Rom J Rheumatol 2024, 33(3):105-108 ISSN (print) 1843–0791, ISSN (online) 2069–6086

Revista Română de Reumatologie
Romanian Journal of Rheumatology

ORIGINAL PAPER

Systemic Sclerosis-Associated ILD: A Tertiary Center Experience During the Pandemic

MAIA IOANA MIHON[1)], ANCA ROXANA GHERASIM[1)], CRISTINA PAMFIL[1,2)], IUSTIN CALAGIU[3)], SIMONA REDNIC[1,2)]

[1)]*Department of Rheumatology, Cluj Emergency County Clinical Hospital, Cluj-Napoca, Romania*
[2)]*"Iuliu Haţieganu" University of Medicine and Pharmacy Cluj-Napoca, Cluj-Napoca, Romania*
[3)] *3rd Internal Medicine Department, Colentina Clinical Hospital, Bucharest, Romania*

Abstract

Systemic sclerosis (SSc) is a chronic autoimmune disorder associated with interstitial lung disease (ILD), significantly contributing to morbidity and mortality among patients [1–6]. This study evaluates imaging findings and the extent of pulmonary fibrosis in SSc-associated ILD during the COVID-19 pandemic.

Methods: A retrospective analysis was conducted on 70 SSc patients at Cluj Emergency Clinical County Hospital from 2019 to 2020, adhering to the 2013 ACR/EULAR criteria. Data on demographics, immunological profiles, organ involvement, and imaging findings from chest CT scans were collected and statistically analyzed.

Results: The cohort comprised 62 females (89%) and 8 males (11%), with a mean age of 51 years. Among the patients, 79% exhibited pulmonary involvement; 98% of these had ILD. The distribution of ILD was highest in diffuse SSc (87%) compared to limited SSc (62%). Common radiological patterns included non-specific interstitial pneumonia (58%) and usual interstitial pneumonia (28%). A significant correlation was found between anti-Scl70 antibodies and ILD ($p=0.004$). CT imaging revealed reticular and micronodular patterns in all patients, with 80% exhibiting ground-glass opacities. Notably, patients with UIP demonstrated a greater extent of fibrosis than those with NSIP ($p<0.05$).

Conclusions: This study highlights the prevalence and imaging characteristics of ILD in systemic sclerosis patients during the pandemic, reaffirming the association of ILD with specific autoantibodies. The findings suggest that even in a tertiary center setting, challenges such as reduced access to imaging during the pandemic may affect ILD assessment.

Keywords: systemic sclerosis, interstitial lung disease, COVID-19 pandemic, anti-Sc170 antibodies.

Introduction

Systemic sclerosis (SSc), an autoimmune connective tissue disorder, is characterized by widespread microvascular damage, excessive extracellular matrix deposition, and progressive fibrosis of the skin and internal organs [7–9]. One of the most significant complications of SSc is interstitial lung disease (ILD), which affects up to 66% of patients and accounts for nearly one-third of all SSc-related deaths [2,10–12].

The most common radiologic manifestation of ILD in systemic sclerosis is non-specific interstitial pneumonia (NSIP), observed in approximately 65% of cases [5]. NSIP is typically characterized by ground-glass opacities with a peripheral distribution, predominantly affecting the basal and subpleural regions [10,13]. In contrast, usual interstitial pneumonia (UIP), identified in approximately 25% of cases, presents with architectural distortion, dense fibrosis, and the characteristic honeycomb pattern, also with a subpleural distribution [10,13].

This study aims to characterize the imaging findings of ILD in systemic sclerosis and assess the extent of pulmonary fibrosis in affected individuals during the time of the pandemic. Additionally, it seeks to provide demographic insights into the patient cohort, including age and sex distribution, while highlighting the clinical features of those who developed ILD.

