TIME-COURSE OF INTERSTITIAL LUNG DISEASE IN SYSTEMIC SCLEROSIS: INCIDENCE, PREVALENCE, AND PROGNOSTIC TIMING

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OBJECTIVE

To analyze the chronological pattern of interstitial lung disease (ILD) in patients with systemic sclerosis (SSc) and to assess whether the timing of ILD onset (early vs. late) impacts prognosis.

METHODS

A total of 313 patients with SSc from a multicenter ambispective study were included. We evaluated the incidence and prevalence of ILD based on annual diagnoses of new cases and their cumulative evolution over the first 10 years following SSc diagnosis. The mean annual incidence proportion (MAIP) and overall prevalence of ILD in the cohort were calculated. We also characterized the distribution of cases at specific time intervals and their cumulative progression. A comparative analysis was performed between early and late ILD, using 3-year and 5-year cut-offs from SSc diagnosis.

RESULTS

Among the 313 patients, 116 (37.1%) developed ILD during follow-up. The MAIP was 6.45 cases per 100 person-years. In 27.6% (32/116) of these ILD patients, ILD was either the presenting feature or the main clinical manifestation leading to SSc diagnosis.

Overall, 35.3% (41/116) of ILD cases were diagnosed in the first year, with 27.6% (32/116) identified in the first 6 months and 7.7% (9/116) in the subsequent 6 months. Of the 240 patients without ILD at the end of the first year, 17.9% (43/240) developed ILD later. Beyond the first year, the incidence rate of ILD in SSc patients declines and remains relatively stable (see Table 1 and figure 1), except for a marked peak in the eighth year, after which it returns to average levels.

When comparing early ILD onset (≤3 years) to late onset (>3 years) [see Table 2], the only notable difference was a lower %pFVC at study inclusion in early cases (mean 79.8 vs. 93; p=0.006). No significant differences were observed in %pDLCO, the distance covered in the 6MWT, or other variables, including the development of type 3 pulmonary arterial hypertension (PAH), lung transplant, mortality, or treatment needs (cyclophosphamide and biologics). Using a >5-year cut-off similarly revealed no statistically significant between-group differences

CONCLUSION

The prevalence of ILD in our cohort was 37.1%, with a MAIP of 6.45 cases per 100 person-years. ILD can occur at any time after SSc diagnosis, with a relatively consistent incidence during the disease course, emphasizing the importance of continued screening for new onset SSc-ILD over time. The timing of ILD onset does not appear to significantly influence its prognosis.

Table 1: Incidence of ILD in SSc over time

Period	New Cases	Cumulative Cases	Cumulative Percentage	Incidence Rate (100 PY)	Total patients	Missing patients due to insufficient follow-up	Incidence rate per 100 person-years
Prior to or at diagnosis	32	32	10.2% (32/116)	10.22	313	40	10,22
First year	41	73	23.3% (73/116)	13.1	241	19	17,01
Second year	5	78	24.9% (78/116)	1.6	217	15	2,30
Third year	3	81	25.9% (81/116)	0.96	199	17	1,51
Fourth year	3	84	26.8% (84/116)	0.96	179	17	1,68
Fifth year	1	85	27.2% (85/116)	0.32	161	13	0,62
Sixth year	4	89	28.4% (89/116)	1.28	144	23	2,78
Seventh year	1	90	28.8% (90/116)	0.32	120	20	0,83
Eighth year	7	97	31.0% (97/116)	2.24	93	11	7,53
Ninth year	3	100	32.0% (100/116)	0.96	79	17	3,80
Tenth year	1	101	32.3% (101/116)	0.32	61	11	1,64
After 10 years	15	116	37.1% (116/116)	4.79	50		30,00

