Background: Systemic sclerosis (SSc) carries a significant burden of disease-related morbidity and life-threatening complications. Unlike other rheumatic disorders (e.g., systemic lupus erythematosus and rheumatoid arthritis), the concepts of “disease activity” and “damage” have only recently been defined in SSc.

Objectives: We aimed to identify clinical and serological predictors of persistence of disease activity and remission in a monocentric prospective cohort of systemic sclerosis patients. Our second aim was to evaluate potential predictors of persistence or new onset of moderate-to-severe damage in our cohort.

Methods: Adult patients fulfilling the ACR/EULAR 2013 classification criteria for SSc and referring to our center from 2013 to 2021 were enrolled. Clinical findings, serological indices and internal organ involvement (pulmonary, cardiac, gastrointestinal, renal and musculo-skeletal) at baseline and at each visit during follow-up were retrospectively analyzed. At least one follow-up visit was required to be included in the study. EUSTAR-AI (European Scleroderma Trials and Research group Activity Index) [1], Medsger severity scale (MSS) [2] and SCTC (Scleroderma Clinical Trials Consortium) damage index [3] were calculated at each visit, at baseline and during follow-up. Follow-up period was defined as the time between baseline and the last available visit. Active disease was defined as an EUSTAR-AI ≥ 2.5, while remission as an EUSTAR-AI < 2.5; activity persistence was defined as an EUSTAR-AI ≥ 2.5 in more than 50% of follow-up visits. According to the literature, damage was classified as mild (SCTC damage index < 6) and moderate-severe (SCTC damage index ≥ 6).

Results: 173 SSc patients (87.9% females) were enrolled in our study and followed up for a median time of 3.5 years. The median disease duration at baseline was 9 years while the median age at diagnosis was 45 years; 34.6% of patients had diffuse cutaneous SSc. Patients with persistently active disease during follow up (12.2%) had at baseline a significantly higher frequency of diffuse cutaneous subset (34% vs 17%, p<0.001) and cardiac involvement (43.4% vs 20.7%, p=0.036) than persistently inactive patients; erythrocyte sedimentation rate (ESR) values were higher (p=0.002) and total lung capacity (TLC) values were lower (p=0.034) in persistently active patients. Positive antinuclear antibodies (ANA) were associated with persistent remission (p=0.042). Persistent disease activity was associated with higher disease severity [MSS 6.3 (s=3.5) vs 3.5 (s=1.7)], p<0.001 and more severe damage (SCTC-DI 3.7 (s=4) vs 1.3 (s=1.9), p<0.001) at baseline. At the multivariate analysis, ESR values (OR 1.04 95% CI 1.01-1.07) and MSS values at baseline (OR 1.75, 95% CI 1.29-2.37) were independent predictors of activity persistence. Patients with persistent or new onset of moderate-severe SCTC at the end of the follow up (9%) had more frequently telangiectasia (81.3% vs. 36.6%, p<0.001) and ILD (62.5% vs. 31.6%, p=0.013) at baseline than patients with mild damage; they also showed lower DLOC values (p=0.047) and lower TLC values (p<0.001), as well as higher systolic pulmonary arterial pressure (sPAP) on transthoracic echocardiography (p=0.0001) at baseline. Multivariate analysis showed that TLC values (OR 0.95, 95% CI 0.92-0.98) and telangiectasia (OR 4.7, 95% CI 1.18-18.54) were independent predictors of moderate-severe damage. An association was found between persistence of disease activity and moderate severe damage at the end of follow up (p<0.003).

Conclusion: Identifying predictors of disease activity persistence and damage accrual at baseline may help to improve the risk stratification of SSc patients, through the identification of those patients who require prompt treatment and a more thorough clinical follow-up.