According to observational studies conducted in last decades, mean survival of SSc patients had improved with significant changes in causes of death.

Objectives: To assess the 10-years survival in a large Italian multicentre cohort of SSc patients in the last decade compared to previous periods published since the 1980s, and to identify features that can justify any change.

Methods: We retrospectively analysed all medical records of our longitudinal SSc cohorts, fulfilling 1980 ARA and/or 2013 EULAR/ACR Classification Criteria, with a median (IQR) follow-up of 91.5 (51-120) months from 4 Scleroderma Units since January 2009. All clinical, laboratory and instrumental findings have been recorded and analysed. Survival rate was calculated with Kaplan-Meier curves and log-rank tests, and Cox proportional hazards models were used to identify any predictor. Then, observed SSc survival was compared to those previously published and to that expected in the general population, calculated using official data published on the website United Nation World Population Prospects (www.macrotrands.net/countries/ITA/italy/death-rate).

Results: Of 912 SSc patients (91.6% female; mean (SD) age at first non-Raynaud symptom (RS) 51 (15.4) years; median (IQR) disease duration from non-RS 24 (0-84.7) months) diffuse cutaneous involvement was defined in 182 (20%) patients. Anti-centromere and anti-topoisomerase-I were detected in 390 (42.8%) and 302 (33.1%) patients, respectively, while 220 (24.1%) presented antibodies for other extractable nuclear antigens. Prevalent non-Raynaud manifestations were interstitial lung disease detected in 459 (50.3%), digital ulcers in 395 (43.3%) and oesophagopathy in 371 (40.7%) patients, respectively, while other gastrointestinal manifestations were reported in 234 (25.7%) patients. Chronic renal failure was observed in 61 (6.7%) patients and pulmonary arterial hypertension (PAH) was confirmed at right heart catheterization in 38 (4.2%) patients. Three hundred twenty-two (35.3%) patients received immunosuppressant, 215 (23.5%) assumed an endothelin receptor antagonist and/or a 5-phosphodiesterase inhibitor, and 72 (7.9%) were treated with a biologic agent. The global 10-years survival was 89.4%; female gender (HR 0.33, CI95% 0.17-0.67), diffuse cutaneous involvement (HR 2.14, CI95% 1.17-3.91), presence of pulmonary hypertension (HR 2.61, CI95% 1.31-5.16) and older age at non-RS (HR 1.1, CI95% 1.06-1.12) affected survival. Furthermore, as compared to previous Italian studies, our cohort showed a significant improvement in rate (see Figure 1).

Conclusion: Survival in SSc patients has improved in last 5 decades but still reduced compared to that expected in general population above all 5 years after diagnosis. Early diagnosis, with reduced renal involvement, along with better screening and innovative therapeutic strategies may explain these achievements.

Figure 1. Ten-years survival in SSc patients since 2009 (left); comparison of survival across different Italian SSc cohorts (box: current analysis) (right).

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POS0892

QUANTITATIVE CT INDEXES: PROMISING TOOLS FOR OBJECTIVE ASSESSMENT OF PULMONARY FIBROSIS IN SYSTEMIC SCLEROSIS

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Background: Pulmonary fibrosis (PF) occurs in the majority of patients with SSc and is a leading cause of SSc-related death. SSc related PF has heterogeneous disease progression: many patients will have a chronic, indolent course while others may develop the progressive, life-threatening disease.

Objectives: The objective of this study is to investigate the discrimination performance of quantitative CT indexes in identifying the parenchymal differences between the SSc and the control groups. We also aimed to demonstrate the

correlation among quantitative indexes (QI), spirometric pulmonary function tests, and visual CT scores in patients with PF.

Methods: A total of 135 SSc patients (female 87.4%; age, 50±13 years), 41 of whom had pulmonary fibrosis (PF), and 38 healthy subjects (female 89.5%; age, 52±6 years) were enrolled. All participants underwent volume thin-section CT in the supine position at full inspiration and spirometry. Quantitative indexes (QIs) were obtained using dedicated software for the segmentation of the lung (Vital Images Vitrea Workstation; Version 7.12.3.133). QIs included total lung volume (TLV), low attenuation (LA) volume (-1020 HU<pixel<-920 Hounsfield units [HU]), medium attenuation (MA) volume (-920 HU<pixel<-0 HU), and high attenuation (HA) volume (-720<pixel<0 HU). The global extent of pulmonary parenchymal abnormality was measured semiquantitatively by visual scoring (VS) and functional lung volume was derived. The functional lung volume, total MA volume, and ratio of total MA to total lung volume were assumed as the indexes of normal lung parenchyma.

