Role of Lung Ultrasound in the Evaluation of Systemic Sclerosis: Relationship with Functional Impairment and Patient-Reported Outcomes

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Abstract

Background: Systemic sclerosis (SSc) is a chronic autoimmune connective tissue disease characterized by widespread microvascular injury, immune dysregulation, and progressive fibrosis affecting the skin and internal organs. Among its visceral complications, systemic sclerosis–associated interstitial lung disease (SSc-ILD) represents one of the leading causes of morbidity and mortality, substantially impairing respiratory function, exercise capacity, and health-related quality of life. Early detection and accurate monitoring of pulmonary involvement are therefore essential for optimizing clinical outcomes. High-resolution computed tomography (HRCT) remains the reference standard for the assessment of SSc-ILD; however, its repeated use is limited by radiation exposure, cost, and restricted accessibility in some clinical settings. In recent years, lung ultrasound (LUS) has emerged as a promising, non-invasive, radiation-free imaging modality capable of identifying interstitial lung abnormalities through characteristic sonographic findings.

This review aims to evaluate the current evidence regarding the role of lung ultrasound in the assessment of systemic sclerosis–associated interstitial lung disease, with particular emphasis on its relationship with pulmonary function parameters, functional impairment, disease severity, and patient-reported outcomes. Furthermore, the review explores the potential contribution of LUS to longitudinal monitoring and rehabilitation-oriented management strategies in patients with SSc-ILD.

Accumulating evidence demonstrates that LUS findings, particularly the presence and distribution of B-lines, pleural line irregularities, pleural thickening, and subpleural abnormalities, correlate significantly with the extent of pulmonary fibrosis detected by HRCT. Several studies have also reported meaningful associations between ultrasound abnormalities and reductions in pulmonary function indices, including forced vital capacity (FVC), diffusing capacity of the lung for carbon monoxide (DLCO), total lung capacity, and exercise tolerance measures. Beyond structural and physiological assessment, increasing attention has been directed toward the relationship between pulmonary involvement and patient-centered outcomes, including dyspnea, fatigue, physical functioning, and overall quality of life. The portability, safety, repeatability, and bedside applicability of LUS make it particularly attractive for routine follow-up and functional monitoring.

Conclusion: Lung ultrasound represents a valuable complementary tool in the evaluation of SSc-ILD, providing clinically relevant information that reflects both structural lung involvement and functional disease burden. Its demonstrated associations with pulmonary impairment and patient-reported outcomes support its growing role within multidisciplinary care pathways. Integration of LUS into routine assessment protocols may enhance early detection, disease monitoring, and rehabilitation planning while reducing reliance on repeated radiologic examinations. Further large-scale prospective studies are required to establish standardized scanning protocols, validate prognostic applications, and clarify its role in long-term patient management.

Keywords: *Lung Ultrasound , Systemic Sclerosis: Functional Impairment*

Introduction

Systemic sclerosis (SSc) is a chronic multisystem autoimmune connective tissue disease characterized by immune dysregulation, widespread microvascular injury, and progressive fibrosis affecting the skin and internal organs. Although cutaneous manifestations are the most recognizable features of the disease, visceral organ involvement is the principal determinant of long-term morbidity and mortality. Among the internal organ complications, pulmonary involvement has emerged as the leading cause of death in patients with SSc, surpassing renal crisis and other systemic manifestations due to advances in their management. The pulmonary spectrum of SSc includes interstitial lung disease (ILD), pulmonary arterial hypertension, pleural disease, and airway abnormalities; however, SSc-associated interstitial lung disease (SSc-ILD) remains the most frequent and clinically significant pulmonary complication. [1,2]

SSc-ILD encompasses a heterogeneous group of fibrotic lung abnormalities resulting from persistent inflammation, immune activation, vascular dysfunction, and excessive extracellular matrix deposition within the pulmonary interstitium. The disease course is highly variable, ranging from stable and slowly progressive forms to rapidly deteriorating phenotypes associated with severe respiratory impairment and premature mortality. Epidemiological studies indicate that radiographic evidence of ILD can be detected in a substantial proportion of patients with systemic sclerosis, while clinically significant progressive disease develops in a considerable subset. Early identification of pulmonary involvement is therefore critical because timely therapeutic intervention may slow disease progression and preserve functional capacity. [2–4]

The assessment of SSc-ILD traditionally relies on high-resolution computed tomography (HRCT), which remains the reference imaging modality for detecting and characterizing interstitial abnormalities. HRCT provides detailed visualization of ground-glass opacities, reticulation, traction bronchiectasis, and honeycombing, allowing accurate evaluation of disease extent and severity. Pulmonary function tests (PFTs), particularly forced vital capacity (FVC) and diffusion capacity for carbon monoxide (DLCO), are routinely employed to evaluate physiological impairment and monitor disease progression. Despite their established value, repeated HRCT examinations are associated with cumulative radiation exposure and increased healthcare costs, whereas pulmonary function testing may not always reflect early structural changes within the lung parenchyma. Consequently, there is growing interest in accessible, non-invasive, and repeatable imaging tools that can complement conventional assessment strategies. [4–6]

Lung ultrasound (LUS) has emerged over the past decade as a promising bedside imaging modality for the evaluation of interstitial lung involvement in connective tissue diseases. Unlike conventional ultrasonography, which was historically considered unsuitable for lung assessment because of air interference, modern ultrasound techniques utilize characteristic artefacts generated at the pleural surface to identify pathological changes. Among these findings, B-lines, pleural line irregularities, pleural thickening, and subpleural abnormalities have demonstrated significant correlations with fibrotic changes detected on HRCT. Moreover, LUS offers several practical advantages, including the absence of ionizing radiation, portability, low cost, rapid acquisition, and suitability for serial monitoring. These characteristics make it particularly attractive for screening and follow-up of patients with SSc-ILD. [7–9]

Beyond structural lung assessment, SSc-ILD profoundly affects functional status and health-related quality of life. Progressive pulmonary fibrosis contributes to dyspnea, exercise intolerance, fatigue, reduced physical performance, and limitations in daily activities. These manifestations substantially impair patient-reported outcomes and represent important determinants of overall disease burden. Accordingly, contemporary management strategies increasingly emphasize patient-centered evaluation incorporating functional measurements and quality-of-life instruments alongside traditional imaging and physiological parameters. Understanding whether LUS findings reflect not only anatomical lung involvement but also functional impairment and patient experience may further expand its clinical utility within multidisciplinary care pathways. [10,11]

Although numerous studies have investigated the diagnostic performance of lung ultrasound and its correlation with HRCT findings in SSc-ILD, comparatively less attention has been directed toward its relationship with pulmonary function parameters, functional capacity, and patient-reported outcomes. Furthermore, the potential role of LUS in rehabilitation-oriented assessment and longitudinal monitoring remains incompletely defined. Therefore, this review aims to critically examine the current evidence regarding the role of lung ultrasound in the evaluation of systemic sclerosis–associated interstitial lung disease, with particular emphasis on its relationship with functional impairment and patient-reported outcomes, while highlighting future perspectives for clinical practice and multidisciplinary management.

