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Between diffuse and limited: the unique identity of systemic sclerosis–overlap syndromes

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ABSTRACT

Aims: Systemic sclerosis–overlap syndrome (SSc-OS) constitutes a distinct clinical phenotype within the spectrum of systemic sclerosis, marked by unique immunological and clinical characteristics that differentiate it from the classical subsets. The present study aimed to characterise the demographic, serological, and organ involvement patterns of patients with SSc-OS, and to assess their disease manifestations and prognostic trajectories in comparison with diffuse cutaneous and limited cutaneous SSc.

Methods: This study included patients followed at the Gazi University Hospital Rheumatology Department between January 2010 and July 2025. SSc-OS was defined as patients fulfilling classification criteria for systemic sclerosis together with other autoimmune diseases as rheumatoid arthritis, polymyositis, and or Sjögren's syndrome. Baseline and 1-year characteristics were compared between SSc and SSc-OS.

Results: A total of 160 patients were included: 68 diffuse cutaneous (dcSSc), 67 limited cutaneous (lcSSc), and 25 SSc-OS. Age at disease onset was lower in dcSSc (42.5±13.7 years) compared with lcSSc (50.6±13.7) and SSc-OS (47.2±13.9; p=0.003). Anti-topoisomerase I positivity was highest in dcSSc (83.8%) versus lcSSc (43.3%) and SSc-OS (16%; p=0.001), whereas anti-centromere was most frequent in lcSSc (41.8%; p=0.001) and anti-SSa in SSc-OS (44%; p=0.002). Interstitial lung disease (ILD) occurred in 89.7% of dcSSc, 76% of SSc-OS, and 56.7% of lcSSc (p=0.001), with extensive disease more common in dcSSc (61.7%; p=0.001). Myopathy was higher in SSc-OS (44%) and dcSSc (35.3%) than lcSSc (12.1%; p=0.001). Immunosuppressive therapy was most frequent in dcSSc (88.2% vs. 35.8% lcSSc and 60% SSc-OS; p=0.001). At one year, SSc-OS patients showed greater improvements in force vital capacity (FVC) and diffusing capacity for carbon monoxide (DLco), though not statistically significant. Mortality occurred in 25% of dcSSc, 14.9% of lcSSc, and 8% of SSc-OS (p=0.113); Kaplan–Meier analysis demonstrated numerically better survival in SSc-OS (mean 25.3 years) compared with lcSSc (19.8) and dcSSc (19.5; log-rank p=0.249).

Conclusion: This study identified SSc-OS in 15.6% of patients, most commonly SSc–Sjögren's. Distinct autoantibody profiles and prominent musculoskeletal involvement differentiated SSc-OS from classical subsets. While dcSSc showed the highest ILD burden and lcSSc was linked to pulmonary arterial hypertension, SSc-OS demonstrated intermediate pulmonary disease and numerically better survival, supporting its recognition as a clinically distinct phenotype within the SSc spectrum.

Keywords: Mortality, overlap syndrome, prognosis, systemic sclerosis

INTRODUCTION

Systemic sclerosis (SSc) is a rare autoimmune connective tissue disease (CTD) characterised by immune dysregulation, widespread vasculopathy, and progressive fibrosis affecting the skin and internal organs.[1] SSc is classified into three subsets based on the extent of cutaneous involvement: diffuse cutaneous SSc (dcSSc), limited cutaneous SSc (lcSSc), and sine scleroderma.[2] However, these subsets may coexist with features of other CTDs, such as systemic lupus erythematosus, rheumatoid arthritis (RA), polymyositis/dermatomyositis (PM/DM), or Sjögren's syndrome (SjS). When the classification criteria for SSc and another CTD are fulfilled simultaneously, the condition is defined as SSc-overlap syndrome (SSc-OS).[3] The reported prevalence of SSc-OS varies considerably across cohorts, ranging from 10% to 32.9%.[4-7]

Clinically, SSc-OS patients exhibit distinct features compared with the classical SSc subsets.[8] Anti-topoisomerase I positivity is observed less frequently in SSc-OS than in dcSSc, while the overall disease course more closely resembles lcSSc. With respect to organ involvement, interstitial lung disease (ILD) is reported more frequently in SSc-OS compared with lcSSc.[4] In contrast, arthritis and myositis are significantly more common than in dcSSc and lcSSc. Synovitis and myositis have been consistently highlighted as characteristic features of SSc-OS,[4] whereas the prevalence of digital ulcers is lower compared with patients with isolated lcSSc.[9] Some studies have suggested