Materials and Methods

This retrospective study included patients diagnosed with systemic sclerosis (SSc) who were treated at the Cluj Emergency Clinical County Hospital between 2019 and 2020. To be included in the study, patients were required to meet the 2013 ACR/EULAR diagnostic criteria for systemic sclerosis, and no exclusion criteria were applied. For each patient, data were collected from medical records, including age at the time of assessment, sex,

and the specific subtype of systemic sclerosis, which was determined based on the extent of skin involvement. Immunologic profiles were also recorded, focusing on the presence of specific autoantibodies such as anti-centromere, anti-Scl70, anti-RNA polymerase and anti-Pm-Scl.

In addition, the presence of Raynaud's phenomenon, capillaroscopic findings, and any organ involvement related to systemic sclerosis were documented. Special attention was given to pulmonary involvement, particularly the presence of interstitial lung disease (ILD), which was evaluated using chest computed tomography (CT) scans. The extent of pulmonary fibrosis, as visualized on CT, was also noted for each patient.

The collected data were compiled into a Microsoft Excel database for statistical analysis. Descriptive statistics were used to summarize the data, and further statistical analyses were conducted using Fisher's exact test, the Chi-square test, and Spearman's correlation coefficient.

Results

General characteristics of the cohort

The study included 70 patients, comprising 62 (89%) females and 8 (11%) males, yielding a female-to-male ratio of 7:1.

Of the 70 patients, 67% (n=47) had the diffuse form, 30% (n=21) had the limited form, and 3% (n=2) were diagnosed with scleroderma sine scleroderma.

Diffuse SSc was present in 88% of males and 56% of females; however, the difference was not statistically significant (p=0.192). Notably, the cohort included, 3% of female patients with scleroderma sine scleroderma.

The study population ranged in age from 23 to 83 years, with a mean age (+SD) of 51 ± 6.76 years. The majority of patients (64%) were within the 40–60-year age group.

Table 1. *Organ involvement distribution.*

Type of involvement	Percent [%]
Cardiac	40
Renal	4.3
Gastrointestinal	63
Musculoskeletal	53

Rodnan score was evaluated in 75% of the patients. The mean(+SD) Rodnan score was 9.9 ± 9.2.

Lung involvement and imaging findings

Of the 70 study participants, 79% (n=55) exhibited pulmonary involvement, and 98% (n=54) of these individuals were diagnosed with interstitial lung disease (ILD); the remaining 2% (n=1) were diagnosed with pulmonary hypertension only.

All male participants, as well as 67% female participants were diagnosed with ILD.

The distribution of ILD across different systemic sclerosis subtypes was as follows: 87% of patients with diffuse systemic sclerosis had ILD, 62% of patients with limited systemic sclerosis, and all with scleroderma sine scleroderma exhibited ILD.

Regarding the immunological profile of participants with ILD, 5% tested positive for anti-centromere antibodies, 60% for anti-Scl70 antibodies, 1.43% for anti-RNA polymerase antibodies, and 2% for anti-PmScl antibodies. Additionally, 37% of patients with ILD displayed other autoantibodies not specifically targeted in the study.

We found that both anti-SCL70 and anticentromere antibodies were associated with lung involvement (p=0.004).

Screening or reassessment of ILD during the pandemic was in 58% (n=41) of patients. Of these, 90% (n=37) showed evidence of interstitial lung involvement on CT imaging. The imaging patterns observed in patients with ILD were distributed as follows: 58% had non-specific interstitial pneumonia (NSIP), 28% had usual interstitial pneumonia (UIP), and 15% had mixed features.

Table 2. *Sex-Specific differences in CT imaging patterns*.

Sex	NSIP [%]	UIP [%]	Unclassifiable [%]
F	60	22	18
M	50	50	0

Patient's sex was not found to be linked with a certain CT pattern (p=0.269).

CT findings revealed that all 41 patients exhibited reticular and micronodular patterns. Ground-glass opacities were observed in 80% (n=33) patients, honeycombing in 27% (n=11) patients, consolidations in 10% patients (n=4), and bronchiectasis in 56% patients (n=23).

The extent of pulmonary fibrosis among the 41 patients who underwent CT evaluation was as follows: 39% of patients had less than 10% fibrosis, 17% patients had 10-25% fibrosis, another 17% of patients had 25-50% fibrosis, and 27% of patients had 50-75% fibrosis. Notably, all patients with unclassifiable CT features had less than 10% fibrosis.