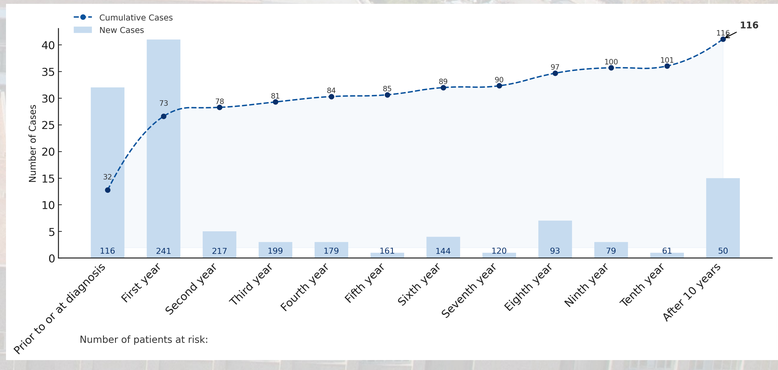
Table 2: Comparative study of prognostic variables between patients with early versus late ILD.

2A: using a diagnostic cut-off point within the first 3 years from disease diagnosis

	Early ILD (≤ 3 years) N=81	Late ILD (> 3 years) N=35	P value
Symptomatic ILD at diagnosis	39 (48.1%)	10 (28.6%)	0.050
Increased fibrosis on HRCT	26 (32.1%)	7 (20%)	0.350
Physiological evidence of disease progression	25 (30.9%)	8 (22.9%)	0.680
Fulfilment of PPF criteria	23 (28.4)	5 (14.3%)	0.103
%pFVC at study inclusion, mean±SD, (IQR 25th-75 th)	79.8±20 (64-92)	93 ±29 (70-115)	**0.006**
Percentage of patients with %pFVC<70 at study inclusion	25 (30.9%)	8 (22.9%)	0.528
%pDLCO at study inclusion, mean±SD, (IQR 25th-75 th)	59 ±15 (46-69)	64±20 (45-84)	0.126
Percentage of patients with %pDLCO<60 at study inclusion	46 (56.8%)	17 (48.6%)	0.302
Distance covered in 6MWT at study inclusion, mean± SD, (IQR 25th-75 th)	392±108 (347-450)	406±88 (360.5-468)	0526
Need for cyclophosphamide treatment	10 (12.3%)	3 (8.6%)	0.554
Need for biologic therapy	30 (37%)	11 (31.4%)	0.562
Lung transplant	8 (9.9%)	4 (11.4%)	0.905
Development of type 3 PAH	8 (9.9%)	1 (2.8%)	0.274
Death	6 (7.4%)	0 (0%)	0.178

2B: using a cut-off point of 5 years.

	Early ILD (≤ 5 years) N=86	Late ILD (> 5 years) N=30	P value
Symptomatic ILD at diagnosis	40 (46.5%)	9 (30%)	0.115
Increased fibrosis on HRCT	26 (30.2%)	7 (23.3%)	0.663
Physiological evidence of disease progression	26 (30.2%)	7 (23.3%)	0.504
Fulfilment of PPF criteria	23 (26.7%)	5 (16.7%)	0.267
%pFVC at study inclusion, mean±SD, (IQR 25th-75 th)	81±21 (64-94)	90±29 (68-116)	0.104
Percentage of patients with %pFVC<70 at study inclusion	25 (29.1%)	8 (26.7%)	0.805
%pDLCO at study inclusion, mean±SD, (IQR 25th-75 th)	59±15 (46.5-71)	63±20 (45-83)	0.361
Percentage of patients with %pDLCO<60 at study inclusion	47 (54.7%)	16 (53.3%)	0.790
Distance covered in 6MWT at study inclusion, mean± SD, (IQR 25th-75 th)	395±108 (352-450)	398±89 (358-450)	0.910
Need for cyclophosphamide treatment	10 (11.6%)	3 (10%)	0.808
Need for biologic therapy	32 (37.2%)	9 (30%)	0.477
Lung transplant	8 (9.3%)	4 (13.3%)	0.617
Development of type 3 PAH	8 (9.3%)	1 (3.3%)	0.443
Death	6 (7%)	9 (30%)	0.206



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