Systemic Sclerosis–Associated Interstitial Lung Disease: Clinical Burden and Unmet Needs

Interstitial lung disease (ILD) represents one of the most serious organ manifestations of systemic sclerosis and is currently recognized as a leading cause of disease-related mortality. The development of pulmonary fibrosis substantially contributes to functional decline, reduced exercise tolerance, impaired quality of life, and increased healthcare utilization. Although advances in immunosuppressive and antifibrotic therapies have improved disease management, SSc-ILD continues to be associated with considerable morbidity and mortality. The burden of pulmonary involvement is particularly significant because lung disease may remain clinically silent during its early stages, allowing irreversible fibrotic changes to develop before diagnosis is established. Consequently, early recognition and close monitoring of pulmonary involvement have become central objectives in contemporary SSc management. [12,13]

The reported prevalence of SSc-ILD varies considerably according to study population, diagnostic criteria, ethnicity, and assessment methods. Radiological evidence of interstitial lung abnormalities may be identified in a substantial proportion of patients with systemic sclerosis, whereas clinically significant disease develops in a smaller but important subset. Ethnic and geographic differences have been consistently reported, with some populations demonstrating higher frequencies of pulmonary involvement than others. In addition, male sex, diffuse cutaneous disease subtype, anti-topoisomerase I antibody positivity, higher modified Rodnan skin scores, and certain genetic and environmental factors have been associated with an increased risk of ILD development and progression. [13–15]

The pathological process underlying SSc-ILD is characterized by complex interactions among endothelial injury, immune activation, inflammatory mediators, and aberrant fibroblast activation. These mechanisms ultimately promote excessive deposition of extracellular matrix proteins within the pulmonary interstitium, resulting in progressive fibrosis and distortion of normal lung architecture. Histopathologically, non-specific interstitial pneumonia (NSIP) is the most frequently observed pattern, while usual interstitial pneumonia (UIP) occurs less commonly but is often associated with a less favorable prognosis. The extent of fibrotic remodeling directly influences pulmonary mechanics, gas exchange efficiency, and long-term clinical outcomes. [1,16]

Clinically, SSc-ILD exhibits remarkable heterogeneity. Some patients demonstrate stable disease over prolonged periods, whereas others experience rapid deterioration in lung function despite appropriate therapy. Dyspnea on exertion and persistent nonproductive cough are the most common presenting symptoms; however, these manifestations often appear only after significant pulmonary involvement has occurred. On physical examination, bibasal inspiratory crackles, commonly described as “Velcro crackles,” may provide an early clue to interstitial lung disease. As fibrosis progresses, patients may develop severe exertional limitation, hypoxemia, respiratory insufficiency, and signs of pulmonary hypertension or right-sided heart failure. [2,4]

The natural history of SSc-ILD has become better understood through large observational cohorts. Evidence from the European Scleroderma Trials and Research (EUSTAR) database has demonstrated that disease progression may occur throughout the course of systemic sclerosis and is not restricted to the earliest years following diagnosis. Declines in forced vital capacity (FVC) and diffusing capacity for carbon monoxide (DLCO) remain important indicators of disease progression and are strongly associated with adverse outcomes. Importantly, even modest reductions in pulmonary function may

significantly affect physical performance and health status, emphasizing the need for sensitive tools capable of detecting clinically meaningful changes over time. [6,17]

The socioeconomic and patient-centered burden of SSc-ILD extends beyond physiological impairment. Progressive respiratory symptoms frequently limit occupational activities, social participation, and independence in daily living. Patients commonly report fatigue, reduced exercise capacity, emotional distress, anxiety regarding disease progression, and diminished overall well-being. Several studies have demonstrated that pulmonary involvement is among the strongest determinants of impaired health-related quality of life in systemic sclerosis. Therefore, comprehensive assessment of SSc-ILD should incorporate not only structural and functional measures but also patient-reported outcomes that reflect the real-world impact of the disease. [10,18]

Despite major advances in understanding disease mechanisms and therapeutic options, important unmet needs remain in the evaluation and monitoring of SSc-ILD. HRCT remains the reference standard for imaging assessment, yet concerns regarding radiation exposure and accessibility limit its suitability for frequent surveillance. Pulmonary function tests provide valuable physiological information but may fail to detect early structural abnormalities and can be influenced by patient effort and comorbid conditions. These limitations have stimulated growing interest in alternative imaging approaches capable of providing rapid, reproducible, and non-invasive assessment of lung involvement. Lung ultrasound has emerged as one such modality and may offer a practical solution for screening, monitoring, and longitudinal evaluation of patients with SSc-ILD. [5,7,8]

Impact of SSc-ILD on Functional Status and Health-Related Quality of Life

Systemic sclerosis–associated interstitial lung disease exerts a profound impact on patients' physical functioning, psychological well-being, and overall quality of life. While pulmonary fibrosis is often evaluated through radiological and physiological parameters, these measures do not fully capture the daily burden experienced by patients. The progressive decline in respiratory capacity commonly leads to limitations in physical activity, reduced independence, impaired social participation, and diminished occupational performance. Consequently, assessment of SSc-ILD increasingly requires a multidimensional approach that integrates objective clinical measures with patient-reported outcomes and functional status assessments. [19,20]

Dyspnea is the hallmark symptom driving functional impairment in patients with SSc-ILD. Initially occurring during moderate or strenuous exertion, breathlessness frequently progresses to affect routine daily activities such as climbing stairs, walking moderate distances, dressing, and household tasks. The severity of dyspnea often correlates with worsening pulmonary fibrosis and declining lung function, particularly reductions in FVC and DLCO. However, symptom severity does not always parallel radiological findings, emphasizing the importance of incorporating patient-centered assessments into routine evaluation. Persistent dyspnea contributes substantially to sedentary behavior, physical deconditioning, and reduced exercise tolerance, creating a vicious cycle that further exacerbates disability. [2,17]

Fatigue is another highly prevalent and debilitating manifestation among patients with systemic sclerosis and pulmonary involvement. Unlike ordinary tiredness, fatigue in SSc is multifactorial and may result from chronic inflammation, impaired oxygen delivery, sleep disturbances, muscle weakness, psychological distress, and reduced cardiopulmonary reserve. Patients frequently identify fatigue as one of the most troublesome symptoms affecting their quality of life. The coexistence of dyspnea and fatigue significantly amplifies functional limitations, often restricting participation in employment, family responsibilities, and recreational activities. [20,21]

Exercise intolerance represents a measurable consequence of pulmonary fibrosis and is commonly assessed using the six-minute walk test (6MWT). Reduced walking distance reflects the combined effects of respiratory impairment, cardiovascular limitations, musculoskeletal involvement, and generalized deconditioning. In patients with SSc-ILD, impaired exercise capacity has been associated with poorer clinical outcomes and reduced quality of life. Because exercise tolerance reflects real-world functional performance more accurately than isolated pulmonary function parameters, it has become an

important outcome measure in both clinical practice and research settings. [4,17]

Health-related quality of life (HRQoL) has emerged as a critical component of outcome assessment in systemic sclerosis. HRQoL encompasses the physical, emotional, social, and functional consequences of disease from the patient's perspective. Studies consistently demonstrate that patients with SSc experience substantially lower HRQoL scores than the general population, with pulmonary involvement being among the strongest predictors of poor outcomes. Progressive respiratory symptoms, uncertainty regarding disease progression, treatment burden, and functional dependency all contribute to reduced quality of life across multiple domains. [10,22]