Patients presenting with UIP pattern have been found to have a more extensive fibrosis than the ones presenting with NSIP ($p<0.05$).

In patients with NSIP, the extent of pulmonary fibrosis was distributed as follows: 39% patients had less than 10% fibrosis, 30% of patients had 10-25%, 22% patients had 25-50%, and 13% patients had 50-75% fibrosis. In patients with UIP, 9% patient had less than 10% fibrosis, 18% patients had 25-50% fibrosis, and 73% patients displayed 50-75% fibrosis.

Discussions

This study reflects the assessment of ILD patients during the pandemic and its limitation secondary to the ambulation and resource allocation constraints. Also, the data on ILD extent in these patients might be biased as SSc-ILD and COVID19 have several similarities [14].

The study population consisted of 70 patients, with

a clear sex imbalance as 62 were women and only 8 were men, resulting in a female-to-male ratio of 7:1. This ratio is consistent with the literature, which reports a range between 3:1 and 11:1 for the female-to-male distribution in systemic sclerosis [15]. Furthermore, the data revealed that men more often presented the diffuse form of the disease, with 7 out of 8 male participants displaying this clinical subtype.

The majority of patients in the study, 60%, had the diffuse form of systemic sclerosis. This finding may be attributed to the study setting, a tertiary referral center for rheumatology diagnosis and treatment.

Within the group of patients with the diffuse form, anti-Scl70 antibodies predominated, accounting for 89% of cases. This observation is supported by previous studies that have demonstrated an association between the diffuse form of systemic sclerosis and the presence of anti-Scl70 antibodies [16]. In the limited form, an equal distribution of anti-centromere and anti-Scl70 antibodies was observed.

The study found that all male patients and 67% of female patients had pulmonary involvement, slightly lower than reported in the literature (12), possibly because a portion of patients did not have access to proper medical services. The majority of patients with diffuse scleroderma had interstitial lung disease, consistent with previous findings [2,11,15,17].

Anti-Scl70 antibodies were the most common antibodies detected, and they were associated with the presence of interstitial lung disease, as determined by Fisher's exact test, suggesting they are a risk factor for this complication.

More than half of the patients underwent computed tomography imaging, with the rest likely unable to due to the COVID-19 pandemic. The most common CT appearance was non-specific interstitial pneumonia, in line with current literature [13,18]. The NSIP pattern was correlated with less extensive pulmonary fibrosis, as indicated by Spearman's correlation coefficient.

The majority of patients showed less than 10% fibrosis extension in both lung fields. Additionally, 39% of the study participants had fibrosis extension less than 10%, suggesting the majority had a milder form of the disease. The appearance of common interstitial pneumonia was correlated with greater fibrosis extension, while unclassifiable patterns were associated with less severe fibrosis, likely due to early-stage investigation of these patients.

An attempt to link patient sex with CT imaging patterns was inconclusive, possibly due to the small number of male participants.

Most women had less than 10% fibrosis, while most men had extensive fibrosis between 50-75%. This indicates men may be prone to more aggressive disease, as previously described in the literature. All participants showed a reticular and micronodular pattern on CT, suggesting mild interstitial lung involvement in all systemic sclerosis patients.

Conclusions

This study investigated the prevalence and imaging characteristics of ILD in SSc patients during the COVID-19 pandemic. Our findings indicate a high frequency of ILD in SSc patients, with NSIP being the most common pattern. A significant association between anti-Sc170 antibodies and ILD was observed. CT imaging revealed a predominance of reticular, micronodular, and ground-glass opacities, with UIP demonstrating a greater extent of fibrosis compared to NSIP. These results highlight the importance of early CT imaging in SSc patients to assess lung involvement and guide clinical management.

Conflicts of Interest: The authors declare no conflicts of interest.

