health Maintenance—The medical complexity of SSc often overshadows the importance of routine health maintenance (RHM). RHM addresses preventive strategies (table 17) directly related to SSc complications. Vaccinations prevent severe pneumonia and influenza in ILD/PH. Age-appropriate cancer screening becomes increasingly significant given the higher malignancy risk in SSc particularly with anti-polymerase III positivity. Screening for cardiovascular disease and OSA may prevent worse outcomes in those already with cardiopulmonary and circulatory impairment. SSc portends a higher risk of osteoporosis[94,95] and fractures, and lower vitamin D absorption with chronic PPI use.

Other essential pre-treatment RHM include infectious hepatitis and tuberculosis screening, consideration of antibiotic prophylaxis, and recurrent pregnancy planning with females on immunosuppression. As with exercise, keeping RHM as part routine documentation framework will protect health outcomes in SSc.

VII. PRACTICAL CONSIDERATIONS FOR PATIENT AND CLINICIAN SUPPORT

A. Pre-Visit Preparations

Patients require time to be heard and time to hear important concepts related the condition they are living with. Protecting one's attention and time to address pivotal patient care issues is crucial to outcomes when caring for people with multi-organ system disease with multiple debilitating manifestations. Attention to patient environment and comfort, anticipatory scheduling to consolidate medical appointments and employing operational throughputs e.g medical record attainment and chart review that support pre-visit data collection, scheduling realistic visit appointments (with appropriate billing) facilitate a greater ease of communication for patient and clinician and protects one's dedicated time with the patient. (Tables 18–19 and resources).

B. Implementing the Plan

SSc is a health condition whereby timely treatment initiation of active disease is key to reversibility of impairment and prevention of permanent damage; and whereby even palliative intervention of irreversible damage can immediately optimize HRQoL, workability, nutrition, mental health and physical well-being and function. Patient education on self-management and engagement with SSc education and advocacy organizations such as the Scleroderma Foundation, Scleroderma and Raynaud's UK (SRUK), Federation of European Scleroderma Associations (FESCA), Scleroderma Australia and Scleroderma India, are central to successful care.

Delays occur in scheduling diagnostic procedures, therapist and consultant referrals, and treatment initiation greatly impacts patient outcomes. Enlisting an 'extended team' of scheduling contacts in other hospital areas who understand the precarious nature of SSc, facilitates teamwork in proactive timely and patient-centered scheduling and prior-authorizations.

Prior Authorizations (PAs): Advocacy for streamlining PAs[96] is essential to improve patient survival and outcomes. Further, denials lead to higher insurance company costs,[97] as most clinicians finally attain authorization.[98] An organized approach can expedite most procedures and medication authorizations, including an appeal, within 72 hours in the US. Correspondence logs to track initiation, requests for additional information and appeals (see Appendix) streamline response times. In the US, any licensed health professional (medical assistant, nurse) are considered 'peers' in a 'peer-to-peer' review; and can obtain approval with increasing efficiency overtime.

The Scleroderma Foundation attained Medicare approval for MMF as a first-line therapy in SSc. However important treatments, e.g. rituximab, may not initially receive authorization. However, adding 'co-existent diagnoses' that satisfy authorization requirements is reasonable from insurance peer reviewers' perspective, e.g. 'seronegative rheumatoid arthritis' or 'lupus', as long as manifestations (e.g. inflammatory arthritis, ANA positivity) can be supported with documentation[99] that states '*clinical features consistent with____*' (co-existent diagnosis). Insurance company requirements for TNFinhibitors failure before rituximab or tocilizumab, are easily refuted explaining contraindication in patients high risk for fibrotic lung disease. Conveying SSc statistics e.g. 50% mortality and ensuing disability without appropriate treatment is generally effective.

Proactive Procedure Scheduling: Again, consolidating procedures and clinic appointments enhances overall HRQoL. Appointments can be costly to patients and their families in terms of travel expenditures and time, work productivity and income loss[100] but also over-medicalizes patients' lives.

Referral Fulfillment: Clinician-to-clinician communication is key to conveying the expeditious nature of clinical concerns. 'Extended teams', mentioned above, serve to expedite timely scheduling for therapy and specialist consultations.

C. Benefits of Concurrent Care between SSc Specialists and General/Local Specialists

Concurrent care, mutual decision-making and close communication between a recognized SSc-center and a patients' local rheumatologists, pulmonologists and other specialists, benefit SSc patients. SSc remains a complex disease, with professional education disproportionately represented by industry's easily misinterpreted therapeutic messaging. Patient volume at SSc-centers habituates attention to the subtleties and complexities of SSc care and therapeutics. SSc-centers offer specialty and experimental treatments, availability of clinical trials, registries, and consultation with specialty PT/OT/nutritionists.

D. Future of SSc Care

Telehealth offsets the frequency of travel burden for patients and family (e.g. time, logistics, financial, work) with its immediacy possibly expediting initiation of appropriate care. During the COVID-19 pandemic, supplementing history to target physical exam findings and guiding patients in physical exam elements has proven helpful to establish degree of vascular, cutaneous and musculoskeletal complications. Home spirometry, may also support expansion of telehealth visits.[101]

Patient self-management are a critical aspect of patient self-management with well-being strategies and therapeutic practices that influence inflammation, fibrotic mechanisms, respiratory function, fatigue and pain such as home exercise practices, therapeutic singing,.[102–104]

Practice Points:

- Serial screening detects potentially lethal complications and is key to decreasing disability and mortality in SSc
- Organ-based documentation optimizes comprehensive assessment, treatment and counselling. Documenting serial patient metrics, such as testing and symptoms, detects ominous early trends of progressive disease that warrants aggressive intervention, such as dropping PFTs despite normal values
- Coexistent ILD and PH is common. Co-existent WHO PH groups is also common. Clinical tools exist to help detect and distinguish pulmonary involvement in SSc
- SSc is very heterogeneous and requires an individualized approach to patient care
- Concurrent care between SSc centers and general/local rheumatologists and pulmonologists is an increasingly common care model that may enhance patient health outcomes
- Patient-centered and outcome-centered care in SSc demands time. Optimizing clinical infrastructure and appropriate billing can help protect clinical time with SSc patient
- Optimal health outcomes in SSc demands a multi-specialty multi-disciplinary approach

- Exercise has multiple-organ based benefits in SSc and may be a disease modifying intervention

Research Agenda:

- Investigate the impact of standardized clinical data collection using customizable open source interfaces like OpenEMR[105] on health outcomes and health disparities in SSc and other complex multi-organ diseases
- Investigate health economics, health outcomes when clinicians optimize appropriate billing to protect clinician-patient visits time related to optimized in SSc
- Investigate the potential of early systemic treatment as preventive in the development of severe gastrointestinal SSc disease (and other manifestations association with disease duration)
- Characterize the degree and dosage of exercise on SSc local and systemic effects.
- Assess the use of pre-visit intake apps (compared to no app), on patients' clinic visit experiences and outcomes.

VIII. SUMMARY

SSc is a devastating multi-system disease, requiring extensive, thoughtful assessment, organized documentation and management of multiple organ-related manifestations that can directly impact a patient's survival and HRQoL. An optimal approach coordinates healthcare services and empowers access to disease-related education and resources. The future of SSc care depends on effective communication along with expeditious assessment and treatment with appropriate pharmacological and non-pharmacological therapeutics. Quality healthcare in SSc is reliant upon sustainable clinical operations and policy-making that optimize survival and HRQoL in SSc.

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APPENDIX of MEDICATION TABLES

Please note medications marked with '^' are either formally approved by drug agencies for use in SSc or part of national formularies e.g. MMF in the US.

Raynaud's and Digital Ulcer Medications

Drug Class	Drug Names	General Side Effects
Calcium Channel Blocker (CCB)		Hypotension, flushing, dizziness, and edema.
Angiotensin Receptor Blocker (ARB)	Losartan Valsartan	Dizziness, diarrhea, hypotension, muscle cramps, and headache.
Angiotensin Converting Enzyme (ACE) Inhibitors	Captopril, Enalapril, Quinapril, Ramipril, Lisinopril	
Alpha Blockers	Prazosin	Hypotension, dizziness, drowsiness
Nitrates	Topical Nitroglycerin 2%	Rash, headache, facial flushing, hypotension, dry mouth, tachycardia.
Phosphodiesterase-5 Inhibitors^	Sildenafil Tadalafil	Blurred vision, flushing, headache, hypotension, visual impairment, tachycardia.

Drug Class	Drug Names	General Side Effects
Prostacyclin/prostacyclin analog^	Epoprostenol Treprostinil Iloprost	Hypotension, dizziness, muscle cramps, nausea and vomiting, edema, headache
Endothelial Receptor Blockers^	Bosentan Ambrisentan Macitentan	Hepatoxicity, headache, flushing, edema, fatigue, hypotension, pruritus, and weight gain.
Topical lidocaine		Avoid getting into eyes or sensitive areas
Botulin Toxin Injections		

Analgesic Medications

Drug Class	Drug names	Concerns for use in SSc
NSAIDS	ibuprofen, naproxen,	• Esophageal concerns • Gastritis / gastric bleeding • Hypertension • Kidney impairment • Gastric bleeding • Fluid Retention • Cardiac events with long-term use
Opioids	Hydrocodone Oxycodone Tramadol	• Decreased motility in GI tract ○ Constipation in general population → may be exaggerated in scleroderma patients • Risk of respiratory depression • Fractionated sleep, impaired sleep • Pruritus
Anti-convulsants	Gabapentin Pregabalin	• Dizziness • Somnolence • Swelling

Pharmacological Therapy for Gastrointestinal Manifestations in SSc *(Courtesy of Monika Lammi, rights reserved)*

Drug Class	Drug Name	Concerns for use/Comments
GERD		
Proton Pump Inhibitors	Pantoprazole* Omeprazole* Lansoprazole* Esomeprazole* Rabeprazole* Dexlansoprazole	*Bioavailability reduced if taken with food Take 30–60 min before breakfast. Decreased absorption of: Mg, B12, Fe Risks (prolonged use): renal insufficiency, osteoporosis, atypical fractures, pneumonia, and dementia.
Histamine 2 Antagonists	Famotidine Cimetidine	Possible inhibition of cytochrome P450 with possible enhanced effects of drugs with P450 reliant metabolism
Antiacids	Calcium carbonate	Hyperkalemia, alkalosis and acute or chronic renal injury.
	Aluminum hydroxide	Aluminum retention with neurotoxicity and anemia in renal failure. Hypophosphatemia.
Surface agents	Gaviscon +/− alginate	
	Sucralfate	Can bind to other drugs if taken simultaneously. Hypophosphatemia. Combining with antiacids can amplify these side effects.