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that ILD occurs at comparable rates between SSc and SSc-OS, although the frequency of pulmonary arterial hypertension (PAH) may be lower in overlap cases.[5] Importantly, overlap patients are often reported to have a milder global clinical course than patients with isolated CTDs, and the occurrence of overlap syndromes appears to be more frequent in lcSSc than in dcSSc. Like classical SSc, pulmonary, gastrointestinal, renal, and cardiac involvement can also be observed in SSc-OS, although the reported frequencies vary widely among studies.[3,9,10]

These findings suggest that SSc-OS represents a distinct clinical phenotype within the spectrum of SSc, with unique immunological, clinical, and prognostic implications. The present study aimed to comprehensively evaluate the clinical, serological, and organ involvement characteristics of patients with SSc-OS, and to compare them with classical SSc subsets in terms of both disease manifestations and prognosis.

METHODS

Ethics

Ethical approval for this study was obtained from the Gazi University Clinical Researches Ethics Committee (Date: 22.10.2024, Decision No: 2024-1594). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

Study Design and Patients

This retrospective, single-centre cohort study was conducted at the Department of Rheumatology, Gazi University Hospital (Ankara, Turkiye). Patients aged ≥18 who fulfilled the American College of Rheumatology 1980[11] or 2013 American College of Rheumatology/European League Against Rheumatism (ACR/EULAR) classification criteria for SSc[12] and were followed between January 2010 and July 2025 were screened for eligibility. In addition, patients were evaluated for overlap syndromes according to the respective classification criteria for RA,[13] SjS,[14] systemic lupus erythematosus,[15] and idiopathic inflammatory myopathies.[16] At baseline, patients were categorised into three subgroups according to their clinical phenotype: dcSSc (n=68), lcSSc (n=67), and overlap syndrome patients (n=25).

Demographic, Clinical and Laboratory Features

Demographic data and disease duration (calculated from the time of first non-Raynaud's symptom) were recorded for all patients. Disease subset was classified as diffuse or lcSSc according to the criteria of LeRoy and colleagues.[2] Patients were considered to have ILD if thoracic high-resolution computed tomography (HRCT) demonstrated radiological features such as ground-glass opacities, reticular thickening, traction bronchiectasis, or honeycombing. Patients with HRCT findings involving ≥20% of the lung parenchyma were classified as having diffuse extended lung involvement.[17] PAH was defined as a mean pulmonary arterial pressure >20 mmHg confirmed by right heart catheterisation. Oesophageal involvement was considered present in patients with a clinical history of gastroesophageal reflux disease and/or dysphagia. Scleroderma renal crisis was defined as new-onset acute kidney injury with hypertension, not attributable to other causes. Digital ischemic complications included the presence of digital ulcers, pitting scars, auto-amputation, or pulp atrophy.

Serological profiles, including relevant autoantibodies, were collected from patient records. Pulmonary function test (PFT) data were retrieved: the earliest available measurement within 12 months of diagnosis was defined as the baseline PFT, and the subsequent measurement obtained within the following 12 months was considered the follow-up PFT. Both forced vital capacity (FVC) and diffusing capacity for carbon monoxide (DLco) were recorded. Immunosuppressive therapies received during the disease course were also documented.

Follow-up and Mortality Data

The primary outcomes of this study were defined as follows:

- **Comparison of clinical characteristics across disease subsets**–The frequency and distribution of demographic, clinical, serological, and treatment-related factors were compared among patients with dcSSc, lcSSc, and overlap syndrome.
- **Assessment of interstitial lung disease progression**–PFT parameters and HRCT-defined lung involvement were evaluated in patients with ILD. The earliest available PFT within 12 months of diagnosis was defined as the baseline, and the subsequent PFT obtained within the following 12 months was considered the follow-up measurement. Changes in FVC and DLco between baseline and follow-up were compared across subsets.
- **Evaluation of mortality during follow-up**–Mortality data were collected for all patients, and survival outcomes were compared among the three disease subsets over the follow-up period.