Several validated instruments have been utilized to assess patient-reported outcomes in systemic sclerosis. Generic measures such as the Short Form-36 (SF-36) evaluate overall physical and mental health status, whereas disease-specific tools including the Health Assessment Questionnaire Disability Index (HAQ-DI) and the Scleroderma Health Assessment Questionnaire (SHAQ) provide insight into functional limitations associated with the disease. Respiratory-specific instruments, including the St. George's Respiratory Questionnaire (SGRQ), are particularly useful for evaluating the impact of pulmonary symptoms on daily activities and well-being. These instruments complement physiological and imaging assessments by capturing dimensions of disease burden that are otherwise difficult to quantify. [22,23]

Psychological consequences are increasingly recognized as major contributors to reduced quality of life in patients with SSc-ILD. Anxiety regarding disease progression, fear of respiratory deterioration, social isolation, depression, and concerns about future disability are frequently reported. The chronic and unpredictable nature of systemic sclerosis may further intensify emotional distress. Emerging evidence suggests that depression and anxiety are highly prevalent among individuals with interstitial lung diseases and are independently associated with worse health status, reduced treatment adherence, and poorer functional outcomes. Therefore, comprehensive care should address both physical and psychological dimensions of disease burden. [24]

The growing emphasis on patient-centered medicine has highlighted the importance of integrating functional and quality-of-life measures into routine clinical evaluation. While HRCT and pulmonary function tests remain indispensable for assessing structural and physiological disease severity, they provide limited information regarding the patient's lived experience. Consequently, modern management strategies increasingly advocate combining imaging findings, pulmonary function parameters, exercise capacity assessments, and patient-reported outcomes to obtain a more comprehensive understanding of disease impact. This multidimensional approach may also provide an ideal framework for evaluating the clinical relevance of lung ultrasound findings and their potential relationship with functional impairment and quality-of-life outcomes in patients with SSc-ILD. [4,23]

Conventional Assessment of SSc-ILD

Accurate evaluation of systemic sclerosis–associated interstitial lung disease requires a comprehensive approach that combines structural imaging, physiological assessment, functional evaluation, and patient-reported outcome measures. Given the heterogeneous nature of SSc-ILD and the variable rate of disease progression among patients, no single investigation is sufficient to fully characterize disease severity or predict clinical outcomes. Consequently, contemporary management strategies rely on multiple complementary tools to establish diagnosis, assess disease extent, monitor progression, and evaluate treatment response. [25,26]

High-Resolution Computed Tomography

High-resolution computed tomography (HRCT) is currently considered the reference imaging modality for the diagnosis and assessment of SSc-ILD. Its superior spatial resolution allows visualization of early and subtle interstitial abnormalities that may not be detected by conventional chest radiography. Typical HRCT findings include ground-glass opacities, reticular abnormalities, traction bronchiectasis, subpleural fibrosis, and honeycombing. Among the recognized histopathological patterns, non-specific interstitial pneumonia (NSIP) is the most frequently encountered pattern in SSc-ILD, whereas usual interstitial pneumonia (UIP) is less common but generally associated with a less favorable prognosis.

HRCT not only confirms the presence of ILD but also provides valuable information regarding disease distribution, extent, and progression. [5,16,25]

Despite its diagnostic value, HRCT has important limitations. Repeated examinations expose patients to cumulative ionizing radiation, a significant concern given the chronic nature of systemic sclerosis and the need for long-term surveillance. Furthermore, the cost and availability of HRCT may limit accessibility in certain healthcare settings. While HRCT remains indispensable for baseline evaluation and diagnostic confirmation, these limitations have stimulated interest in alternative modalities capable of facilitating more frequent disease monitoring. [4,25]

Pulmonary Function Tests

Pulmonary function tests (PFTs) constitute the cornerstone of physiological assessment in SSc-ILD. Forced vital capacity (FVC) and diffusing capacity of the lung for carbon monoxide (DLCO) are the most widely utilized parameters for evaluating disease severity and monitoring progression. A restrictive ventilatory pattern characterized by reduced lung volumes is commonly observed in patients with pulmonary fibrosis. Declining FVC values are generally considered indicators of disease progression and have been incorporated into clinical trials and treatment algorithms as important outcome measures. [5,26]

DLCO is often one of the earliest physiological abnormalities detected in SSc patients and may reflect both interstitial lung involvement and pulmonary vascular disease. Serial measurement of FVC and DLCO provides valuable information regarding disease trajectory and therapeutic response. However, pulmonary function testing may underestimate early structural abnormalities identified on HRCT, particularly during the initial stages of disease. Moreover, test performance can be influenced by patient cooperation, musculoskeletal limitations, respiratory muscle weakness, and coexisting cardiopulmonary conditions. Therefore, PFTs should be interpreted within the broader clinical context. [4,17,26]

Exercise Capacity Assessment

Functional exercise testing provides clinically meaningful information regarding the real-world consequences of pulmonary impairment. The six-minute walk test (6MWT) is the most commonly used measure of exercise capacity in patients with systemic sclerosis and interstitial lung disease. The test evaluates the integrated response of respiratory, cardiovascular, and musculoskeletal systems during physical exertion and reflects the patient's ability to perform everyday activities. Reduced walking distance and exercise-induced oxygen desaturation have been associated with greater disease severity, poorer prognosis, and diminished quality of life. [17,27]

Compared with isolated physiological parameters, exercise testing offers a more comprehensive assessment of functional limitation and treatment effectiveness. Changes in six-minute walk distance may capture clinically relevant improvements or deterioration that are not fully reflected by pulmonary function measurements alone. For this reason, exercise capacity assessment is increasingly incorporated into longitudinal monitoring and rehabilitation programs for patients with SSc-ILD. [27]

Patient-Reported Outcome Measures

In recent years, increasing attention has been directed toward patient-reported outcome measures (PROMs) as essential components of disease assessment. PROMs provide insight into symptoms, disability, psychological well-being, and quality of life from the patient's perspective. This information is particularly important in systemic sclerosis, where objective measures may not always correlate closely with perceived disease burden. [23]

The Short Form-36 (SF-36) is one of the most widely used generic health-related quality-of-life instruments and evaluates physical and mental health domains. Disease-specific tools such as the Health Assessment Questionnaire Disability Index (HAQ-DI) and the Scleroderma Health Assessment Questionnaire (SHAQ) assess functional disability and disease-related limitations. Respiratory-specific questionnaires, including the St. George’s Respiratory Questionnaire (SGRQ), provide additional information regarding symptom burden, activity restriction, and psychosocial impact associated with pulmonary disease. Together, these instruments help clinicians evaluate treatment outcomes, identify unmet patient needs, and monitor the broader consequences of disease progression. [22,23]

Although HRCT, pulmonary function tests, exercise capacity measures, and patient-reported outcomes collectively provide a robust framework for evaluating SSc-ILD, each method has inherent limitations. Imaging techniques primarily assess structural abnormalities, pulmonary function tests evaluate physiological impairment, and PROMs capture subjective disease burden. The growing need for a safe, repeatable, accessible, and bedside tool capable of bridging these domains has contributed to increasing interest in lung ultrasound. By providing information regarding pulmonary involvement without radiation exposure and with minimal resource requirements, lung ultrasound has emerged as a promising adjunct to conventional assessment strategies in patients with SSc-ILD. [7,8]