Drug Class	Drug Name	Concerns for use/Comments
Promotility/LES	Metoclopramide	May increase gastric motility in patients with systemic sclerosis. FDA advised against use for more than 3 months SE: traditive dyskinesia, cardiac arrythmia (monitor with EKG)
	Domperidone	Not FDA approved in US. Can be obtained with Investigational New Drug Application. SE: cardiac arrhythmia
	Buspirone	Increases the lower esophageal sphincter pressure, amplitude of esophageal contractions. Appears more effective for GERD-related symptoms not esophageal hypomotility symptoms (dysphagia and chest pain).
	Baclofen	Shown to augment lower esophageal sphincter pressure in patients with GERD. Not studied in patients with SSc.
Gastroparesis		
Promotility agents	Metoclopramide	May increase gastric motility in patients with systemic sclerosis FDA advised against use for more than 3 months Risk: traditive dyskinesia, cardiac arrythmia (monitor with EKG) FDA advised against use for more than 3 months
	Domperidone	Not FDA approved in US. Can be obtained with Investigational New Drug Application. SE: cardiac arrhythmia (monitor with EKG)
	Erythromycin	Not recommended long term: tachyphylaxis, may cause small bowel dysmotility. SE: cardiac arrhythmia (monitor with EKG)
	Prucalopride	Improves gastric, small bowel and colonic transit. FDA approved for constipation.
	Cisapride	Improves postprandial symptoms and gastric emptying. More potent acutely than metoclopramide. Withdrawn from the US market because of cardiac arrhythmia.
Antiemetics	Ondansetron	SE: Prolongs GI transit, headache, cardiac arrhythmia.
	Granisetron	SE: constipation, headache, cardiac arrhythmias
	Prochlorperazine	SE: Sedation, tardive dyskinesia
	Promethazine	SE: Central, cardiac arrhythmia
Dyspepsia		
Neuromodulators	Buspirone	Improves gastric accommodation and symptoms of dyspepsia, but decreases gastric emptying of liquids.
	Mirtazapine	Improves dyspepsia, sleep, depression SE: weight gain, drowsiness
Herbal	FDgard (caraway oil and I-menthol)	
SIBO		
Antibiotics	Rifaximin Metronidazole Amoxicillin/clavulanic acid Norfloxacin	Treat for 2 weeks. High risk of recurrence due to small bowel dysmotility. Cycle regimens to limit antibiotic resistance. May consider use of prokinetics, see below. Antibiotics, e.g. fluoroquinolones may contribute to clostridium difficile overgrowth
Chronic Intestinal pseudo-obstruction		
Prokinetics	Metoclopramide Erythromycin Prucalopride	See above. May also be considered for SIBO.
Cholinesterase inhibitor	Pyridostigmine	SE: bradycardia, excessive bronchial secretions, cholinergic crisis

Drug Class	Drug Name	Concerns for use/Comments
Somatostatin analog	Octreotide	Used in patients who failed to respond to other prokinetic agents. Inhibits gastric motility.
Constipation		
Bulk forming laxatives	Psyllium Methylcellulose	Patients with gastric dysmotility and visceral hypersensitivity may not be able to tolerate.
Osmotic laxatives	Polyethylene glycol	SE: abdominal pain, distention, bloating.
Stimulant laxatives	Bisacodyl Glycerol	
Guanylate cyclase-C receptor agonists	Linaclotide	Diarrhea, bloating.
	Plecanatide	Improves gastric, small bowel and colonic transit. Diarrhea.
Chloride channel activator	Lubiprostone	Nausea, diarrhea.
Promotility agent	Prucalopride	Improves gastric, small bowel and colonic transit. FDA approved for constipation.

Systemic Treatment/Immune Suppression / Anti-Fibrotics

Drug	Side Effects	Monitoring/Counseling	Common Uses
Mycophenolate mofetil (MMF) mycophenolic acid ^	Diarrhea, increased risk of infection, headache, fatigue, leukopenia, thrombocytopenia, teratogenic	CBC, serum electrolytes especially with ongoing diarrhea, drug interactions; REMS (pregnancy) If side effects occur, decrease dose to side effect free level, and keep at this dose for longer period before increasing again. Use of contraception	Anti-fibrotic immunosuppressant First-line for progressive ILD Skin-tightening, Joint involvement
Cyclophosphamide	Increased risk of infection Hair loss, GI upset, decreased appetite, stomatitis, amenorrhea, interstitial cystitis, infertility, oligospermia/azoospermia, Stevens-Johnson syndrome, increased risk of bladder cancer	CBC, urinalysis (monthly if on IV therapy)	Progressive ILD Progressive skin-tightening
Rituximab	Risk of infection Infusion reaction common Very rare, demyelinating disorders		Progressive skin-tightness Progressive ILD Joint involvement, possibly PH
Tocilizumab ^	Risk of Infection Transaminitis, hepatotoxicity Very rare, demyelinating disorders Rare risk of GI perforation Hyperlipidemia	Serum lipids CBC Transaminases	Skin-tightness Joint involvement Slowing down progressive ILD Possibly PH
Intravenous Immunoglobulin G	Headache, fatigue, renal dysfunction, transient ischemic episodes, cerebrovascular event, urticaria, flushing, hypertension, aseptic meningitis		Progressive SSc
Hematopoietic Stem Cell Transplantation	Extreme immunosuppression High risk of infection and	Per protocol	Progressive SSc prior to significant organ damage

Drug	Side Effects	Monitoring/Counseling	Common Uses
	sepsis Heart failure, arrhythmia		
Methotrexate	Nausea, diarrhea, hepatotoxicity, stomatitis, alopecia, myelosuppression, teratogenic Medication-induced pneumonitis, rare Increased risk of infection	CBC, Serum creatinine, Transaminases, Concomitant use of folic acid Avoidance of alcohol Use of contraception	Joint involvement
Azathioprine	GI upset, myalgia, leukopenia, thrombocytopenia, risk of infection, hepatotoxicity	Signs of bleeding, jaundice, change in color of stool; TPMT deficiency, drug interactions	Joint involvement
Glucocorticoids	Scleroderma Renal Crisis Amongst many other potentially detrimental side effects	Opportunities to lower dose or discontinue	Restricted use of very low doses
Leflunomide	Hepatotoxicity Nausea, Diarrhea, Hypertension, Rash, Headache, Abdominal pain, Alopecia; Peripheral neuropathy	CBC and transaminases, signs of infection Avoid alcohol, use of contraception	Joint involvement
Sulfasalazine	Nausea, Diarrhea, Headache, Photosensitivity, Myelosuppression	CBC GI distress, SPF use	Joint involvement
Hydroxychloroquine	Nausea, Diarrhea, Headache, vision changes Rarely myopathy Rarely myelosuppression	Baseline eye exam Screening according to published protocols Visual changes at night or peripheral	Joint involvement
Anti-Fibrotic e.g. nintedanib^, pirfenidone	Gastrointestinal distress, hepatotoxicity, fatigue, swelling	Transaminase levels Electrolytes with vomiting or diarrhea	Slowing down lung progression. Uncertain regarding whether these have systemic effects, thus far there has been no demonstrated improvement on skin, joint, or quality of life.

APPENDIX OF CLINICIAN and PATIENT RESOURCES

Clinical Skills Resources:

Functional Index-2: https://www.youtube.com/watch?v=qw4XvWKQErU

Manual Muscle Test 8 (MMT-8): https://www.niehs.nih.gov/research/resources/assets/docs/mmt8_grading_and_testing_procedures_for_the_abbreviated_8_muscle_groups_508.pdf

Modified Rodnan Skin Score: https://www.youtube.com/watch?v=Bl3EX_2PaUc

Timed Up and Go Test: https://youtu.be/auqAb_AWM1U

TImed sit to stand test: https://www.youtube.com/watch?v=puJhQXUlbdA

30-seconds Sit to Stand Test: https://www.youtube.com/watch?v=PzCTwkJVhWg

DETECT Algorithm for PH Screening: https://www.suspectpahctd.com/DETECT/

Examples of Clinic Operations Documents:

Medical Records Intake Form for Scheduling New Patients: https://www.dropbox.com/s/wapuv8p8dkoz2n3/PATIENT%20SCHEDULING%20INTERVIEW.docx?dl=0

New Patient Questionnaire: https://www.dropbox.com/s/jynfaq5ax3cyo8a/SSc%20Patient%20Intake%20Form.docx?dl=0

Infusion Order Record: https://www.dropbox.com/s/v1vkwiegpjhead4/INFUSION%20ORDER%20RECORD.docx?dl=0

Oral Medication Authorization Record: https://www.dropbox.com/s/algr06i6upndtmf/RECORD%20ORAL%20MEDS%20PRIOR%20AUTH.docx?dl=0

Patient Questionnaires:

StopBang Questionnaire Online Calculator: http://stopbang.ca/osa/screening.php

Epworth Sleepiness Scale: https://www.thecalculator.co/health/Epworth-Sleepiness-Scale-Calculator-905.html

http://epworthsleepinessscale.com/

Scleroderma Health Assessment Questionnaire: https://www.dropbox.com/s/gd9847e9bw82101/SHAQ%20-%20SF36%20-%20Cochin%20Hand%20Function.doc?dl=0

SF-36 form: https://www.rand.org/health-care/surveys_tools/mos/36-item-short-form/scoring.html

https://www.rand36calculator.com/

Cochin Hand Function Questionnaire: https://www.dropbox.com/s/gd9847e9bw82101/SHAQ%20%20SF36%20-%20Cochin%20Hand%20Function.doc?dl=0

Giessen GI Form: https://www.dropbox.com/s/o2i68d7f4ojvu4h/Giessen%20Gastrointestinal%20Questionnaire%20for%20Scleroderma.doc?dl=0

SSc-GIT: https://www.dropbox.com/s/yi5wzl3yezgmqn7/GIT%20Questionnaire%20-%20The%20Actual%20Survey.doc?dl=0

Patient Specific Functional Scale (PSFS) User Manual: https://www.physiopedia.com/Patient_Specific_Functional_Scale

Patient and Physician Education and Advocacy Resources:

Scleroderma Foundation: www.scleroderma.org

FESCA: www.fesca-scleroderma.eu/wordpress/

Scleroderma Australia: https://www.sclerodermaaustralia.com.au/

Scleroderma & Raynaud's UK: https://www.sruk.co.uk/scleroderma/

Scleroderma Societies of Canada and Ontario: www.scleroderma.ca, https://www.sclerodermaontario.ca/, https://sclerodermie.ca/en/