Statistical Analysis

Descriptive statistics were used to summarise patients' characteristics. Categorical variables were presented as absolute frequencies and percentages. Continuous and normally distributed variables were expressed as mean (±standard deviation; SD), and constant and not normally distributed variables as median (and interquartile range; IQR). The normality of continuous variables was evaluated using the Shapiro–Wilk test and confirmed by visual inspection of histogram plots. Comparisons among the three patient subsets were performed using one-way analysis of variance (ANOVA) for normally distributed continuous variables and the Kruskal–Wallis test for non-normally distributed variables. Post-hoc pairwise comparisons were conducted using Bonferroni correction. Where appropriate, categorical variables were compared using the Chi-square or Fisher's exact test. The log-rank test compared survival data plotted on the Kaplan-Meier curves. Survival rates at 15 years were calculated. Statistical analyses were performed using SPSS software (version 23, IBM Corp., Armonk, NY). A two-tailed p-value <0.05 was considered statistically significant.

RESULTS

Patient Characteristics

A total of 160 patients with SSc were included in the analysis: 68 with dcSSc, 67 with lcSSc, and 25 with SSc-OS. Among the 25 patients classified as having SSc-OS, 19 fulfilled criteria for SSc–SjS overlap, four for SSc–myositis overlap, and two for SSc-RA overlap. The mean age at study entry was significantly higher in the lcSSc (58.2±13.27 years) and SSc-OS groups (57.7±13.47 years) compared with dcSSc (52.6±13.75 years; p=0.037). Similarly, age at disease onset was significantly earlier in dcSSc (42.5±13.66 years) compared with lcSSc (50.6±13.67 years) and SSc-OS (47.2±13.92 years; p=0.003). Most patients were female across all subsets (>90%). Mortality was observed in 17 dcSSc (25%), 10 lcSSc (14.9%), and 2 SSc-OS (8%) patients, with no significant difference among groups (p=0.113).

Disease Characteristics

Autoantibody profiles differed significantly between groups. Anti-centromere antibody positivity was most frequent in lcSSc (41.8%) compared with SSc-OS (28%) and dcSSc (4.4%; p=0.001). Conversely, anti-topoisomerase I positivity was markedly more common in dcSSc (83.8%) compared with lcSSc (43.3%) and SSc-OS (16%; p=0.001). Anti- SjS type A (anti-SSa) antibody was more prevalent in SSc-OS (44%) compared with dcSSc (16.2%) and lcSSc (11.9%; p=0.002).

Raynaud's phenomenon was highly prevalent across all subsets (>88%), without significant differences. However, telangiectasia was more frequent in dcSSc (66.2%) and SSc-OS (60%) compared with lcSSc (30.3%; p=0.001). Similarly, a history of digital ulcers was significantly higher in dcSSc (51.5%) compared with lcSSc (25.8%) and SSc-OS (32%; p=0.007). Catheterisation-confirmed PAH was observed more often in lcSSc (14.9%) than in dcSSc (2.9%) or SSc-OS (8%; p=0.048).

ILD on HRCT was most frequent in dcSSc (89.7%), compared with 76% in SSc-OS and 56.7% in lcSSc (p=0.001). Extensive lung involvement (≥20% of lung parenchyma) was also more frequent in dcSSc (61.7%) compared with lcSSc (29.9%) and SSc-OS (36%; p=0.001). Baseline PFTs demonstrated lower FVC% % predicted in dcSSc (84.1±20.0) compared with lcSSc (102.1±20.7) and SSc-OS (93.7±26.9; p=0.001). DLco % predicted values were lowest in dcSSc (68.8±19.0), intermediate in SSc-OS (73.1±22.8), and highest in lcSSc (78.2±22.6), although this did not reach statistical significance (p=0.066). Articular involvement was common across groups (76–92%) without significant differences. Myopathy was significantly more frequent in SSc-OS (44%) and dcSSc (35.3%) compared with lcSSc (12.1%; p=0.001). Upper gastrointestinal involvement and renal crisis were observed at similar frequencies among the three subsets.

Immunosuppressive therapy was used most frequently in dcSSc (88.2%) compared with lcSSc (35.8%) and SSc-OS (60%; p=0.001). Mycophenolate mofetil and cyclophosphamide were predominantly administered in dcSSc (73.5% and 47.1%, respectively), followed by SSc-OS (36% and 24%) and lcSSc (20.9% and 10.4%; both p=0.001). Rituximab use was more common in dcSSc (22.1%) compared with lcSSc (3%) and SSc-OS (8%; p=0.002). These data was shown in **Table 1**.