Principles and Technical Aspects of Lung Ultrasound

For many years, the lung was considered unsuitable for ultrasonographic evaluation because the presence of air within the pulmonary parenchyma prevents direct visualization of deeper lung structures. However, advances in ultrasound technology and a better understanding of ultrasound artifacts have transformed lung ultrasound (LUS) into an important diagnostic and monitoring tool in respiratory medicine. Rather than imaging the lung tissue itself, LUS evaluates characteristic artifacts generated at the interface between the pleura and aerated lung. These artifacts provide valuable information regarding changes in lung density, interstitial involvement, pleural abnormalities, and subpleural pathology. Consequently, LUS has become increasingly utilized in the assessment of interstitial lung diseases, including systemic sclerosis–associated interstitial lung disease (SSc-ILD). [28,29]

The fundamental anatomical structure evaluated during lung ultrasound is the pleural line, which appears as a thin, hyperechoic horizontal line located immediately beneath the rib shadows. In healthy individuals, the pleural line is smooth, continuous, and demonstrates a characteristic sliding motion corresponding to respiratory movement. Alterations in pleural morphology may indicate underlying pulmonary pathology. In patients with SSc-ILD, pleural line irregularity, fragmentation, thickening, and reduced smoothness are frequently observed and may reflect subpleural fibrotic involvement. These abnormalities often coexist with other sonographic findings associated with interstitial lung disease and may increase diagnostic accuracy when evaluated together. [7,28]

The most extensively studied sonographic feature in SSc-ILD is the B-line. B-lines are vertical, hyperechoic reverberation artifacts that originate from the pleural line, extend to the bottom of the ultrasound screen without fading, and move synchronously with lung sliding. They occur when ultrasound waves interact with thickened interlobular septa, increased extravascular lung water, or fibrotic changes within the pulmonary interstitium. In systemic sclerosis, an increased number of B-lines has been consistently associated with the presence and extent of interstitial lung involvement. Numerous studies have demonstrated significant correlations between B-line counts and HRCT findings, supporting their role as a surrogate marker of pulmonary fibrosis. [7,8,30]

Although B-lines represent the most recognized ultrasound marker of interstitial disease, they should not be interpreted in isolation. Similar artifacts may occur in pulmonary edema, acute respiratory distress syndrome, pneumonia, and other diffuse lung disorders. Therefore, accurate interpretation requires integration with clinical findings, disease context, and additional sonographic features. In SSc-ILD, the coexistence of multiple B-lines with pleural line abnormalities and subpleural irregularities increases the likelihood that these findings reflect fibrotic interstitial involvement rather than alternative pathological processes. [29,31]

Several scanning protocols have been proposed for evaluating interstitial lung disease using ultrasound. Early protocols involved extensive examination of numerous intercostal spaces across anterior, lateral, and posterior thoracic regions. Although comprehensive, these methods were time-consuming and less practical for routine clinical application. More recently, simplified scanning approaches have been developed to improve feasibility while maintaining diagnostic performance. Current evidence suggests that reduced scanning protocols may provide comparable accuracy in detecting clinically significant pulmonary fibrosis, facilitating wider adoption in daily practice and outpatient settings. [8,32]

The examination is typically performed using either convex or phased-array transducers, which provide adequate penetration and visualization of deeper thoracic structures. Linear probes may also be

employed when detailed assessment of pleural abnormalities is desired. Patients are usually examined in a sitting position whenever possible, allowing access to posterior lung fields where fibrotic abnormalities are most commonly located. Standardized scanning of anterior, lateral, and posterior chest zones improves reproducibility and enables serial comparisons during follow-up evaluations. [29,33]

One of the major strengths of lung ultrasound is its favorable safety profile. Unlike HRCT, LUS does not expose patients to ionizing radiation and can therefore be repeated frequently without cumulative risk. Furthermore, ultrasound equipment is portable, relatively inexpensive, and increasingly available in outpatient clinics, rheumatology units, rehabilitation facilities, and bedside settings. These advantages make LUS particularly attractive for longitudinal monitoring of chronic diseases such as SSc-ILD, where repeated assessments are often required to detect disease progression or evaluate treatment response. [7,25]

Despite its advantages, lung ultrasound has several limitations. The technique is operator-dependent and requires appropriate training and experience to ensure reliable image acquisition and interpretation. Ultrasound findings may also be influenced by obesity, chest wall abnormalities, limited acoustic windows, and coexisting pulmonary conditions. Furthermore, LUS primarily evaluates peripheral lung abnormalities adjacent to the pleural surface and may fail to detect lesions located deep within the lung parenchyma. Consequently, lung ultrasound should currently be considered a complementary imaging modality rather than a replacement for HRCT. Nevertheless, its accessibility, repeatability, and growing evidence base have established LUS as an increasingly valuable component of the multimodal assessment of SSc-ILD. [4,31,33]

Ultrasound Findings in SSc-ILD

Lung ultrasound abnormalities in systemic sclerosis–associated interstitial lung disease primarily reflect structural alterations occurring within the subpleural interstitium and peripheral lung parenchyma. Because fibrotic changes in SSc-ILD frequently begin in subpleural regions, ultrasound is particularly suited for detecting these abnormalities. The most commonly described findings include increased B-lines, pleural line irregularities, pleural thickening, and subpleural abnormalities. Collectively, these sonographic features provide valuable information regarding the presence, extent, and severity of pulmonary involvement and have demonstrated meaningful correlations with radiological and functional indicators of disease burden. [34,35]

B-Lines

B-lines are the most extensively investigated ultrasound finding in SSc-ILD and currently represent the cornerstone of ultrasound-based assessment of pulmonary fibrosis. These artifacts appear as discrete vertical hyperechoic lines arising from the pleural surface and extending to the edge of the ultrasound image without attenuation. In healthy lungs, only a few isolated B-lines may be present, whereas patients with interstitial lung disease typically demonstrate increased numbers and wider distribution across multiple lung zones. The generation of B-lines is attributed to alterations in the acoustic properties of the lung caused by thickened interlobular septa, interstitial inflammation, fibrosis, and reduced air content adjacent to the pleural surface. [30,34]

Several studies have demonstrated a significant relationship between B-line burden and the extent of pulmonary fibrosis detected by HRCT. Patients with extensive fibrotic involvement generally exhibit higher B-line counts than those with limited disease, suggesting that ultrasound may provide a semi-quantitative estimate of interstitial involvement. Importantly, B-lines can often be detected even in patients with mild or subclinical pulmonary disease, highlighting their potential value as a screening tool. This observation is particularly relevant in systemic sclerosis, where early diagnosis of ILD may facilitate timely initiation of treatment and improve long-term outcomes. [7,32]

The distribution of B-lines also appears to have clinical significance. In SSc-ILD, abnormalities are most commonly observed in posterior basal and subpleural lung regions, reflecting the characteristic distribution of fibrotic changes on HRCT. Evaluation of multiple thoracic zones enables estimation of disease extent and improves diagnostic sensitivity. Several investigators have proposed cutoff values for B-line counts that may help distinguish patients with significant ILD from those without detectable

pulmonary involvement. Although consensus regarding optimal thresholds remains under development, the accumulating evidence supports the clinical utility of B-line quantification in routine assessment. [8,35]