Pulmonary Fibrosis Foundation: https://www.pulmonaryfibrosis.org/

Pulmonary Hypertension Association: https://phassociation.org/

Renal Crisis Card: https://ard.bmj.com/content/74/Suppl_2/1136.1

Educational Resources for Patients:

Oxygen Use (for patients in the U.S.): https://www.dropbox.com/s/3d8wyikb8204ira/What%20Patients%20Should%20Know%20About%20OXYGEN%20THERAPY%20-%208%20-2-2017.pdf?dl=0

Patient Information on Medications: www.rheuminfo.com

Janet Poole Hands / Face Instructional Links: https://www.youtube.com/watch?v=1F02FxdOgwI

https://www.youtube.com/watch?v=8MztM3zItik

https://www.youtube.com/watch?v=YwWP7mgcYhU

Stretching exercises for the hand and face.
The Scleroderma Foundation, http://www.scleroderma.org/site/DocServer/Form_16c_low_res.pdf?docID=19809&AddInterest=1281

Taking Charge of Systemic Sclerosis (TOSS): an internet program for systemic sclerosis. https://www.selfmanagescleroderma.com/

Living Well: Heart, Lung, Muscle & Mind: A collection of videos dedicated to yoga rehab and dance rehab for heart, lung, muscle and autoimmune conditions https://www.youtube.com/channel/UCRgvkbyzep-Q3LGBiAksQZw/videos

3-3-1 Exercise Tutorial https://www.youtube.com/watch?v=zsBRxmkzAnM&t=2s

Move Towards Health: UMC CPHC Instructional Booklet on Safe Home-based Dance Practice https://doi.org/10.13140/RG.2.2.25576.49927

Sleep Booklet: https://www.dropbox.com/s/0axd782mi818smc/SF%20Arizona%20Conference%20%20-SLEEP%20-%20DOUBLE%20Booklet.docx?dl=0

Mindfulness Booklet: https://www.dropbox.com/s/mrpl33zxjsk20br/SF%20Arizona%20Conference%20%20-RESTORE%20YOURSELF-%20DOUBLE%20Booklet.docx?dl=0

Mindfulness in Scleroderma Videos: https://www.youtube.com/watch?v=pNK9RP4Abyw https://www.youtube.com/watch?v=lmQKOCDJ19Y

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Box 1.

Checklist to Support Shared Decision-Making *(Courtesy of LA Saketkoo, rights reserved)*

Shared Decision-Making Checklist

- **Name the patient's items of concern** as presented by the patient and if possible which are highest priority
- **Ascertain patient's thoughts** on the potential underlying cause/s
- **Name the items of concern** from the clinical perspective including short and long-term (e.g. potential progressive damage, associated abrupt complications etc)
- **Respond to patient's perceptions** of potential cause in support of & clarifying divergence from patient perceptions. Remain transparent in what is known, unknown, yet to be known and that which requires researching by the clinician.
- **Name the treatment options available**, including any non-pharmacological with particular attention those suggested by the patient
- **Discuss safety, side effects and efficacy** (including anticipated onset) of available therapies and those suggested by the patient.
- **Assess Patient Expectations of treatment**
- **Set Treatment Expectations** including prognosis, anticipated degree of symptom/impairments resolution, cure versus slowing progression, disease activity versus damage

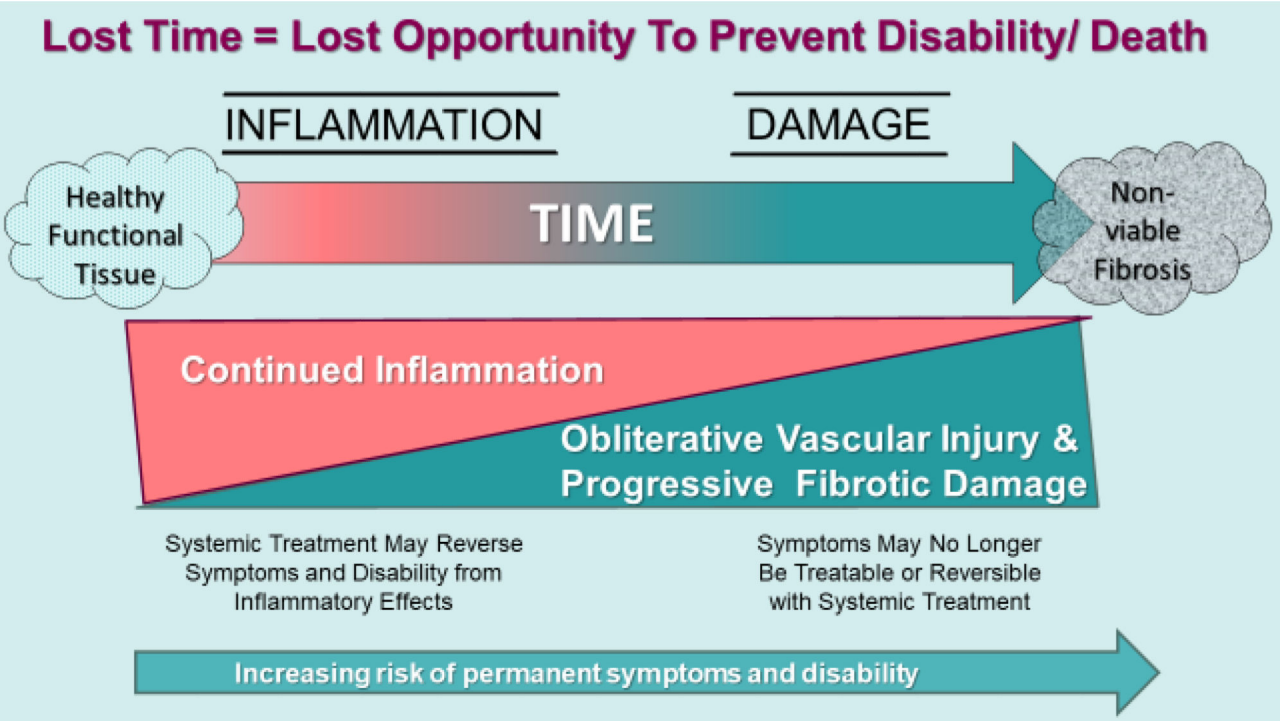
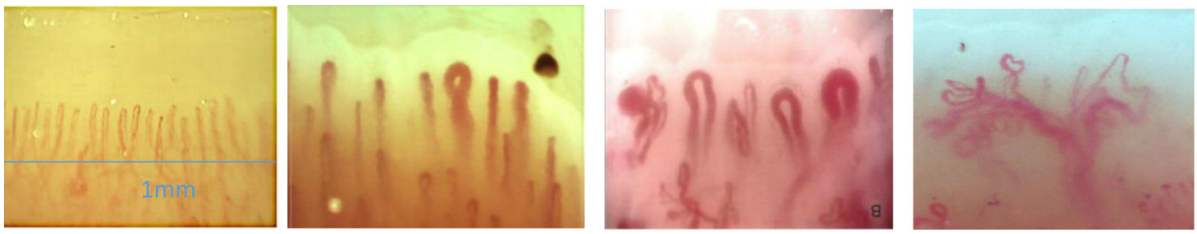


Figure 1.

SSc involved tissue, of which the lung is one example, experiences transition from healthy tissue to fibrosis as inflammation is incited and progressively extends within resident organs. Vascular injury with tissue hypoxia is an important factor to the development of tissue fibrosis. Symptoms and disability can be transient with active inflammation with systemic treatment. Over time untreated inflammation irreparably injures effected tissue resulting in scarring and fibrosis. Fibrosis is irreversible and results in permanent organ-related disability. *(Courtesy of LA Saketkoo, rights reserved)*



Normal pattern with >9 capillaries in 1 mm across the top row. one giant capillary and bleeding known as “early” pattern.

‘Early’ SSc pattern with one giant capillary and bleeding (brown cloud is micro-hemorrhage from below capillary.

“Active” SSc pattern with giant capillaries and abnormal shapes – with significant loss of capillaries.

‘Late’ SSc pattern with capillary loss and very abnormal, disorganized shapes due to neo-angiogenesis as vessels struggle to re-grow.

Figure 2.

Demonstration of ‘normal’ and various SSc patterns on nail fold video capillaroscopy. (*Images courtesy of Vanessa Smith; University of Ghent, Belgium.)*

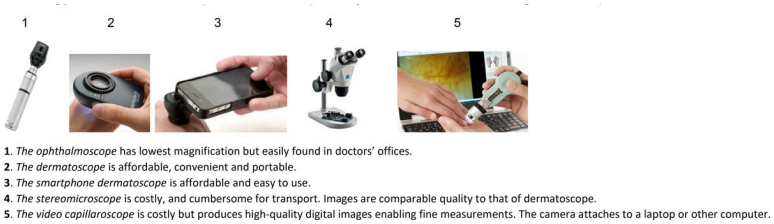


Figure 3. Capillaroscopy is an essential rheumatologic service.