Lung Function and 1-Year Changes in SSc-ILD

In patients with SSc-ILD, baseline pulmonary function differed significantly between subsets. The mean baseline FVC % predicted was lower in dcSSc (84.4±19.2) compared with lcSSc (104.9±20.0) and SSc-OS (89.5±26.4; p=0.001). At one year, although the difference did not reach statistical significance (p=0.115), patients in the SSc-OS group demonstrated a greater improvement in FVC% compared with the other subsets.

Similarly, the predicted baseline DLco % was lowest in dcSSc (67.4±16.9), intermediate in SSc-OS (73.1±23.4), and highest in lcSSc (79.1±19.8), with a statistically significant difference across groups (p=0.033). At one year, although the differences in FVC and DLco did not reach statistical significance (p=0.115 and p=0.289, respectively), patients in the SSc-OS group demonstrated greater improvements in both parameters than the other subsets. These data was shown in **Table 2**.

Survival Analysis

During follow-up, 29 deaths occurred among the 160 patients (17 in dcSSc, 10 in lcSSc, and 2 in SSc-OS). Among the 29 deceased patients, SSc-related causes constituted a considerable proportion. PAH was responsible for 4 deaths (13.7%), PH-ILD for 2 deaths (6.9%), ILD progression for 3 deaths (10.4%), and gastrointestinal complications for 1 death (3.4%). Other causes of death included infections, malignancies, and cardiovascular or cerebrovascular events. Infections were common, with bacterial pneumonia in 3 patients (10.4%), COVID-19 pneumonia in 4 patients (13.7%), and sepsis in 2 patients (6.9%). Malignancies accounted for 5 deaths (17.3%), cardiovascular causes for 3 (10.4%), and cerebrovascular events for 1 (3.4%). The cause of death remained unknown in 1 patient (3.4%). Kaplan–Meier survival analysis showed numerically higher survival in the SSc-OS group compared with dcSSc and lcSSc, with mean survival estimates of 25.3 years for SSc-OS, 19.8 years for lcSSc, and 19.5 years for dcSSc. However, the overall difference between groups did not reach statistical significance (log-rank p=0.249). The Kaplan–Meier survival curves of patients with SSc and SSc-OSs are presented in **Figure**.

DISCUSSION

In the present study, we provided a detailed comparison of dcSSc, lcSSc, and SSc-OS. SSc-OS was revealed in 25 (15.6%) of our SSc patients. Our result is consistent with the broad prevalence ranges previously documented among cohorts,[4-7,18] underscoring the frequent occurrence and clinical relevance of overlap syndromes within the SSc spectrum. Moreover, our series's distribution of overlap subtypes (1.2% SSc-RA, 2.5% SSc-myositis, 11.9% SSc-SjS) fell within the ranges reported in prior studies.[6,8,9]

Patients with lcSSc and SSc-OS were significantly older at inclusion than those with dcSSc, while the onset of disease occurred earlier in the latter group. This observation aligns with reports suggesting that secondary autoimmune diseases

Table 1. Patient, disease and treatment characteristics of patients with overlap syndrome and a SSc control population

Patient characteristics	dcSSc (n=68)	lcSSc (n=67)	SSc-OS (n =25)	p-value
Age, years, mean ±SD	52.6±13.75	58.2 ±13.27	57.73±13.47	0.037
Age at disease onset, years, mean ±SD	42.53±13.66	50.65±13.67	47.2±13.92	0.003
Disease duration, years, mean ±SD	10.07±6.4	7.59±6.59	9.10±6.5	0.05
Female sex, n (%)	63(92.6)	63(94)	25(100)	0.389
History of smoking (ever), n (%)	7(10.3)	11(16.9)	4(16)	0.199
Death, n (%)	17(25)	10(14.9)	2(8)	0.113
Immunological characteristics				
Anti-centromere antibody, n (%)	3(4.4)	28(41.8)	7(28)	0.001
Anti-topoisomerase I antibody, n (%)	57(83.8)	29(43.3)	4(16)	0.001
Anti-SSa antibody, n (%)	11(16.2)	8(11.9)	11(44)	0.002
Disease characteristics				
Raynaud phenomenon, n (%)	66(97.1)	63(94)	22(88)	0.24
Telangiectasia, n (%)	45(66.2)	20(30.3)	15(60)	0.001
History of digital ulcer, n (%)	35(51.5)	17(25.8)	8(32)	0.007
Catheterisation-confirmed PAH, n (%)	2(2.9)	10(14.9)	2(8)	0.048
Respiratory involvement				
CT-scan-defined ILD, n (%)	61(89.7)	38(56.7)	19(76)	0.001
Diffuse extended ILD, n (%)	42(61.7)	20(29.9)	9(36)	0.001
FVC% % predicted, mean ±SD	84.1±20.03	102.1±20.7	93.7±26.9	0.001
DLco % predicted, mean± SD	68.8±19.0	78.2±22.6	73.1±22.8	0.066
Articular involvement, n (%)	52(76.5)	51(76.1)	23(92)	0.211
Myopathy, n (%)	24(35.3)	8(12.1)	11(44)	0.001
Oesophageal dysphagia, n (%)	28(41.2)	28(42.4)	15(60)	0.241
Renal crisis, n (%)	2(2.9)	1(1.5)	1(4)	0.754
Treatment characteristics (ever use)				
Immunosuppressive therapy, n (%)	60(88.2)	24(35.8)	15(60)	0.001
Methotrexate therapy, n (%)	1(25)	(10.4)	6(24)	0.073
Azathioprine, n (%)	18(26.5)	6(9)	5(20)	0.029
Mycophenolate mofetil, n (%)	50(73.5)	14(20.9)	9(36)	0.001
Cyclophosphamide, n (%)	32(47.1)	7(10.4)	6(24)	0.001
Rituximab, n (%)	15(22.1)	2(3.0)	2(8)	0.002
Anti-IL6R Ab, n (%)	3(4.4)	1(1.5)	2(8)	0.32