Results: MA volumes, HA volumes, total lung volumes and the ratio of MA volume to total lung volume differed significantly between the patients with PF, patients without PF, and the control group. In the PF group, FVC showed significant correlation with functional lung volume ($r=0.45$, $p=0.014$) and total MA volume ($r=0.48$, $p=0.009$); DLCO showed significant correlation with VS of normal lung parenchyma ($r=0.65$, $p<0.001$), functional lung volume ($r=0.53$, $p=0.006$), total MA volume ($r=0.54$, $p=0.005$) and ratio of total MA to total lung volume ($r=0.42$, $p=0.031$). The functioning lung volume obtained by VS and total MA volume showed excellent correlation ($r=0.78$, $p<0.001$).

Conclusion: Quantitative indexes measured by soft-ware differentiated the patients with PF from the patients without PF and healthy subjects. The indexes used to evaluate the normal lung parenchyma showed a good correlation with pulmonary function test results. Quantitative indexes can be used as an objective complementary tool for the evaluation of the lung areas unaffected by PF.

Table 1. Quantitative Indexes of CT in the Control, SSc without PF and SSc with PF Groups

	Control	SSc without PF	SSc with PF	p
Right lung LA volume (ml)	372±375	420±446	254±308	0.102
Right lung MA volume (ml)	1230±408	1377±441	987±451	<0.001
Right lung HA volume (ml)	531±152	494±177	625±215	0.004
Left lung LA volume (ml)	342±370	367±383	221±271	0.089
Left lung MA volume (ml)	1014±383	1170±433	805±402	<0.001
Left lung HA volume (ml)	563±176	516±251	620±289	0.037
Total lung LA volume (ml)	712±736	827±959	517±653	0.119
Total lung MA volume (ml)	2212±863	2548±862	1756±850	<0.001
Total lung HA volume (ml)	1072±343	1009±406	1290±522	0.005
Total lung volume (ml)	3996±1237	4385±1256	3563±1236	0.002
Mean lung density (HU)	-799±61.4	-798±63	-730±75	<0.001
Total MA volume/Total lung volume	0.55±0.12	0.59±0.13	0.49±0.15	0.002

Figure 1. Segmentation of lung parenchyma

Disclosure of Interests: None declared

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POS0893

NON-INVASIVE CUTANEOUS ASSESSMENT OF SYSTEMIC SCLEROSIS- THE NEW OUTLOOKS

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Background: Systemic sclerosis (SSc) is a rare connective tissue disease with abnormalities in vasculopathy, immune dysregulation and fibrosis resulting in skin and internal organ damages. Severity of skin involvement is known to correlate with organ-related mortality in particular pulmonary involvement. Variables skin assessment tools are available, modified Rodnan Skin Score (mRSS) is currently best validated and used widely. The immediate action of finding an ideal,

clinically convenient objective methods is crucial to better clinicians' care for SSc patents.

Objectives: Explore the potential of commercially available handheld, non-invasive devices for SSc skin analysis.

Methods: 1.Measure skin surface Adenosine Triphosphate (ATP) level with handheld ATP bioluminator (SystemSURE Plus, Hygiene) over the forearm of SSc(n= 51) and controls (n=50) 60seconds after sterilization to eliminate extrinsic factors. The bioluminometer expresses ATP test results in Relative Light Units (RLU) that is directly proportional to the amount of ATP on the test sample (Unit conversion: 1RLU = 1fM).

2.In-vivo Raman Spectra measurement of SSc skin comparing with matched healthy controls on proximal phalangeal, area between 2nd and 3rd metacarpal and forearm. Our measurements include laser power of 250mw, excitation length of 785nm and spectral range from 500 to 2800cm⁻¹. Measurements were analysed with patients' phenotypes and clinical characteristics.

Results: Flow cytometry showed increase expression of P2X7 (purinergic) receptor and CD206 in M2-Macrophage in SSc compare to controls [(724.4 vs 472.9, 776.1 vs 632.2)]. CD206 expression positively correlated with P2X7 levels (p<0.001, r²=0.76) and mRSS (p<0.05, r²=0.26). In real life scenario, measurement of purinergic metabolites is laboratorial tedious. ATP bioluminator measurement reviewed significant higher skin surface ATP in SSc than controls (188fM ± 53 [95% CI = 84, 300] vs 44fM ± 6 [95% CI = 33, 56], p< 0.003). And the intensity is negatively correlate with duration of disease in SSc (r = - 0.25, p = 0.096).