An abnormal capillaroscopy satisfies >20% of SSc criteria and confers 96% predictive power for development of CTD; making it an essential part of the rheumatologic exam. With any method capillaries become increasingly easier to visualize with practice over time. *(Courtesy of T Frech & LA Saketkoo, rights reserved)*

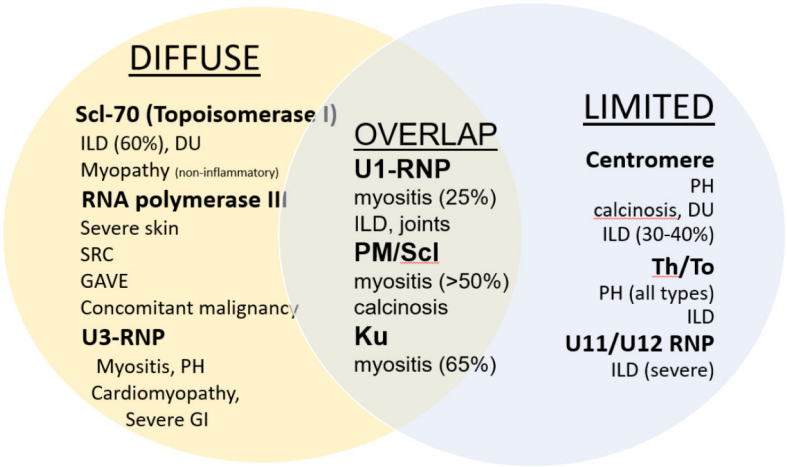


Figure 4. Clinical-Serologic Classification and Internal Organ Associations

(Courtesy of RT Domsic, rights reserved)

ILD = interstitial lung disease; DU = digital ulcers; SRC = scleroderma renal crisis; PH = pulmonary hypertension

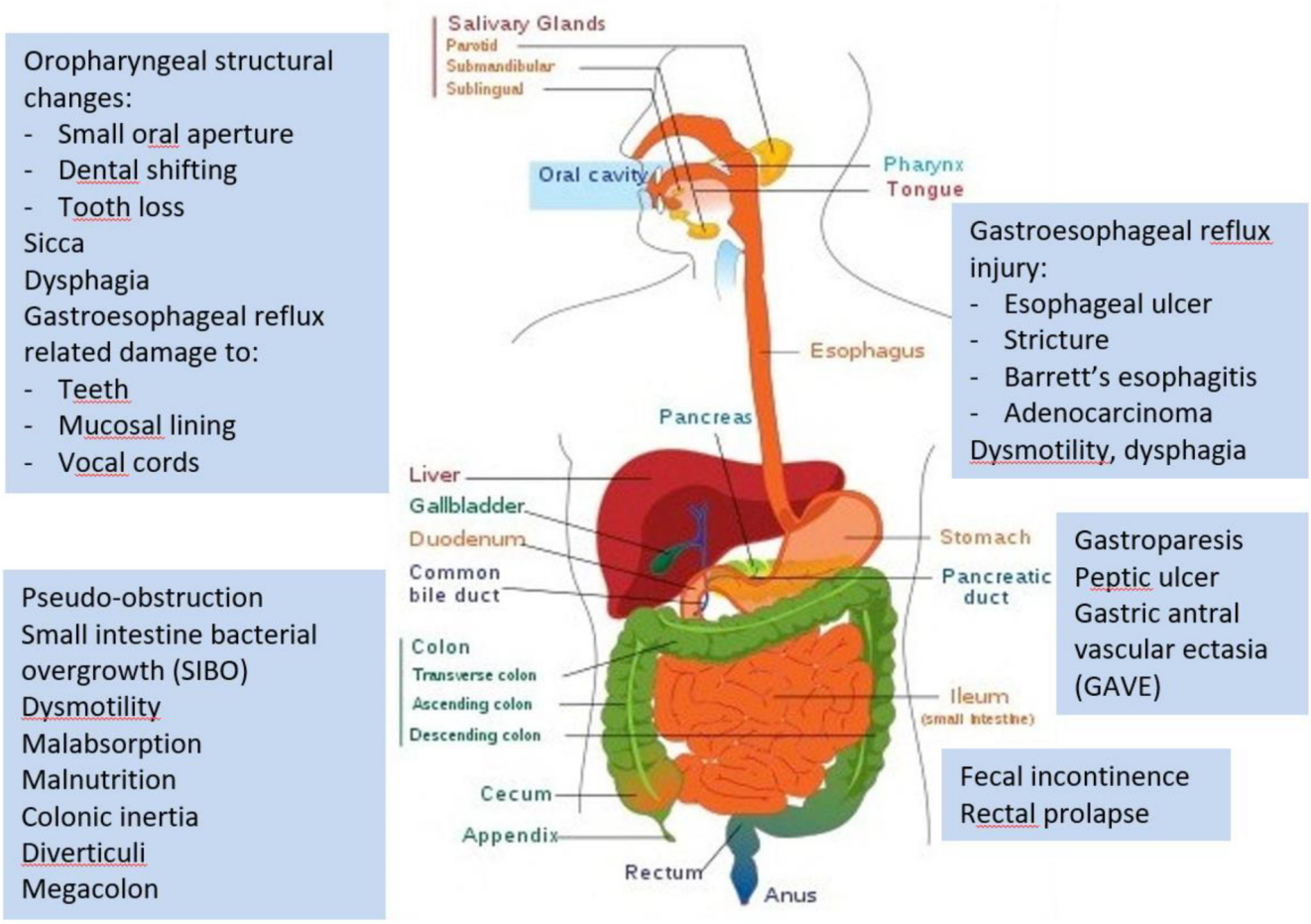


Figure 5. Depiction of the diffuse nature of gastrointestinal involvement in SSc.
Courtesy of T Frech, rights reserved.

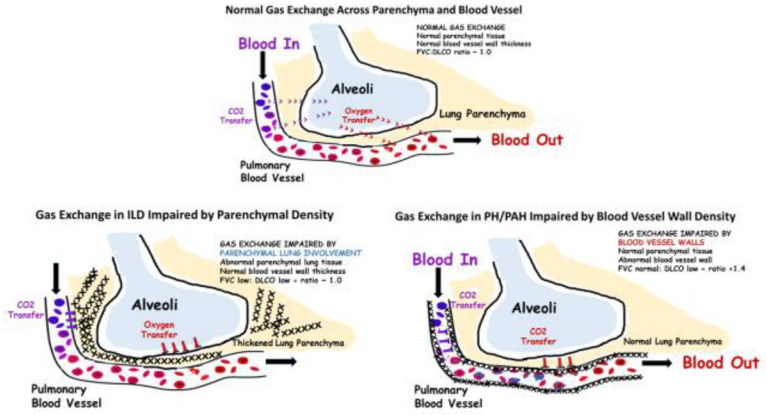


Figure 6.

Diffusion Capacity of the Lung for Carbon Monoxide Measures the Ability of Gas Transfer *(illustrations courtesy of LA Saketkoo, rights reserved.)*

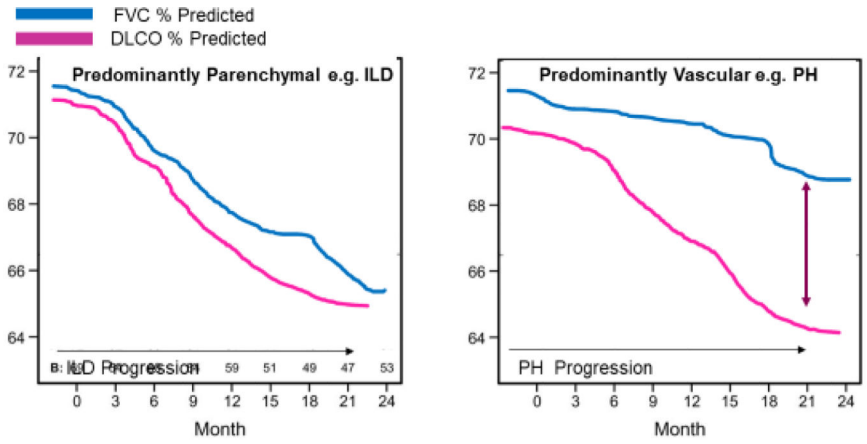


Figure 7. DLCO behavior in ILD versus PH Predominance.

The closer the ratio of FVC:DLCO is to 1 the more likely abnormal changes are related to restrictive lung disease. (*illustration courtesy of LA Saketkoo*)

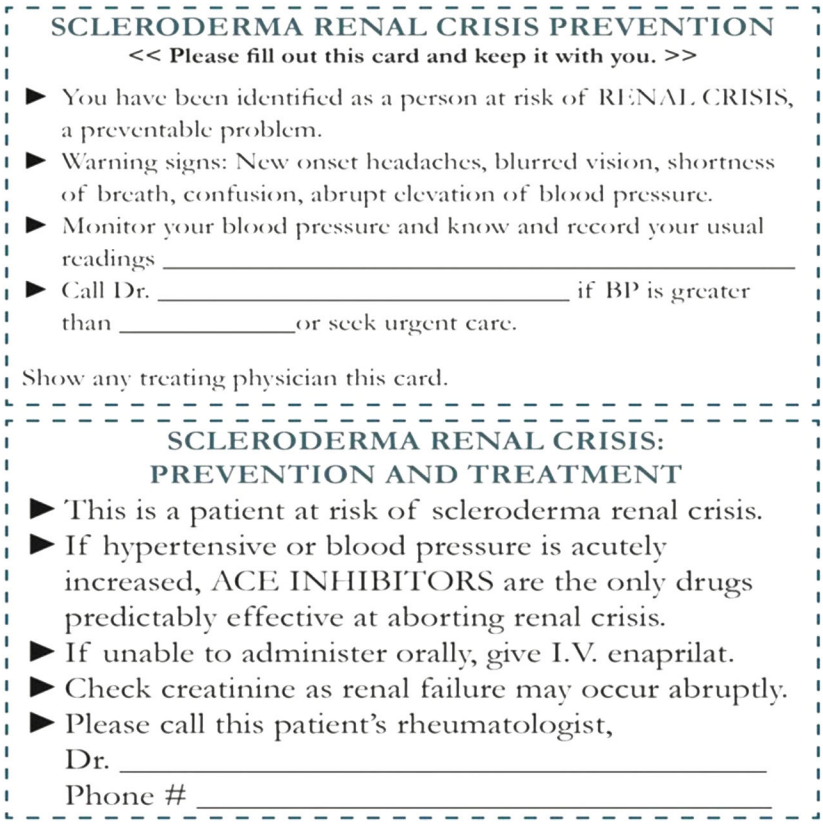


Figure 9.

The Renal Crisis Prevention Card may help patients direct emergency healthcare providers to abort a crisis and avoid adverse outcomes.[83]

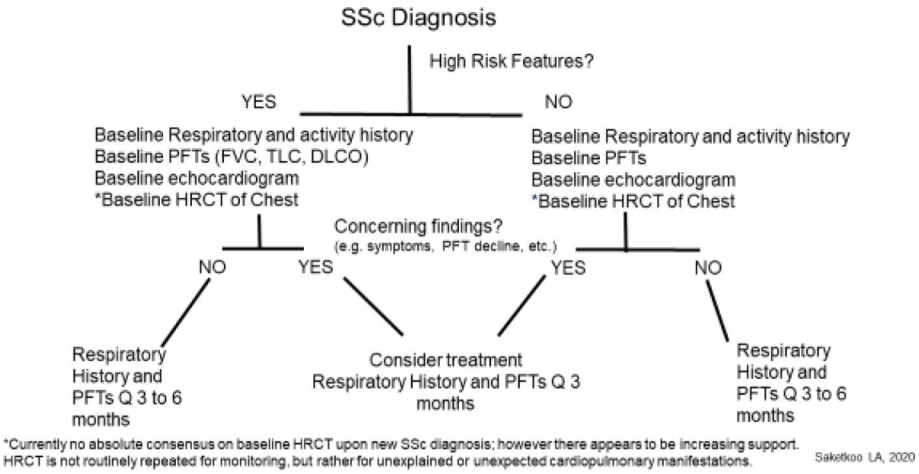


Diagram 1.