SSc: Systemic sclerosis, dcSSc: Diffuse cutaneous systemic sclerosis, lcSSc: Limited cutaneous systemic sclerosis, OS: Overlap syndrome, SD: Standard deviation, anti-SSa: Anti–Sjögren's Sjögren's-syndrome-related antigen, PAH: Pulmonary arterial hypertension, CT: Computed tomography, ILD: Interstitial lung disease, FVC: Forced vital capacity, DLco: Diffusing capacity of the lungs for carbon monoxide, IL6R Ab: Interleukin-6 receptor antibody

Table 2. Baseline FVC and DLCO values and 1-year changes in patients with SSc-ILD according to disease subsets

Pulmonary function fests	dcSSc (n =61)	lcSSc (n=38)	SSc-OS (n=19)	p-value
FVC% predicted, mean±SD	84.37±19.21	10.4.9±20.0	89.53±26.35	0.001
Δ FVC, mean	-2.0	5.1	12.5	0.115
DLco% predicted, mean±SD	67.41±16.87	79.11±19.8	73.1±23.4	0.033
Δ DLco, mean	4.0	-1.2	10.4	0.289

SSc: Systemic sclerosis, dcSSc: Diffuse cutaneous systemic sclerosis, lcSSc: Limited cutaneous systemic sclerosis, OS: Overlap syndrome, SD: Standard deviation, FVC: Forced vital capacity, DLco: Diffusing capacity of the lungs for carbon monoxide

may develop later in the natural course of SSc.[8] Similar to earlier cohorts, the majority of our overlap patients were female.[3,9]

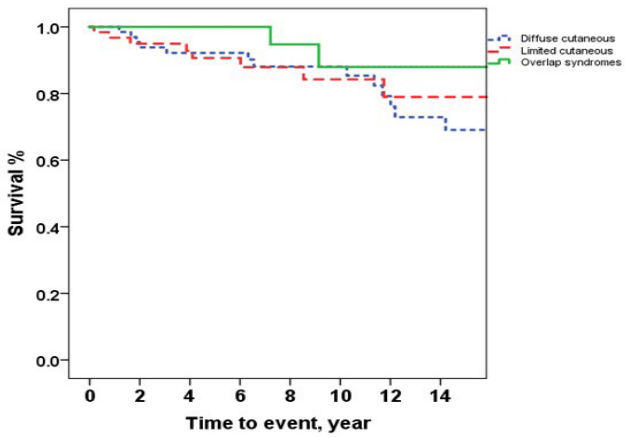

Figure. Kaplan–Meier survival curves of systemic sclerosis (SSc) patients stratified by disease subset (diffuse cutaneous SSc, limited cutaneous SSc, and overlap syndromes)

Serological profiles differed markedly between subsets. Anti-topoisomerase I antibody predominated in dcSSc, anti-centromere antibodies in lcSSc, and anti-SSa antibodies in SSc-OS, confirming previously described associations.[9] The relatively high prevalence of rheumatoid factor and anti-citrullinated protein autoantibodies in overlap syndromes, particularly SSc-RA, may contribute to the increased frequency of erosive arthritis and usual interstitial pneumonia (UIP).[3] These findings reinforce the view that autoantibody signatures reflect distinct pathogenic mechanisms and help delineate clinical phenotypes.