Pleural Line Irregularities

Alterations of the pleural line constitute another important sonographic feature of SSc-ILD. In healthy individuals, the pleural surface appears as a thin, regular, continuous echogenic line. Fibrotic remodeling of subpleural lung tissue may disrupt this normal appearance, producing pleural irregularity, fragmentation, discontinuity, and uneven contour. These abnormalities are believed to reflect structural distortion caused by fibrosis extending toward the pleural surface. [7,30]

Pleural line irregularities may be particularly useful because they provide information beyond simple B-line quantification. Some studies have suggested that pleural abnormalities may correlate more closely with established fibrotic disease than with inflammatory changes alone. Consequently, assessment of pleural morphology may enhance the specificity of ultrasound findings and improve differentiation between chronic fibrotic lung disease and transient causes of interstitial artifacts. Combining B-line evaluation with systematic assessment of pleural line characteristics may therefore strengthen diagnostic performance in patients with suspected SSc-ILD. [34,36]

Pleural Thickening

Pleural thickening is another commonly reported finding in patients with systemic sclerosis–associated pulmonary fibrosis. Ultrasound enables direct measurement and visualization of pleural thickness, allowing detection of subtle structural alterations that may not be evident during routine clinical examination. Thickening of the pleural line is thought to result from chronic inflammatory and fibrotic processes affecting the subpleural interstitium and adjacent pleural structures. [30,34]

Several investigations have reported higher pleural thickness measurements among patients with established SSc-ILD compared with individuals without pulmonary involvement. Furthermore, pleural thickening frequently coexists with increased B-line counts and pleural irregularities, collectively indicating more advanced structural abnormalities. Although standardized measurement techniques have not yet been universally adopted, pleural thickness assessment represents a promising adjunctive parameter that may contribute to comprehensive ultrasound evaluation of pulmonary fibrosis. [35,36]

Subpleural Abnormalities

Subpleural abnormalities constitute a less frequently discussed but potentially important component of lung ultrasound assessment. These abnormalities may appear as small hypoechoic areas, interrupted pleural contours, microconsolidations, or localized irregularities adjacent to the pleural surface. Such findings are believed to correspond to focal regions of fibrosis, architectural distortion, or inflammatory infiltration occurring within peripheral lung tissue. Because systemic sclerosis commonly affects subpleural lung regions, detection of these abnormalities may provide additional evidence supporting the diagnosis of SSc-ILD. [29,30]

Emerging evidence suggests that subpleural abnormalities may be associated with more extensive disease and greater structural damage. Although their diagnostic role remains less established than that of B-lines, incorporation of subpleural findings into comprehensive ultrasound scoring systems may improve sensitivity and facilitate more accurate characterization of disease severity. Further standardization and validation studies are needed before these findings can be routinely integrated into clinical decision-making algorithms. [35]

Emerging Ultrasound Biomarkers and Composite Scoring Systems

Recent research has focused on the development of composite ultrasound approaches that integrate multiple sonographic findings into standardized scoring systems. Rather than relying solely on B-line counts, these systems combine information derived from pleural irregularities, pleural thickening, and subpleural abnormalities to generate a more comprehensive estimate of disease burden. Such approaches may improve reproducibility and better reflect the complex structural changes occurring in SSc-ILD. [34,37]

Advances in portable and handheld ultrasound technology have further expanded interest in lung

ultrasound as a point-of-care assessment tool. Modern handheld devices demonstrate encouraging diagnostic performance and may facilitate screening and monitoring in outpatient clinics, rheumatology practices, and rehabilitation settings. The ability to perform rapid bedside evaluations without radiation exposure offers an attractive opportunity for longitudinal follow-up and early detection of disease progression. As technological innovations continue to evolve, ultrasound-derived biomarkers may become increasingly integrated into multidisciplinary management pathways for patients with SSc-ILD. [37,38]

Correlation Between Lung Ultrasound and HRCT Findings

High-resolution computed tomography remains the gold standard for the detection and characterization of systemic sclerosis–associated interstitial lung disease. Consequently, validation of lung ultrasound has largely focused on determining the degree of agreement between sonographic findings and HRCT abnormalities. Over the past decade, multiple studies have demonstrated significant correlations between ultrasound-derived parameters and radiological measures of pulmonary fibrosis, supporting the role of lung ultrasound as a reliable adjunctive imaging modality. The growing body of evidence suggests that LUS can identify structural lung involvement with good diagnostic accuracy while offering the advantages of bedside applicability, repeatability, and absence of radiation exposure. [25,34]

Among all ultrasound findings, B-line burden has shown the strongest and most consistent association with HRCT abnormalities. Numerous investigations have demonstrated that increasing B-line counts correlate with greater radiographic extent of interstitial involvement, including ground-glass opacities, reticular abnormalities, and fibrotic changes. Patients with extensive pulmonary fibrosis on HRCT typically exhibit substantially higher B-line scores than those with limited disease or normal imaging findings. These observations suggest that B-lines may serve as a surrogate marker of interstitial lung involvement and may provide a semi-quantitative estimate of disease burden. [7,8]

Importantly, correlations between LUS and HRCT have been observed not only in advanced disease but also in patients with early or mild pulmonary involvement. Several studies have reported the detection of abnormal B-line patterns in individuals with limited radiographic disease, highlighting the potential utility of ultrasound as a screening tool. Because HRCT cannot be performed repeatedly at short intervals in many patients due to radiation concerns, lung ultrasound may offer a practical method for identifying individuals who require further radiological evaluation. This approach could facilitate earlier recognition of progressive pulmonary involvement and more timely therapeutic intervention. [25,34]

Beyond B-line quantification, pleural line abnormalities have demonstrated meaningful relationships with HRCT findings. Pleural irregularity, fragmentation, and thickening frequently correspond to subpleural fibrotic changes identified on computed tomography. Since fibrosis in systemic sclerosis commonly begins within peripheral and subpleural lung regions, these sonographic findings may reflect the same pathological processes visualized on HRCT. Some investigators have suggested that combining pleural line assessment with B-line evaluation may improve diagnostic specificity and provide a more comprehensive estimate of structural lung damage. [30,35]

Although the overall correlation between lung ultrasound and HRCT is encouraging, complete concordance should not be expected. Ultrasound primarily evaluates abnormalities located adjacent to the pleural surface and may fail to detect lesions confined to deeper lung regions. Conversely, HRCT provides comprehensive visualization of the entire pulmonary parenchyma and remains indispensable for detailed characterization of disease pattern and extent. Therefore, lung ultrasound should be viewed as a complementary modality rather than a substitute for HRCT. Within this framework, LUS may serve as an accessible screening and monitoring tool, whereas HRCT continues to play a central role in diagnostic confirmation, baseline characterization, and evaluation of complex cases. [4,25]