Proposed Screening and Monitoring Algorithm for Clinically Significant SSc-ILD. *Courtesy of LA Saketkoo, rights reserved.*

Table 1.

Risk Factors for Death, Disability and Rapidly Progressive Disease

Risk Factor	Clinical measures	Indication of Rapidly Progressive SSc or Severe Disease
Diffuse skin involvement	Modified Rodnan total Skin thickness Score (mRSS)	Increasing diffuse skin thickness, mRSS > 29
Tendon Friction Rub	Palpable presence on exam	Palpable presence on exam
Anti-topoisomerase I	See measures for ILD, dcSSc, renal crisis, and cardiac fibrosis	
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 arterial hypertension (PAH)	Echocardiography	Estimated sPAP >40 mmHg Right atrial or ventricular enlargement Septal flattening
	Right heart catheterization	mPAP>20mmHg
	WHO / NYHA Classification	PVR ≥ 3 Wood units Class III / IV
Cardiac Involvement	ECG Echocardiography Cardiac MRI	ECG arrhythmia, heart block, valve disease, Diastolic dysfunction >grade 2 left ventricular ejection fraction <45%
Digital ulcers, gangrene	Nailfold capillaroscopy	Severe capillary loss, with fibrotic infiltration
Scleroderma renal crisis	Hypertension	Abnormal or an unusually elevated value for patient Normotensive possible if on prednisone, vasodilators or anti-hypertensive
	Serum biomarkers	Rising serum creatinine Anti-RNA 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/Pre-albumin	
Polyarthritis	HAQ-DI DAS-28	HAQ-DI >2.00
General health status	Weight loss/BMI Serum biomarkers	Weight loss > 10% Low albumin, Low Hb
Comorbidities	Presence of : COPD, malignancy, diabetes mellitus	Anti-polymerase III in relation to malignancy

GAVE: gastric antral vascular ectasia, ILD: Interstitial lung disease; PAS: estimated pulmonary artery systolic pressure by Doppler echo; HAQ-DI : Health Assessment Questionnaire-Disability Index

Table 2.

Risk factors for the development of severe organ manifestations of systemic sclerosis[19,39–44]

Organ manifestation	Risk factors with Associated Findings
Heart	Diffuse cutaneous SSc Elevated ultra-sensitive CRP Myocardial fibrosis on CMR Anti-topoisomerase 1 antibody Male gender 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, i.e. >10mg prednisone daily Significant cardiac manifestation Joint contractures Tendon friction rubs
Interstitial lung disease (ILD)	African ancestry Male gender High mRSS Diffuse cutaneous SSc Anti-topoisomerase I antibody (Scl-70) Anti-Th/To antibody Anti-U11/U12 (RNPC) antibody Increased ESR or CRP FVC<70 %, DLCO<70 %
Progressive ILD	Active polyarthritis Increased ESR or CRP Disease onset over 55 years High mRSS Reflux (GERD) NYHA III-IV heart disease Decreased SpO_2 during 6MWT Progressive drop in %FVC corroborated by HRCT and symptoms Advanced ILD (traction bronchiectasis, honeycombing) within 5 years of disease onset
Pulmonary arterial hypertension	Disease onset over 55 years Long disease duration African ancestry for early onset Skin telangiectasia (increased number and size) Isolated DLCO decrease FVC/DLCO ratio > 1.6 Severe Raynaud's Severe digital ulcers Decreased capillary density by nail fold capillaroscopy

Organ manifestation	Risk factors with Associated Findings
	Increased serum uric acid Presence of anti-nucleolar (anti-Th/To, and anti-U3 RNP) autoantibodies
Gastrointestinal	Disease duration Anti-U3-RNP Dysbiosis (microbiome composition) End-stage vasculopathy features such as DU, calcinosis Dysphagia Frequent food regurgitation Small Intestinal Bacterial Overgrowth and related chronic diarrhea Chronic intestinal pseudo-obstruction Fecal soiling Weight loss Low albumin/pre-albumin
Digital ulcers	Diffuse cutaneous SSc 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 DAS-28 Presence of overlap SSc Presence of anti-RNA Polymerase III and anti-Scl-70 (anti-Topoisomerase I) autoantibodies

6MWT: 6-minute walk test, CMR: Cardiac MRI, CRP: C-reactive protein, DAS-28: Disease Activity Score-28, DLCO: diffusion capacity of the lung for carbon monoxide, ESR: erythrocyte sedimentation rate, FVC: forced vital capacity, GERD: gastroesophageal reflux disorder, mRSS: modified Rodnan Skin Score, NYHA: New York Heart Association; SpO2: blood oxygen saturation; WHO: World Health Organization

Table 3.

Domain Organization for Clinical Assessment and Documentation in SSc. Each sub-domain is often characterized by *onset, coincident intervention*, and *changes over time*.

Domains	Sub-Domains	Assessment Considerations
Background	Biological sex	
	Ethnicity and race	
	Environmental exposure history	e.g. chemicals via occupation or proximity
	Cardiovascular history	Especially noting hypertension
Disease Duration	Raynaud's phenomenon onset (month/year)	
	What was 1st non-Raynaud's phenomenon symptom	
	Onset of 1st non-Raynaud symptom (month/year)	
	Physician diagnosis of SSc (month/year)	
Skin Thickening	Onset month/year	
	Distribution (mRSS)	
	Pruritus	
	Pigmentation disturbances	e.g. hypo-, hyer- or poikiloderma
	Telangiectasia and Calcinosis	Recorded here or under the vascular domain
Vascular Manifestations Please see and incorporate components of Table 7 for document template		
HEENT	Facial Changes	Oral aperture
	Eyes	Dry Eyes
	Oral	Tooth loosening, Chewing difficulty Oral pain Dry mouth Dental caries
	Naso-pharyngeal	Post Nasal Drip (lung irritant) Hoarseness of voice (vocal cord fibrosis or acid injury)
Cardiopulmonary	History of symptoms Dyspnea/Cough / Exercise Intolerance NYHA Symptom Category	1st noticed symptoms to now Tables 9–10 for contextualizing history taking Although a categorical variable that limits utility, a worsening NYHA classification marks significant clinical worsening
	Cardiac symptoms including lower extremity edema, orthopnea	Arrhythmias/conduction disturbances, heart failure

Domains	Sub-Domains	Assessment Considerations
Gastrointestinal Consider following SCTC-GIT or Geissen tools for overall GI impact	Swallowing difficulty	Proximal Distal Choking, coughing
	Acid related	Heartburn Hoarseness Cough, timing e.g. morning
	Gastric	History of GAVE Early satiety Regurgitation of food Emesis of food Bloating / distension / pain
	Biliary	History of primary biliary cholangitis Itching, jaundice, pruritus, but may be asymptomatic Bilirubin and transaminase profiles, possible anti-mitochondrial antibody presence
	Small bowel	Diarrhea, pain, weight loss, malabsorption Cramping Bloating
	Large bowel	Constipation Fecal soiling
Muscular	Atrophy, Muscle strength, Muscle endurance, Aerobic capacity (submaximal test) Hand grip and pinch strength	MMT-8 TST/30-sec CST[^] FI-2/FI-3 [^] Ebbeling treadmill test [*] Astrand cycle test [*] 6 MWT [*] Jamar or Grippit dynamometer [*] Pinch meter [*]
Joint	AROM upper extremity, AROM/PROM hands/fingers	FSA [*] Goniometer [*] HAMIS [*] Cochin Hand Function Scale [*] DAS-28

6MWT: 6 minute walk test for distance, CST: Chair-Stands Test, DAS-28: Disease Activity Scale-28, FI-2: Functional Index 2, FI-3: Functional Index 3, FSA: Function Shoulder Assessment, HAMIS: Hand Mobility in Scleroderma, mRSS: modified Rodnan Skin Score, NYHA: New York Heart Association

[*] implemented routinely by OT, PT

[^] implemented by PT, OT but can be performed in clinic by physician or staff

Table 4.

Snapshot Diagram of Common Diagnostic Testing in SSc

VITALS	CARDIOPULMONARY		GASTROINTESTINAL as indicated by history and clinical findings	LABORATORY
Weight	FVC	*Consider smaller, softer mouth piece*	^pH Probe, 24 Hour monitoring	CBC
Blood Pressure	TLC		^Esophagram / Swallow study	CMP
Heart Rate	DLCO		^Esophagogastroduodenoscopy	Inflammatory markers: ESR, CRP, albumin, platelets
Respiratory Rate	6 MWT for distance and saturation with forehead oximeter		^Gastric Emptying Study	Muscle assessment: CK, aldolase, LDH
Oxygen saturation	HRCT of chest		^Stool for Ova, Parasite and Culture	Cardiac markers: BNP/NTproBNP, Troponin, Uric acid
	Echocardiogram		^Colonoscopy	Tuberculosis/HBV if considering therapy with Rituximab or Tocilizumab
	^ECG		^Glucose or Lactose H2 breath test for SIBO	25-OH Vitamin D
	^Right Heart Catheterization			HIV for new PH diagnosis
	^VQ Perfusion Scan – should be considered at new PH diagnosis			

^As indicated by history or clinical findings

SIBO: small intestine bacteria overgrowth

Table 5.