References

[1] Caron M, Hoa S, Hudson M et al. Pulmonary function tests as outcomes for systemic sclerosis interstitial lung disease. Eur Respir Rev [Internet]. 2018;27(148). Available from: http://dx.doi.org/10.1183/16000617.0102-2017

[2] Ananyeva LP. Interstitial lung disease associated with systemic sclerosis. Nauchno-Prakticheskaya Revmatol. 2017;55(1):87–95.

[3] Adler S, Huscher D, Siegert E et al. Systemic sclerosis associated interstitial lung disease - individualized immunosuppressive therapy and course of lung function: Results of the EUSTAR group. Arthritis Res Ther. 2018;20(1):1–12.

[4] Winstone TA, Assayag D, Wilcox PG et al. Predictors of mortality and progression in scleroderma-associated interstitial lung disease: A systematic review. Chest. 2014;146(2):422–36.

[5] Khanna D, Seibold J, Goldin J et al. Interstitial lung disease points to consider for clinical trials in systemic sclerosis. Rheumatology (Oxford). 2017;56(5):v27–32.

[6] Fischer A, Patel NM, Volkmann ER. Interstitial lung disease in systemic sclerosis: Focus on early detection and intervention. Open Access Rheumatol Res Rev. 2019;11:283–307.

[7] Allanore Y, Simms R, Distler O et al. Systemic sclerosis. Nat Rev Dis Prim. 2015;1(April).

[8] Castelino F V., Dellaripa PF. Recent progress in systemic sclerosis-interstitial lung disease. Curr Opin Rheumatol. 2018;30(6):570–5.

[9] Jaeger VK, Wirz EG, Allanore Y et al. Incidences and risk factors of organ manifestations in the early course of systemic sclerosis: A longitudinal EUSTAR study. PLoS One. 2016;11(10):1–15.

[10] Demizio DJ, Bernstein EJ. Detection and classification of systemic sclerosis-related interstitial lung disease: A review. Curr Opin Rheumatol. 2019;31(6):553–60.

[11] Mango RL, Matteson EL, Crowson CS et al. Assessing Mortality Models in Systemic Sclerosis-Related Interstitial Lung Disease. Lung [Internet]. 2018;196(4):409–16. Available from: http://dx.doi.org/10.1007/s00408-018-0126-6.

[12] Bergamasco A, Hartmann N, Wallace L et al. Epidemiology of systemic sclerosis and systemic sclerosis-associated interstitial lung disease. Clin Epidemiol. 2019;11:257–73.

[13] Goldin JG, Lynch DA, Strollo DC et al. High-resolution CT scan findings in patients with symptomatic scleroderma-related interstitial lung disease. Chest. 2008;134(2):358–67.

[14] Hoffmann-Vold AM, Distler O, Bruni C et al. Systemic sclerosis in the time of COVID-19. Lancet Rheumatol [Internet]. 2022;4(8):e566–75. Available from: http://dx.doi.org/10.1016/S2665-9913(22)00130-8.

[15] Schoenfeld SR, Castelino F V. Interstitial lung disease in Scleroderma. Rheum Dis Clin North Am. 2015;41(2):237–48.

[16] Skare TL, Fonseca AE, Luciano AC et al. Autoantibodies in scleroderma and their association with the clinical profile of the disease. A study of 66 patients from southern Brazil. An Bras Dermatol. 2011;86(6):1075–81.
[17] Roofeh D, Jaafar S, Vummidi D et al. Management of systemic sclerosis-associated interstitial lung disease. Curr Opin Rheumatol. 2019;31(3):241–9.
[18] Aydi Z, Rachdi I, Ben Dhaou B et al. Particularités épidémiologiques, cliniques et évolutives des pneumopathies interstitielles au cours de la sclérodermie systémique. Rev Pneumol Clin [Internet]. 2016;72(2):122–8. Available from: http://dx.doi.org/10.1016/j.pneumo.2015.09.003.

Corresponding author
Maia Ioana Mihon, Department of Rheumatology, Cluj Emergency County Clinical Hospital, Cluj-Napoca, Romania, maia.mihon@gmail.com

Received: 29.10.2024

Accepted: 24.11.2024