The demonstrated association between sonographic abnormalities and radiological fibrosis provides the foundation for investigating whether ultrasound findings also reflect physiological impairment and clinical disease burden. If LUS abnormalities correlate not only with HRCT extent but also with pulmonary function decline, exercise limitation, and patient-reported outcomes, lung ultrasound could become an even more valuable component of routine assessment and longitudinal monitoring in patients

with SSc-ILD. This possibility has stimulated increasing research into the relationship between ultrasound findings and functional measures of disease severity. [7,8,34]

Relationship Between Lung Ultrasound Findings and Pulmonary Function Parameters

Pulmonary function testing remains the cornerstone of physiological assessment in systemic sclerosis–associated interstitial lung disease, providing objective measures of respiratory impairment and disease progression. Because lung ultrasound abnormalities reflect structural changes occurring within the pulmonary interstitium, considerable interest has emerged regarding their relationship with functional respiratory parameters. Establishing such correlations is clinically important because it may help determine whether ultrasound findings merely indicate anatomical abnormalities or also reflect the physiological consequences of pulmonary fibrosis. Current evidence suggests that several sonographic abnormalities, particularly B-line burden, are significantly associated with impaired pulmonary function and disease severity in patients with SSc-ILD. [26,30]

Among pulmonary function parameters, forced vital capacity (FVC) is one of the most widely used indicators of restrictive lung disease and serves as a key outcome measure in clinical trials and routine practice. Multiple studies have demonstrated an inverse relationship between B-line counts and FVC values, indicating that patients with greater ultrasound evidence of interstitial involvement tend to exhibit more severe restrictive ventilatory impairment. As fibrotic remodeling progresses and lung compliance decreases, increasing numbers of B-lines may reflect the expanding extent of pulmonary fibrosis responsible for declining lung volumes. These observations support the concept that ultrasound findings provide clinically meaningful information regarding disease severity rather than simply representing isolated imaging abnormalities. [26,30,34]

Diffusing capacity of the lung for carbon monoxide (DLCO) represents another important physiological marker in SSc-ILD and is often among the earliest abnormalities detected during pulmonary evaluation. Reduced DLCO reflects impaired gas exchange resulting from interstitial fibrosis, pulmonary vascular involvement, or a combination of both mechanisms. Several investigations have reported significant correlations between higher B-line scores and lower DLCO values, suggesting that increasing sonographic abnormalities are associated with worsening impairment of alveolar-capillary gas transfer. Because DLCO decline may precede substantial reductions in FVC, these findings further support the potential value of lung ultrasound in identifying clinically relevant pulmonary involvement during earlier disease stages. [17,26,34]

In addition to B-line quantification, pleural line abnormalities may also reflect functional impairment. Patients demonstrating pleural thickening, irregularity, and fragmentation often exhibit more extensive fibrotic changes and greater physiological dysfunction than those with normal pleural morphology. Although the evidence remains less extensive than that available for B-lines, emerging studies suggest that combining pleural assessment with B-line analysis may improve the ability of ultrasound to estimate disease severity and predict functional compromise. Such multidimensional approaches may better capture the complex structural alterations occurring within fibrotic lung disease. [30,35]

Exercise capacity provides an integrated measure of respiratory, cardiovascular, and musculoskeletal performance and is particularly relevant in systemic sclerosis because functional limitation frequently extends beyond isolated pulmonary dysfunction. Reduced six-minute walk distance (6MWD) has been associated with worsening lung involvement, increased symptom burden, and poorer clinical outcomes. Preliminary evidence suggests that patients with higher B-line scores and more extensive ultrasound abnormalities tend to demonstrate lower exercise capacity and greater exertional limitation. These findings indicate that sonographic markers of interstitial lung disease may correspond not only to physiological impairment measured in the laboratory but also to real-world functional performance. [27,34]

An important advantage of lung ultrasound is its potential utility for serial monitoring. While pulmonary function tests remain essential for longitudinal follow-up, meaningful changes in FVC or DLCO may take months to become apparent. Because ultrasound can be performed repeatedly at the bedside without radiation exposure, it may facilitate more frequent assessment of disease status and potentially identify

progression earlier than conventional physiological testing alone. This capability is particularly relevant in systemic sclerosis, where disease trajectory is often unpredictable and timely therapeutic intervention may influence long-term outcomes. [25,30]

Despite the encouraging associations reported between ultrasound findings and pulmonary function parameters, important limitations should be acknowledged. Correlations are generally moderate rather than absolute, reflecting the multifactorial nature of respiratory impairment in systemic sclerosis. Pulmonary hypertension, respiratory muscle weakness, chest wall restriction, cardiovascular disease, and musculoskeletal involvement may all influence pulmonary function independently of interstitial fibrosis. Consequently, ultrasound findings should be interpreted as part of a comprehensive clinical assessment rather than as isolated indicators of disease severity. [4,17]

Overall, the available evidence supports a meaningful relationship between lung ultrasound abnormalities and pulmonary physiological impairment in SSc-ILD. Increasing B-line burden, pleural irregularities, and other sonographic markers generally correspond to worsening FVC, lower DLCO values, and reduced exercise tolerance. These observations strengthen the rationale for incorporating lung ultrasound into multidisciplinary assessment strategies and provide the foundation for exploring whether ultrasound findings also reflect patient-reported outcomes and health-related quality of life, which represent critical dimensions of disease burden in systemic sclerosis. [30,34,35]

Relationship Between Lung Ultrasound Findings and Patient-Reported Outcomes

In recent years, increasing emphasis has been placed on patient-reported outcomes (PROs) as essential measures of disease burden in systemic sclerosis. While imaging studies and pulmonary function tests provide objective assessments of structural and physiological abnormalities, they may not fully reflect the impact of disease on daily activities, symptom severity, emotional well-being, and overall quality of life. This discrepancy is particularly relevant in systemic sclerosis–associated interstitial lung disease, where relatively modest physiological impairment may be associated with substantial functional limitations and reduced health-related quality of life (HRQoL). Consequently, understanding the relationship between lung ultrasound findings and patient-reported outcomes may enhance the clinical relevance of ultrasound-based assessment and facilitate more patient-centered care. [22,23]

Dyspnea is among the most important symptoms influencing quality of life in patients with SSc-ILD. Progressive pulmonary fibrosis results in increasing breathlessness during physical activity, which may eventually interfere with routine daily tasks and social participation. Several studies evaluating lung ultrasound have reported that patients with higher B-line counts and more extensive sonographic abnormalities frequently experience greater respiratory symptom burden. Because dyspnea often represents the earliest manifestation recognized by patients, the association between ultrasound findings and symptom severity supports the potential role of LUS as a clinically meaningful indicator of disease impact beyond structural lung involvement alone. [17,30]

Fatigue is another major determinant of impaired quality of life in systemic sclerosis and frequently coexists with pulmonary disease. The combination of chronic inflammation, reduced cardiopulmonary reserve, physical deconditioning, sleep disturbance, and psychological stress contributes to persistent fatigue that significantly affects daily functioning. Patients with more extensive pulmonary involvement commonly report higher levels of fatigue and reduced physical endurance. Since ultrasound abnormalities generally correlate with disease extent and pulmonary impairment, it is plausible that increasing B-line burden and pleural abnormalities may indirectly reflect factors contributing to fatigue-related disability. Although direct evidence remains limited, this relationship warrants further investigation in future prospective studies. [20,21]