Common laboratory abnormalities in SSc. *Courtesy of JK Gordon & LA Saketkoo, rights reserved.*

Category	Specific Lab	Common Implications
Antibody Presence		
	ANA, **Anti-nucleolar pattern of any titer	Positive in 90–95% of cases. Perform by immunofluorescence. If negative, consider other fibrosing illnesses.
	*Anti-Scl-70 (Anti-topoisomerase I)	70% diffuse SSc, 30% limited SSc, higher risk ILD and higher risk severe ILD
	*Anti-RNA Polymerase III	Higher risk diffuse SSc, rapidly progressive skin, musculoskeletal involvement, higher risk SRC, GAVE, concomitant malignancy; Raynaud may present later in disease course
	*Anti-centromere	Limited SSc, PAH
	**Anti-Fibrillarin (U3-RNP)	Severe ILD, PAH, cardiomyopathy, severe GI involvement, diffuse SSc,
	**Anti-Th/To	Limited skin involvement, PAH, ILD
	**Anti-PM-Scl	Myositis, overlap
	Anti-U11/U12 RNP	Limited skin, ILD
	Anti-U1-RNP	Myositis, MCTD/Overlap, ILD, PAH, arthritis
	Anti-Ku	Myositis, Overlap
	Anti-NOR 90	Anecdotally associated with SSc, and other CTDs with RP; forgotten antibody
	Anti-Ro52	ILD, overlap
HEMATOLOGIC		
	Hemoglobin/Hematocrit	GI loss, Medication effect, active inflammation
	Schistocytes	Concern for SRC
	Platelets	Elevated: Active inflammation, Low: SRC, medication effect
	Erythrocyte Sedimentation Rate	active inflammation, infection, malignancy
	Serum Protein Electrophoresis	Hypergammaglobulinemia Associated with active disease, severe lung involvement, SSA antibody; More prevalent in African ancestry
Chemistry		
	Creatinine	SRC related renal injury
	Transaminases (ALT/SGOT, AST/SGPT)	Medications, myopathy,
	Creatine Kinase	Myopathy, myocardial infarction
	Albumin	If low: Active inflammation, low nutrition status, malabsorption
	Troponin	Myocarditis

Category	Specific Lab	Common Implications
	C-Reactive Protein	Active inflammation, infection Prognostic indicator
	Aldolase	Myopathy
	Uric Acid	Pulmonary hypertension predictor, cardiovascular disease
	Pro-NT-beta natriuretic protein / Beta-natriuretic protein	Pulmonary hypertension, heart failure
Urine		
	Protein	Prognostic indicator SRC
	Red cells	SRC

* Indicates criteria marker

** Indicates strong correlation with SSc diagnosis

Table 6.

Key Physical Exam Assessments in SSc *Courtesy of T Frech & LA Saketkoo, rights reserved.*

Category	Assessment Area	Observed Finding	Comment
CONSTITUTIONAL	Nutrition	Weight	
		Fit of clothes	
		Temporal muscle atrophy	
	Overall mobility	Observation into room, seating, reaching for coat, bag etc Use of assist device for ambulation	
HEMATOLOGICAL	Pallor	Observation	Anemia can occur from GAVE, medication effect, SRC
	Lymph nodes	Palpation	
HEENT			
Facial appearance	General facial structural features	Lip thinning	Most facial changes are difficult to track
	*Telangiectasia	See below	May indicate increasing vasculopathy
Eyes	Dryness		
	Conjunctival pallor		
Oropharyngeal	Oral Cavity	Dryness	
		Sublingual pallor	
		Dentition/crowding	
	Oral aperture	Aperture diameter in mm	
	*Telangiectasia	See below	Often the first location to appear
	Naso-pharyngeal	Signs of post-nasal drip (PND), i.e. erythema, ‘cobble-stoning’	PND and Reflux are micro-aspirated and irritate sensitive lung tissue causing parenchymal inflammation and possibly worsening ILD.
VASCULAR			
	*Circulation/RP	- color - coolness - location	

Category	Assessment Area	Observed Finding	Comment
		*Capillaroscopy - morphology: Drop-out Hemorrhage Dilated (giant) Tortuous Disorganized	Positive morphology contributes to diagnosis. Ophthalmoscope or dermatoscope easily identify morphologic changes. Nailfold video capillaroscope can mark detailed changes over time.
	*Digital ulcers	- number - location - depth - 'true' vs friction - drainage - infection^	
	*Pitting	- number - location - tenderness	
	Calcinosis	- number - location - consistency (solid v paste) - tenderness - infection^	Size, draining or not
	(Acro)-Osteolysis	Presence of distal to proximal: - Digital shortening - Nailbed tapering from sides - Nailbed blunting from tip	
	*Telangiectasias	- count - location (inner lip, face, chest, palms) - matted v non-matted	- used for diagnostic purposes - followed over time
CARDIOPULMONARY			
Cardiac	Observation	Jugular venous distension	
		Lower extremity edema	
		Positional chest pain	Pericarditis
	Auscultation	Rhythm, presence of gallop, rub	Pericarditis can occur in early phase dcSSc
	Aerobic capacity	6MWT	
Pulmonary	Observation	Respiratory rate	
		Depth of inhalation	Patients with ILD/PF often 'splint' to protect from coughing
		Cough with inhalation	Possible ILD/PH
	Auscultation	From apices to bases, from beginning of inhalation to end of exhalation Listening for crackles, absent breath sounds	If not hearing breath sounds, instruct patient during exam. Splinting occurs commonly in ILD to avoid inspiratory cough. Otherwise, consider pleural effusion

Best Pract Res Clin Rheumatol. Author manuscript; available in PMC 2022 September 15.

Category	Assessment Area	Observed Finding	Comment
		Inspiratory cough	
	Oximetry	SpO2%/Pulse oximetry, at rest and exertion–e.g. walk to exam room. 6MWT	Preferably ear or forehead oximetry Finger may display results not reflective of true SpO2
	Aerobic capacity	6MWT for distance	Musculoskeletal involvement may impact results, but overall 6MWT can reliably tend exercise tolerance
GASTROINTESTINAL	Nutrition	As above	
	Abdomen	Observable, palpable distension	
MUSCULOSKELETAL			
Articular/Peri-articular	Joint extension	To 180 degrees	PIPs, MCPs, wrists, elbows, shoulders, knees, hips, ankle joints
	Joint flexion	Fixed contracture (yes/no)	
	Finger-to-palm		
	Tenderness +/− swollen joints	Palpation especially PIPs, MCPs, wrists	Synovitis is even more difficult to appreciate in SSc than other CTDs
	Tendon Friction Rubs	Localization for documentation	
Muscle	Observation	Mobility	Muscle involvement is: - common in SSc - of variable and combined pathology: atrophy, inflammatory, necrotic, fibrotic - associated with SSc cardiac involvement
		Atrophy	
	Strength/Endurance	MMT 5 or 8 †	
		Functional Index-2 (FI-2) ^∧ FI-3-2 †^∧	Endurance is a more revealing assessment and more problematic for SSc patients than isometric strength. Usually performed by physiotherapist.
	Functional capacity	TST ^∧ or 30-sec CST †^∧	
SKIN	General Appearance	Pigmentation: - Hyper- - Hypo- - Poikiloderma Sheen: - Across chest Telangiectasias (here or detailed in ‘vascular’ domain)	
	Breakdown	Ulceration - Digital	

Category	Assessment Area	Observed Finding	Comment
		- Other areas Pitting	
	*Thickness: Extent and Degree	mRSS†	Skin thickness may also impair ROM
	Phase of Thickness	- Edematous v Bound-down - Initial signs of edematous phase often include puffy fingers; before skin thickening occurs	Edematous phase can cause diffuse pain and itching and often mistaken as fibromyalgia.
			Stretching may reduce inflammation, edema, contractures and skin tightness of hands, fingers, shoulders, chest, hamstrings and hips; as well as increase ROM.

*Indicates SSc classification criteria marker

^Infection = assessing for redness and purulence

^^see corresponding photo/s

†please see resource list for instructional content

^implemented by PT, OT but can be performed in clinic by physician or staff ‡

Table 7.

Vascular history, physical, counseling, therapeutic considerations. *(Table courtesy of T Frech and LA Saketkoo, rights reserved)*

Manifestation	Initial History	Current & Past Symptoms	Physical Function/Self Esteem	Exam	Counseling Considerations	Therapeutic Considerations
Raynaud(RP)	- 1st RP recollection - Provoking factors - Location - Frequency - Pain - Duration of attack -Medication use - History of: Gangrene, Surgical amputation, Sympathectomy, Botox injections	- Pain sensation *quality* and *intensity* (numbness, tingling, burning stinging, pain) - Location (ears, nose, fingers, nipples, toes) - Frequency - Color changes	-Impact on social life -Impact on employment	-Acro-osteolysis	- Stress management - Warming measures - Discontinue exacerbating medications - Avoid tobacco	-See table below for medications
Digital Ulcers	-Location* -Number -Concurrent infection or gangrene - Duration	Severity of Pain -Infection -Size - Location - Frequency - Duration	Impact on social life -Impact on employment	-Number -Location -Size -Infection - Gangrene	-Identifying critical digital ischemia	- OT -Wound care -Salves -See table below for medications -See table below for medications - RP Prevention *Ulcers can appear in other locations
Pitting	-Location -Pain	- Pain - Numbness - Location - Frequency	Impact on social life -Impact on employment	-Number -Size	Protective measures	
Calcinosis	-Location -Pain -Drainage	-Pain -Drainage -Location -Surgical needs	Impact on social life -Impact on employment - Impact on joint function or contractures	-Number -Size -Location - Attachment to tendons, ligaments, muscle planes	Protective measures from trauma to site Surgical options	- RP treatment - RP prevention - Trauma prevention - Surgical removal - Possible IV prostacyclin
Telangiectasia	-Location -Change in number	-Location -Treatment	Impact on social life -Impact on employment	-Number -New lesions for last exam -Location	Cosmetic options	-Laser beam therapies
Erectile Dysfunction (ED)			Impact on self-esteem, intimate life		Aerobic exercise may help, attention to cold prevention may help	Referral to ED specialist, aerobic exercise
GAVE	-See below					
PH	- See below					

Table 8.