As anticipated, patients with dcSSc exhibited the highest burden of ILD, with lower pulmonary function and more extensive HRCT abnormalities. SSc-OS cases demonstrated an intermediate pulmonary profile but showed greater numerical improvements in FVC and DLco over one year. This pattern suggests that ILD in overlap syndromes may be more immunologically mediated and potentially more responsive to treatment. Similarly, Moinzadeh et al.[4] reported comparable findings regarding longitudinal DLco changes in their cohort.

Vascular manifestations such as digital ulcers and telangiectasia were most common in dcSSc, while lcSSc showed stronger associations with PAH. In contrast, overlap syndromes were distinguished by higher rates of myopathy and arthritis. These findings were consistent with the results of Shenavandeh et al.,[9] who reported greater musculoskeletal involvement in overlap patients compared with lcSSc. Gastrointestinal and renal complications were observed at similar frequencies across groups, in keeping with the report of Scherlinger et al.,[8] who found no significant differences in severe organ manifestations between overlap and non-overlap patients.

Therapeutic approaches largely reflected disease severity. Immunosuppressive treatment, particularly with mycophenolate mofetil, cyclophosphamide, and rituximab, was most frequently prescribed in dcSSc. Patients with overlap syndromes demonstrated intermediate rates of immunosuppressive use, which differs from Shenavandeh et al.,[9] who found higher usage in lcSSc compared with overlap patients. Such discrepancies may reflect clinical practice variations and the criteria used to define overlap syndromes. Scherlinger et al.[8] noted that overlap patients were more likely to receive corticosteroids and biologic agents, particularly in SSc-RA.

Although Kaplan–Meier analysis indicated numerically better survival in overlap patients compared with both lcSSc and dcSSc, the differences did not reach statistical significance. In our cohort, the differences observed in the Kaplan–Meier survival curves can largely be explained by cause-specific mortality patterns. Patients with dcSSc more frequently experienced mortality due to ILD progression and infectious complications, whereas in the lcSSc subset mortality was mainly attributable to PAH. These findings confirm that ILD and PAH remain the leading causes of mortality in SSc. These findings agree with several previous studies suggesting that overlap syndromes are not necessarily associated with poorer survival. Nevertheless, subgroups such as SSc-SjS have been associated with increased mortality, mainly related to infectious complications and lymphoproliferative diseases.[8] This heterogeneity underscores the need for larger cohorts and longer follow-up to clarify prognostic outcomes within specific overlap subtypes.

Our results suggest that overlap syndromes constitute a heterogeneous but clinically recognizable subgroup with features intermediate between lcSSc and dcSSc. While dcSSc remains the most aggressive subset, characterized by extensive ILD and greater immunosuppressive requirements, SSc-OS is marked by prominent musculoskeletal manifestations and distinctive serological profiles and may carry a relatively favorable survival trajectory. The variability reported across studies likely reflects differences in study design, classification criteria, follow-up duration, and ethnic distribution of overlap phenotypes.

Limitations

The modest number of overlap cases in our cohort limited the power of subgroup analyses, particularly regarding survival and longitudinal pulmonary function. In addition, treatment practices in our center may not represent those of other institutions, and the absence of systematic testing for all autoantibodies may have influenced the observed frequencies.

This study provides one of the few large single-center analyses directly comparing SSc-OSs with the classical dcSSc and lcSSc subtypes. Our findings highlight that SSc-OS patients display distinct serological and organ involvement patterns, underscoring the clinical relevance of recognizing overlap forms. Early identification of SSc-OS is important because these patients often require tailored immunosuppressive approaches and exhibit variable prognostic trajectories compared with non-overlap SSc.

CONCLUSION

Overall, our findings indicate that SSc-OS represents a distinct clinical and immunological entity within the SSc spectrum. These patients demonstrate intermediate pulmonary involvement, prominent musculoskeletal manifestations, and unique antibody profiles, without excess mortality compared with classical subsets. Larger, multicenter longitudinal studies are warranted to validate these observations and to identify prognostic markers that can better guide management strategies in this complex subgroup.

ETHICAL DECLARATIONS

Ethics Committee Approval

Ethical approval for this study was obtained from the Gazi University Clinical Researches Ethics Committee (Date: 22.10.2024, Decision No: 2024-1594).

Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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