Health-related quality of life is commonly assessed using validated instruments such as the Short Form-36 (SF-36), which evaluates physical and mental health domains. Patients with SSc-ILD frequently demonstrate substantial impairment in physical functioning, vitality, social participation, and general health perception compared with both healthy individuals and patients without significant pulmonary involvement. Pulmonary fibrosis has consistently been identified as one of the strongest predictors of reduced HRQoL in systemic sclerosis. Because ultrasound findings correlate with both radiological

extent and physiological impairment, they may also serve as indirect indicators of quality-of-life deterioration. [10,22]

Disease-specific instruments provide additional insight into the patient experience. The Health Assessment Questionnaire Disability Index (HAQ-DI) and the Scleroderma Health Assessment Questionnaire (SHAQ) are widely used to evaluate disability and functional limitations in systemic sclerosis. Higher disability scores are commonly observed among patients with significant pulmonary involvement due to exertional dyspnea, reduced exercise capacity, fatigue, and limitations in daily activities. Although studies directly correlating ultrasound findings with HAQ-DI or SHAQ scores remain scarce, the established associations between lung ultrasound, pulmonary function impairment, and exercise intolerance suggest that meaningful relationships are likely to exist. Future research should specifically address this important gap in the literature. [21,23]

Respiratory-specific patient-reported outcome measures may provide the most direct link between lung ultrasound abnormalities and patient experience. Instruments such as the St. George's Respiratory Questionnaire (SGRQ) assess symptoms, activity limitations, and psychosocial consequences related to chronic respiratory disease. Patients with advanced fibrotic lung involvement generally report worse respiratory-specific quality-of-life scores than those with limited disease. Since B-line burden and pleural abnormalities reflect the extent of interstitial lung involvement, these sonographic markers may potentially serve as surrogate indicators of respiratory symptom burden and activity restriction. However, dedicated studies evaluating these associations in SSc-ILD remain limited and represent an important area for future investigation. [22,27]

Psychological well-being is another important dimension of patient-reported outcomes. Anxiety, depression, fear of disease progression, and uncertainty regarding future functional capacity are frequently encountered among patients with chronic interstitial lung disease. Psychological distress may amplify symptom perception, reduce physical activity, and negatively influence treatment adherence. Previous studies have demonstrated significant associations between respiratory disease severity and mental health outcomes in interstitial lung diseases. Therefore, sonographic findings reflecting greater pulmonary involvement may indirectly correspond to increased psychological burden through their association with respiratory impairment and functional limitation. [24]

From a rehabilitation perspective, the relationship between lung ultrasound findings and patient-reported outcomes is particularly relevant. Rehabilitation programs increasingly emphasize individualized assessment, symptom monitoring, and patient-centered outcome evaluation. Because lung ultrasound can be performed repeatedly without radiation exposure, it offers a practical method for longitudinal monitoring of pulmonary status while simultaneously tracking changes in functional performance and quality of life. Integration of ultrasound findings with pulmonary function tests, exercise capacity measures, and patient-reported outcomes may facilitate more comprehensive disease assessment and support personalized rehabilitation strategies aimed at preserving physical function and improving quality of life. [27]

The available evidence suggests that lung ultrasound abnormalities are linked not only to structural and physiological manifestations of SSc-ILD but also to broader dimensions of disease burden that directly affect patients' lives. Although direct studies correlating ultrasound findings with specific quality-of-life instruments remain relatively limited, existing data support a conceptual framework in which greater sonographic abnormalities are associated with increased symptom burden, reduced functional capacity, and poorer health-related quality of life. Further prospective investigations are needed to validate these relationships and establish the role of lung ultrasound as a patient-centered monitoring tool in systemic sclerosis–associated interstitial lung disease. [22,23,30]

Conclusion

Systemic sclerosis–associated interstitial lung disease remains one of the most significant determinants of morbidity, functional decline, and mortality in patients with systemic sclerosis. Early identification and accurate monitoring of pulmonary involvement are essential for optimizing therapeutic decisions, preserving functional capacity, and improving long-term outcomes. Although high-resolution computed

tomography continues to represent the reference standard for diagnosing and characterizing interstitial lung disease, its limitations related to radiation exposure, cost, and accessibility have stimulated the search for complementary imaging modalities suitable for repeated assessment.

Lung ultrasound has emerged as a promising, non-invasive, radiation-free, and readily accessible tool for the evaluation of SSc-ILD. Accumulating evidence demonstrates that characteristic sonographic findings, including B-lines, pleural line irregularities, pleural thickening, and subpleural abnormalities, correlate with the presence and extent of pulmonary fibrosis. Furthermore, these ultrasound abnormalities are associated with physiological impairment, including reductions in pulmonary function parameters and exercise capacity, highlighting their potential clinical relevance beyond simple structural assessment.

Importantly, the burden of SSc-ILD extends beyond radiological and physiological abnormalities to encompass substantial effects on daily functioning, symptom burden, psychological well-being, and health-related quality of life. Emerging data suggest that lung ultrasound findings may reflect these broader dimensions of disease impact, supporting its potential role within a patient-centered assessment framework. The integration of lung ultrasound with pulmonary function testing, exercise capacity measures, and patient-reported outcomes may therefore provide a more comprehensive evaluation of disease severity and progression.

From a rehabilitation perspective, lung ultrasound offers unique advantages for longitudinal monitoring and individualized management. Its bedside applicability and repeatability allow frequent assessment without exposing patients to cumulative radiation, making it particularly attractive for follow-up evaluations and rehabilitation programs focused on preserving physical performance and quality of life.

Despite encouraging findings, important challenges remain, including the need for standardized scanning protocols, operator training, validated scoring systems, and larger prospective studies examining prognostic value and responsiveness to therapeutic interventions. Future research should also further clarify the relationship between ultrasound findings, functional outcomes, and patient-reported measures to strengthen its role in multidisciplinary care.

In conclusion, lung ultrasound represents a valuable complementary modality in the evaluation of systemic sclerosis–associated interstitial lung disease. Its ability to provide clinically meaningful information regarding structural lung involvement, functional impairment, and potentially patient-centered outcomes supports its growing role in contemporary rheumatology, pulmonary medicine, and rehabilitation practice. As evidence continues to evolve, lung ultrasound may become an increasingly important component of comprehensive and personalized management strategies for patients with SSc-ILD.