Modifiable causes and treatment of fatigue and pain in SSc. *(Table courtesy of LA Saketkoo, rights reserved.)*

Symptom	System/Origin	Potential Causes	Team Involvement/Interventions
Fatigue	Anemia	GI loss, chronic inflammatory disease	
	Cardiac	PH, diastolic HF, CAD, 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, OSA	OT, PT, PR as for cardiac
	Muscular	Low muscle endurance, muscle strength or reduced aerobic capacity	MT, MMM, PR-PTr, PT for Aerobic exercises, muscle strengthening and endurance exercises, 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
	Neurological	Pain: ischemic, edematous skin, articular, restless leg syndrome	Assess treatable causes, MT MMM, PR
	Malnutrition	Weight loss, malabsorption	Dietary and nutritional counselling
	Sleep-related	OSA, nocturnal pain, pruritus, GI symptoms, depression, anxiety, steroid or opioid use	SH, RSS, MMM, MT
	Medication-Related	Methotrexate, MMF, nintedanib etc.	
Pain/Dysesthesia	Vascular	Raynaud	EC preventive strategies, MT, vasodilators, PT for aerobic exercise to improve blood flow
			Sympathectomy for critical ischemia
		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, OT for stretching and manipulation
		Subcutaneous edema and pressure	MT,ST, OT as above
		Pruritus	MT, SH, ST, opioid receptor blocker, phototherapy
	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, local injections, muscle strengthening, stretching, targeted hand exercises

Symptom	System/Origin	Potential Causes	Team Involvement/Interventions
		Secondary fibromyalgia	MMM, PR-PTr, SH, education
	Gastrointestinal	Heartburn	EC, RH, NH, anti-acid and PPI
		Abdominal cramping	See below
		Abdominal bloating	
	Genitourinary	Dyspareunia	Pelvic floor therapies, sometimes systemic treatment
		Vaginal dryness	Lubricants, topical estrogen
		Erectile dysfunction	Vasodilators, PT for aerobic exercise, specialist referral

Abbreviations: AG = anticipatory guidance, ATT = assessment with targeted treatment, EC = education/counselling, DHS = dental hygiene strategies, ILD= interstitial lung disease, MMM = mindful movement modalities (e.g. gentle yoga, tai chi etc), MT= mindfulness training strategies, OSA= obstructive sleep apnea, OT= occupational therapy, NH = nutrition hygiene (EC on attention to selection, volume, texture, preparation, combination strategies of foods), PAH= pulmonary arterial hypertension, PPI = proton pump inhibitors, POS = practical organizational strategies, PT = physiotherapy, RH = reflux hygiene (including head of bed elevation), RHS = refer to hand specialist, RME = refer to motility expert, THE= targeted home exercises, PR = pulmonary rehabilitationist, PR-EC = pulmonary rehabilitation educational component, PR-PTr = PR physical training component, RSS = refer to sleep specialist, SH = sleep hygiene, SR = specialist referral, ST = systemic treatment, UTPRM = untested patient-reported management[10]

Table 9.

Screening questions to help patients reflect on potential onset and changes in dyspnea and cough. *Courtesy of LA Saketkoo, rights reserved.*

DYSPNEA Screening	COUGH Screening for ILD
Do you notice being more short-winded now than one month ago, six months ago, last year while doing activates (consider activities likely for the patient)?	Have you been coughing? More in the past 3/6 months?
Do you notice it takes you longer to vacuum, mop, make the bed, mowing the lawn?	Do you cough when taking a deep breath in?
Do you notice you are more short of breath when vacuuming, making the bed, 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?

Table 10.

Common causes of dyspnea and cough in SSc. *Courtesy of LA Saketkoo & MB Scholand, rights reserved.*

DYSPNEA	**COUGH**
ILD	ILD – dry inspiratory
Pulmonary Hypertension – any or any combination of the following: Groups I, II, III, IV	PND – possible drip sensation, often in morning, sore throat
Bronchiectasis*	Bronchiectasis*
Cardiac dysfunction or arrhythmia	Heart failure
Anemia	GERD – can be ‘wet’ cough / gastroparesis
Physical deconditioning	
Intrinsic or extrinsic myopathy e.g. restrictive truncal skin involvement (carapace chest), accessory muscle myopathy	
General population considerations: CAD, COPD	
Disordered breath patterns	

** 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)

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Table 11.

Screening and characterization of pulmonary hypertension in SSc. *Courtesy of LA Saketkoo, rights reserved.*

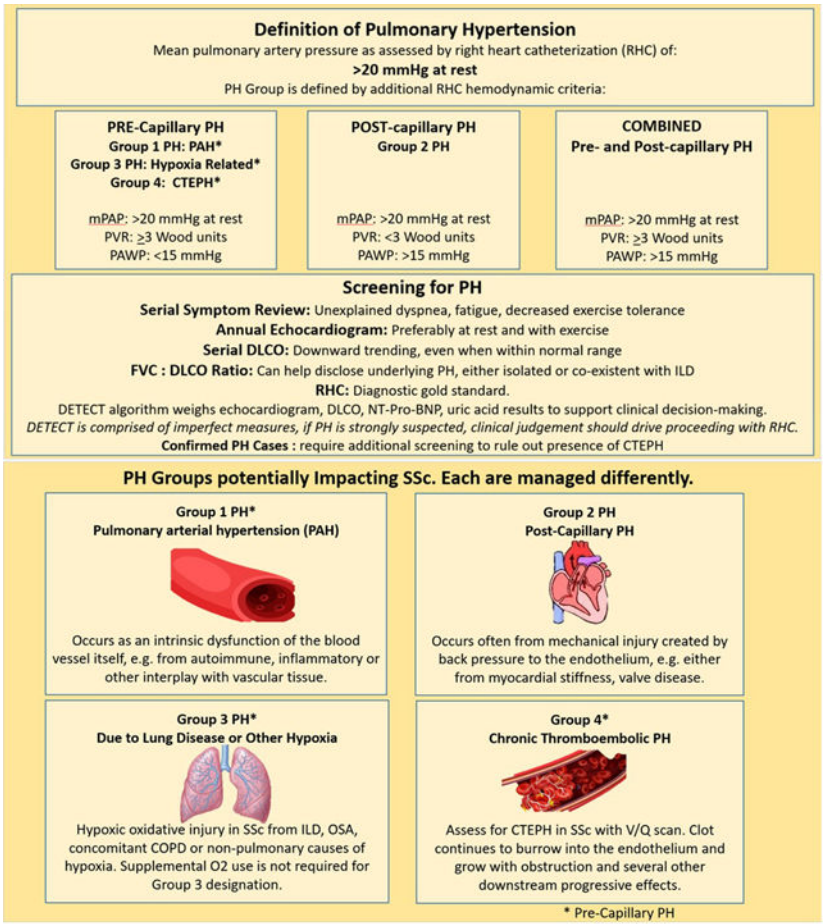

Table 12:

When to Consider Referral for Lung Transplant

Diagnosis	Indications for Referral
Interstitial lung disease	• Radiographic or biopsy proven disease • FVC <= 80% • Need for supplemental oxygen
Pulmonary hypertension	• Severe functional limitation with NYHA functional class III or IV • Rapid decline in functional status • Decreasing 6MWT • Increasing oxygen requirements • Need for intravenous therapies
Myocardial disease	• RV failure without evidence of RV infarction (isolated RV failure related to pulmonary hypertension [any WHO class] recovers after lung transplant) • Irreversible LV involvement, heart-lung transplant evaluation may be warranted

Abbreviations: 6MWT, 6-minute walk test; FVC, forced expiratory volume; LV, left ventricle; NYHA, New York Heart Association; RV, right ventricular; WHO, World Health Organization

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Table 13:

Common Challenges of Lung Transplant Evaluation in Patients with Systemic Sclerosis

Challenge	Considerations
Obesity	• BMI <35, preferably <30 and transplant center dependent • Early counseling regarding healthy weight
Age	• Highly variable and transplant center dependent
Frailty/Deconditioning/Post-transplant rehabilitation potential	• Pulmonary rehab participation • Frailty Assessment Score • Chronic pain/Advanced osteoporosis
Active substance abuse/dependence	• 6 months sobriety with only rare exceptions • Participation in counseling
Esophageal dysmotility	• Full evaluation of esophagus • GJ tube for full nutritional support may be recommended, assessment for willingness and compliance
History of malignancy	• Time free from malignancy is multifactorial and transplant center dependent
Social support	• Identify 24-hour caregiver for at least 3 months • Some transplant centers also require a committed back-up caregiver • Caregivers will be evaluated for appropriateness
Finances	• Financial counseling to establish ability to afford transplant • Fundraising may be required/recommended • Insurance clearance required before evaluation is initiated

Abbreviations: BMI, body mass index; GJ, gastrostomy-jejunostomy

Table 14.

Common Therapeutic and Surgical Referrals Resourced in SSc Care. Cultivating referral relationships with colleagues who are interested in SSc may have best outcomes for people living with SSc

THERAPEUTIC/SURGICAL	INDICATIONS
Occupational Therapy	For hand, face and oral health Joint and skin mobility Self-management, breath pattern training Home and work adaptations
Hand Surgery Vascular Surgery	Early referral (for physician/patient familiarization) for patients at high risk for vascular or wound complications including: Critical ischemia DUs/calcinosis complicated by infection Calcinosis complicated by nerve entrapment Macrovascular occlusion For procedures including sympathectomy, botulin toxin injections
Physiotherapy	For building muscle strength, muscle endurance and aerobic capacity Increasing physical capacity and activity Balance, joint/skin mobility Education on fatigue and pain
Pulmonary Rehabilitation	For enhancing aerobic capacity, endurance and education on cardiopulmonary efficiency Includes Singing, Yoga, Dance for Lung Health programs
Dental care / Oral surgery	At least twice yearly Access to pediatric is a consideration Dry mouth care Preservation of dentition
Speech	For swallowing, exercises for mouth strength and speech production
Nutrition / Dietetic Care	To enhance calorie intake, detailed counselling on gastroparesis and food tolerance strategies
Wound Care	Management of DUs, calcinosis
Hyperbaric Therapy	For DUs, avascular necrosis, general wound healing
Psychological Support and Counselling	For managing anxiety, depression, impact of changing appearance on body image and self-esteem Developing coping skills to manage changing ability, uncertainty

Table 15.

Essential counseling on exercise in SSc. Note: in many countries, physiotherapists also teach breathing exercises to optimise breath patterns and strength of breath. General exercise applications are also a part of cardiopulmonary rehabilitation programs.

EXERCISE GENERAL APPLICATION	STRETCHING	RESISTANCE	AEROBIC	MONITOR
	Both upper and lower extremities with dedicated focus on areas with impaired range of motion (e.g. shoulders/ pectorals, calves, hamstrings and external rotators in hip). Easier to do when warm, after exercise or sauna	Ideally >15 reps for 3 sets at least twice a week To gain muscle mass To preserve overall muscle strength	Warm-up and cool-down important esp PAH, treadmill, ergometer cycle Ideally 30 min, 3 days/ week	At least initially with PAH and/or ILD: SpO2, heart rate, blood pressure. Dyspnea and muscle tiredness with Borg CR-10 and exertion with Borg RPE
OROFACIAL				
	Emphasize -mouth opening -facial grimaces such as smile, pucker lips, etc	Isometric-hold positons - see resources	N/A	-use ruler to monitor - see resources section
HANDS				
	Emphasize -Flexion MCP and IP joints -Extension PIP joints -First commissure) -Finger web spaces (interdigit) -Wrist flexion and extension	-Squeezing foam, dough, putty) -Finger extension – rubber bands/putty as resistance -Rolling out dough/putty with finger -Pinch with foam, dough, putty (finger tips to thumb, thumb to side of index finger)	N/A	Hand tracings: - In extension - In fist Grip and pinch strength - see resources section
	Heat modalities prior to stretching enhances practice (e.g. paraffin wax, warm water, etc)			

Abbreviations: N/A = not applicable, MCP = metacarpophalangeal joint, PIP = proximal interphalangeal joint

Table 16.

Key Elements of Recurrent Counseling *(Courtesy of LA Saketkoo, rights reserved)*

Category	Sub-Category	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, e.g. from cold to warmth - Anticipate cold environments, e.g. 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
		Peripheral	- Gloves / socks always at hand - Should allow for a thin space to trap a warming layer of air - Pocket hand warmers, can be placed in pockets, gloves, socks, undergarments - 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
		Pain management	- Protection as above - Topical lidocaine - Cleansing routine
		Signs of infection	- Increased pain/tenderness - Redness - Purulence
		Prevention	As much as possible avoid: - Cold exposure - Trauma Topical antibiotics with signs of infection
	Additional calcinosis	Advisement	- Avoid digging to prevent infection - If intolerable can try repeated soaking in warm Epsom salt water - Topical antibiotics
	Erectile dysfunction		- Increased physical activity may help protect circulatory and neuronal function - Preventive measures as for RP might have a protective effect
NUTRITION	Calorie intake	Nutritious	- Avocado - Nuts, nut butters - Cheeses, butter - Potatoes, rice - Olive and other oils

Category	Sub-Category	Item	Advisements for Patients
	Food Tolerance	Nutritious	- Pureed foods (soups, dips, stews) - Smaller amounts of a food - 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 - Keeping mouth moist - Adapted and powered devices for teeth and oral care
	SICCA		Wetting and pro-salivation products Possibly singing, humming, chanting and exercise
CARDIOPULMONARY			Graded exercise essential to health
			Control of GERD and PND to avoid lung injury from micro-aspiration
			Vaccination for prevention of infection
	PH and Cardiac	Monitor for symptoms of heart failure	Daily weights as needed; recording of post-void morning weight Alert MD of new onset lower extremity edema
GASTROINTESTINAL			
	GERD	Esophageal Injury & 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 not equate severity - Esophagitis - Esophageal cancer - Dysphagia and potential loss of swallow function - Strictures & Webbing - Need for esophageal stretching - Acid aggravates lung disease
		Medications	- PPI daily or twice daily, especially with esophagitis or esophageal ulcer - Adding PRN or OTC agents (e.g. sucralfate, H2 blockade) -- it is perceived that in SSc the benefits of PPIs greatly outweigh associated risks
		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 - Avoid meals 2–3 hours before lying - Avoid sphincter relaxants at end of day e.g. alcohol, chocolate, caffeine, mint etc.
	Gastroparesis		- Sleep and hygiene as for GERD - Exercise / walking may help

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Category	Sub-Category	Item	Advisements for Patients
			- Gravity strategies for passive digestion - upright position - attention to food consistency e.g. thinner foods - Gastroparesis dietary suggestions for food tolerance
	Bloating		- Exercise for motility - Small frequent meals
	Nausea	SSc or Medication related	- Mobility / exercise to decrease nausea - Ginger sweets, drink - Sucking candies - Cold pops - Instruction on PRN anti-emetics
	Diarrhea	SSc or Medication related	Logistics until controlled: change of clothes, time planning Medication use: risks / benefits / when
MEDICATION	See Appendix of Medications		
VACCINES	See Table 17		Pneumococcal immunizations per CDC guidelines Influenza annually Herpes zoster (killed only i.e. Shingrix) COVID-19
EXERCISE			Improves: - Circulation and vascular responsiveness - Body warmth - Sleep - Self-Esteem - Breathlessness - Joint mobility stiffness and lubrication - Skin function - GI function - Possibly erectile function - Nausea - Salivation - Respiratory performance - Cognitive clarity Decreases: - inflammation - Pain (anywhere) - Joint stiffness - Possibly contractures - Possibly skin tightness - Depression - Stress - Fatigue

Category	Sub-Category	Item	Advisements for Patients
WOMEN OF CHILD-BEARING AGE	Medication toxicity		- Use of contraception essential with specific IS and PAH medications - Discontinuation of specific IS or PAH medications prior to conception
	Conception		- Must be a planned - Medication washout pre-conception - Discuss assessing extent of ILD, PH, cardiac or renal involvement in light of safe pregnancy
	Care of children		-Adaptations for child care - Strategies to manage fatigue
PSYCHOLOGICAL			Advocacy / Education Groups Local support groups
			Online self-management program (see resources)

Table 17.

Routine Health Maintenance in SSc. *Courtesy of N Sandorfi, rights reserved.*

Immunization	HPV (ages 16–26), Influenza (yearly), Hepatitis B, Pneumococcus (at any age with immune disease), Diphtheria/Tetanus/Pertussis (ages 19–64), Varicella Zoster killed (ages 50 or older), (*) COVID-19
Age, sex and risk factor based cancer screening	Gynecological, prostate, gastrointestinal, skin (*) Higher risk exists around the time of disease onset for those with anti-RNA polymerase III positivity (with consideration of breast, lung, prostate and tongue cancer)
General	Hypertension, diabetes cholesterol, sexually transmitted diseases (*)
Osteoporosis	Women ages 65< or earlier if risk factors exist (special considerations in SSc: malabsorption, corticosteroid use, prolonged use of proton pump inhibitors) (*)
Ophthalmology	Special considerations: sicca symptom related complications, hydroxychloroquine associated toxicity (**)
Dental	Routine exam and sicca symptom related complications (***)
Psychological	Chronic disease related psychological conditions (depression/anxiety) (****)
Laboratory	Tuberculosis, hepatitis C/B screening related to pharmacological therapies

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Table 18.

Patient-Centered Visit Preparations

Environment	
Temperature	Cold can be injurious in SSc Control clinic temperature exposure via either: - thermostat adjusted to >72F/22C - or with blankets for dedicated patient use Patients should be advised to bring clothing layers to maintain warmth for areas outside of clinic control
Fragrance-free	A perfume-free policy maintains a safe environment for patients, family members and clinic staff: - fragrance can trigger dyspneic coughing episodes in patients with ILD - fragrance can impede PFT performance for that patient and other nearby patients or those who subsequently in the suite Advisement occurs prior to visit, during scheduling.
Supplemental Oxygen Availability	Many patients with SSc use supplemental oxygen tanks that hold a limited oxygen supply. Upon patient arrival, switching their tank to a clinic tank: - assures sufficient supply for their visit - preserves supply for the patient's journey home If this can't be done, patients should be advised of anticipated length of time at the facility for which they will need to have sufficient supply.
Wait Times	Multiple procedures on a single day can be exhaustive and unanticipated. Helping patients and families anticipate their needs with the following advisements creates a more comfortable (and safe) experience:
Nutrition Needs	- Bringing snacks and lunch
Hydration	- Having water or preferred beverages available
Down time	- Reading materials etc. to pass time waiting between tests and visits
Visit Times	Assessment, intervention and counselling in SSc that is sufficient to reduce SSc-related symptoms and complications requires time.
New Patients	≥90 minutes but can require 3 hours, depending on disease extent, complications and initiating management
Established Patients	45 to 90 minutes as even stable patients with SSc requires multi-organ assessment and SSc-specific counselling that is beyond a usual visit for most other conditions
Chart Review	SSc management is often time-sensitive and relies upon diagnostic testing and symptom history trended overtime. New patients often require extensive data organization; while Interval history is often dense for established patients. Appropriate chart review requires pre-visit attainment of past and interval medical records. Documentation of serial data points prior to visit facilitates proactive management, freeing up clinician attention for meaningful patient-centered discussions. Real-time interventions and counselling may result in: - fairly immediate relief of some disabling symptoms - prevention of disease progression Chart review is reimbursable in the US, whether on same day or other day. See resources list for medical record intake template and other clinic support documents.
Consolidating Testing	Consolidating SSc diagnostic testing in as few visits as possible reduces travel burden, employment impact on patient and family
Out-patient	Past records, pre-visit labs, PFTs, HRCT or echo, ordered prior to scheduled visit, with results forwarded for clinician review, expedites management during the visit. Same day SSc-diagnostic testing, prior to clinician visit: - Common approach at SSc centers: coordinating SSc testing to occur same day, prior to scheduled visit

In-patient	An alternate approach for new and established patients at SSc centers in some countries with: - Approximate 2 day hospital admission - All routine SSc diagnostic testing and any further testing as indicated by - Evaluation and teaching by PT/OT - Management with counselling over one or both days Patients also visit as out-patients for interim monitoring, repeat testing

Table 19.

Quality healthcare provision sufficient to address the most pressing and essential aspects of SSc care and other complex multi-system disorders, demands time. Accounting for time usage is foundational for reimbursement or, especially for countries and provinces where complexity is not accounted for, an advocacy metric for policy revision. Using the 2021 policies from *U.S. Centers for Medicare & Medicaid Services* is used as an example below, similar constructs may exist in other countries.

Discrete Care Events	**Stipulations for billing in the US**		**Coding**	
Chart Review/Pre-visit Charting/Post-visit Charting	If occurs same day as patient clinic visit	See below	Tabulate in the time-based visit coding using prolonged codes	
	If occurs on a day other than actual clinic visit If occurs as a non-visit consultation	Stand alone codes	- 99358 for 31 to 74 minutes on non-direct patient care - 99359 for each additional 15–30 minutes i.e. added for 75–90 min and again for 104 –120 minutes (maximum)	
Clinic Visit	No direct patient time requirement Primary code to which other codes are added e.g. prolonged clinician or staff codes	Complexity-based	See below	
		Time-based		
Patient-initiated queries	Telephone or internet-based communication with patient that is unrelated to a visit 7 days prior nor leads to visit in next 24 hours	Time-based for communication and tasks related to query	99441 5 –10 min 99442 11–20 min 99443 21–30 min	
Clinic Staff Time	Added to clinic visit code, for prolonged services by staff beyond the typical time		99415 45 – 74 min 99416, each additional 15–30 min	
Clinic Visit Breakdown for Time-based Coding				
New Patient		Established Patient		
99202 15–29 minutes		99212 10–19 minutes		
99203 30–44 minutes		99213 20–29 minutes		
99204 45–59 minutes		99214 30–39 minutes		
99205 60–74 minutes		99215 40–54 minutes		
Prolonged Coding				
99205 or 99215 need to be fulfilled then				
Codes that may be obsolete in 2021	99354 additional 30–74 minutes 99355 for each further 15–30 minute increments	**Possible new 2021 codes** Added for each additional 15 min increment	**CMS Code:** G212 **AMA Code** 99417	