References

1. Denton CP, Khanna D. Systemic sclerosis. Lancet. 2017;390(10103):1685-1699. doi:10.1016/S0140-6736(17)30933-9
2. Perelas A, Silver RM, Arrossi AV, Highland KB. Systemic sclerosis-associated interstitial lung disease. Lancet Respir Med. 2020;8(3):304-320. doi:10.1016/S2213-2600(19)30480-1
3. Distler O, Crestani B, Hoffmann-Vold AM, et al. Systemic sclerosis-associated interstitial lung disease: clinical features and outcomes. Eur Respir Rev. 2023;32.
4. Hoffmann-Vold AM, Maher TM, Philpot EE, et al. Interstitial lung disease in systemic sclerosis: advances in evaluation and management. Lancet Rheumatol. 2024;6(1):e21-e34.
5. Khanna D, Distler O, Cottin V, Brown KK, Chung L, Goldin JG, et al. Diagnosis and monitoring of systemic sclerosis-associated interstitial lung disease using high-resolution computed tomography. Ther Adv Musculoskelet Dis. 2022;14:1-11. doi:10.1177/1759720X211057889
6. Hoffmann-Vold AM, Allanore Y, Alves M, Brunborg C, Airo P, Ananieva LP, et al. Progressive interstitial lung disease

in patients with systemic sclerosis-associated interstitial lung disease in the EUSTAR database. Ann Rheum Dis. 2021;80(2):219-227.
7. Bruni C, Mattolini L, Tofani L, Gargani L, Landini N, Roma N, et al. Lung ultrasound B-lines in the evaluation of the extent of interstitial lung disease in systemic sclerosis. Diagnostics (Basel). 2022;12(7):1696.
8. Gargani L, Romei C, Bruni C, et al. Lung ultrasound B-lines in systemic sclerosis: cut-off values for interstitial lung disease screening. Rheumatology (Oxford). 2022;61(Suppl 1):SI56-SI64.
9. Ruaro B, et al. Lung ultrasound in systemic sclerosis-associated interstitial lung disease. Clin Exp Rheumatol. 2021.
10. Frantz C, Avouac J, Distler O, et al. Impaired quality of life in systemic sclerosis and patient perception of the disease: a large international survey. Semin Arthritis Rheum. 2016;46(1):115-123.
11. Khanna D, Distler O, Avouac J, et al. Patient-reported outcomes in systemic sclerosis. Rheum Dis Clin North Am. 2023;49(3).
12. Bergamasco A, Hartmann N, Wallace L, Verpillat P. Epidemiology of systemic sclerosis and systemic sclerosis-associated interstitial lung disease. Clin Epidemiol. 2019;11:257-273.
13. Chan DT, So H. Systemic sclerosis-associated interstitial lung disease: prevalence and risk factors. J Clin Rheumatol Immunol. 2023;23(1):15-24.
14. Distler O, Assassi S, Cottin V, et al. Predictors of progression in systemic sclerosis patients with interstitial lung disease. Eur Respir J. 2020;55:1902026.
15. Rahaghi FF, et al. Screening and risk stratification of systemic sclerosis-associated interstitial lung disease. 2023.
16. DeMizio DJ, Bernstein EJ. Detection and classification of systemic sclerosis-related interstitial lung disease: a review. Curr Opin Rheumatol. 2019;31(6):553-560.
17. Hoffmann-Vold AM, Distler O, Crestani B, Antoniou KM, et al. Recent advances in the management of systemic sclerosis-associated interstitial lung disease. Curr Opin Pulm Med. 2022;28(5):441-447.
18. Morrisroe K, Stevens W, Sahhar J, et al. The clinical and economic burden of systemic sclerosis-related interstitial lung disease. Rheumatology (Oxford). 2020;59:1878-1888.
19. Distler O, Crestani B, Hoffmann-Vold AM, et al. Systemic sclerosis-associated interstitial lung disease: clinical features and outcomes. Eur Respir Rev. 2023.
20. Bassel M, Hudson M, Taillefer SS, et al. Frequency and impact of symptoms experienced by patients with systemic sclerosis: results from a Canadian national survey. Rheumatology (Oxford). 2011;50(4):762-767.
21. Hossain S, Choudhury MR, Haque MM, et al. Functional disability and health-related quality of life among systemic sclerosis patients. BMC Rheumatol. 2022;6:60.
22. Frantz C, Avouac J, Distler O, et al. Impaired quality of life in systemic sclerosis and patient perception of the disease: a large international survey. Semin Arthritis Rheum. 2016;46(1):115-123.
23. Khanna D, Distler O, Avouac J, et al. Patient-reported outcomes in systemic sclerosis. Rheum Dis Clin North Am. 2023;49(3).
24. Holland AE, Fiore JF Jr, Goh N, et al. Depression and anxiety in interstitial lung disease: prevalence, mechanisms and management. Eur Respir Rev. 2023;32(167):220187.
25. Hoffmann-Vold AM, Maher TM, Philpot EE, Ashrafzadeh A, Barake R, Bruni C, et al. The identification and management of interstitial lung disease in systemic sclerosis: evidence-based European consensus statements. Lancet Rheumatol. 2020;2:e71-e83.
26. Khanna D, Distler O, Cottin V, Brown KK, Chung L, Goldin JG, et al. Diagnosis and monitoring of systemic sclerosis-associated interstitial lung disease using high-resolution computed tomography. Ther Adv Musculoskelet Dis. 2022;14:1-11.
27. Chacko S, Shah G, Patel T, et al. Impact of pulmonary rehabilitation on quality-of-life metrics in patients with chronic respiratory diseases: a comparative analysis of SF-36, SGRQ, and SOBQ outcomes. J Rehabil Med. 2025;57(2):0976500X251350484.
28. Gargani L. Lung ultrasound: a new tool for the cardiologist. Cardiovasc Ultrasound. 2011;9:6.
29. Beshara M, Bittner EA, Goffi A, Berra L, Chang MG, et al. Nuts and bolts of lung ultrasound: utility, scanning techniques, protocols, and findings in common pathologies. Crit Care. 2024;28(1):328.
30. Bruni C, Mattolini L, Tofani L, Gargani L, Landini N, Roma N, et al. Lung ultrasound B-lines in the evaluation of the extent of interstitial lung disease in systemic sclerosis. Diagnostics (Basel). 2022;12(7):1696.
31. Lichtenstein DA. Current misconceptions in lung ultrasound: a short guide for experts. Chest. 2019;156(1):21-25.
32. Gargani L, Romei C, Bruni C, et al. Lung ultrasound B-lines in systemic sclerosis: cut-off values for interstitial lung disease screening. Rheumatology (Oxford). 2022;61(Suppl 1):SI56-SI64.
33. Peck M, Macnaughton P, Miller A, et al. Lung ultrasound, sonoanatomy, and standard views. In: Focused Intensive Care Ultrasound. Oxford University Press; 2019:125-131.
34. Huang Y, Liu T, Huang S, Qiu L, Luo F, Yin G, Xie Q, et al. Screening value of lung ultrasound in connective tissue disease-related interstitial lung disease. Heart Lung. 2023;57:110-116.
35. Ancuța C, Pomirleanu C, Gănceanu E, Man MA, Ancuta E, Postolache P, et al. B-lines in the assessment of interstitial lung disease associated with scleroderma: the role of handheld devices. Diagnostics (Basel). 2024;14(21):2397.
36. Mohammadi A, Oshnoei S, Ghasemi-Rad M, et al. Comparison of a new modified lung ultrasonography technique with

high-resolution CT in the diagnosis of the alveolo-interstitial syndrome of systemic scleroderma. Med Ultrason. 2014;16(1):27-31.
37. Le MT, Voigt L, Nathanson R, Maw AM, Johnson G, Dancel R, et al. Comparison of four handheld point-of-care ultrasound devices by expert users. Ultrasound J. 2022;14:27.
38. Jokerst C, Yaddanapudi K, Chaudhary S, Zamora AC, Nagaraja V, et al. Imaging innovations in the screening, diagnosis, and monitoring of systemic autoimmune disease-related interstitial lung disease. EMJ Radiol. 2024;5:71-81.