We obtain Raman spectra in SSc patient and control. Our study both groups have similar Raman curve when Raman Spectrometry were performed on skin surfaces. However, the relative intensity of each peaks of the curve were overtly flatter in SSc. This finding were similar for both Limited and Diffuse SSc in gross review of the graph representative. In addition to that, our analysis reviewed a peak at Raman shift of 2410cm⁻¹ that is characteristically present in forearm of a SSc but not in controls (Figure 1). Its significant yet to be determined.

Conclusion: Both ATP bioluminator and Raman Spectrometry is widely available commercially which are widely used in industrial, agriculture and cosmetology and dermatology in particular for Raman Spectrometry. It is commonly for assessing physically property of skin, determine drug administration and diagnosis of variable skin condition in particular cancer diagnosis. The advantages of these tools in SSc skin analysis include:

- 1.Non-invasive nature of skin analysis (compares to skin biopsy),
 - 2.Portable devices easily mobilized in clinic setting,
 - 3.Advanced technology allows molecular analysis of skin hence able to objectively classify grades of skin inflammation and determine drug efficacy
 - 4.Possible better accuracy compares to other methods (eg. Ultrasound) which are operators dependent,
 - 5.Widely available Raman signal database of different types of chemical compounds and expertise made the collection and analysis of date convenient
- Our study has provide preliminary outlook and idea of utilizing commercially available devices on skin analysis in SSc. Further study in larger cohort are to be considered.

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POS0894

ANTI-IL-6 THERAPY EFFECT FOR REFRACTORY JOINT AND SKIN INVOLVEMENT IN SYSTEMIC SCLEROSIS: A REAL-WORLD, SINGLE CENTER EXPERIENCE

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Background: Emerging evidence during the last two decades supports a pivotal role of Interleukin 6 (IL-6) in the pathogenesis of Systemic Sclerosis (SSc). Standard immunosuppressive agents are often inadequate to control disease activity in SSc patients and treatment failure of multiple regimens is frequent in real-world practice.

Objectives: To examine the efficacy and safety of interleukin-6 receptor inhibition by tocilizumab in selected real-world patients with SSc.

Methods: Twenty-one patients (20 women, 16 diffuse SSc, mean age: 52±10 years, mean disease duration: 6.4±3.7 years, all with negative rheumatoid factor and anti-cyclic citrullinated antibodies, none with overlap syndrome with RA) with active joint and skin involvement refractory to corticosteroids (n=21), methotrexate (n=17), cyclophosphamide (n=10), mycophenolate (n=7), rituximab (n=1), leflunomide (n=2), hydroxychloroquine (n=2), and hematopoietic stem cell transplantation (n=2) who received weekly tocilizumab (162 mg subcutaneously) in an academic center, were monitored prospectively. Changes in Eustar modified activity index (MAI), modified Rodnan skin score (mRSS), disease activity score (DAS)28, lung function tests (LFTs) and patient reported outcomes (PROs) were analyzed at one year of treatment and at the end of follow-up.

Results: One patient discontinued tocilizumab after 3 months due to inefficacy. During the first year of treatment, 12 patients achieved low disease activity (mean MAI change -2.9±1.8, p<0.001) and significant clinical improvement was evident in 12 patients regarding skin involvement (mean mRSS change: -6.9±5.9, p<0.001) and in 16 patients regarding polyarthritis (mean DAS28 change: -1.9±0.8, p<0.001); Accordingly, improvements were recorded for all PROs (all p<0.001) (Table 1). Lung function tests' stabilization was also observed in 16/20 patients. During the second year, 3 patients discontinued tocilizumab (cytomegalovirus infection in 1, inefficacy in 2) and one died. Beneficial effects were sustained in all 16 patients at follow-up end (mean duration of Tocilizumab treatment 2.2 ± 1.1 years), apart from LFTs deterioration in 3. Except for recurrent digital ulcer infection in 3 patients, tocilizumab was well-tolerated.

Conclusion: Tocilizumab was effective in refractory joint and skin involvement irrespective of SSc disease duration or subtype. Long-term retention rates and disease stabilization for most real-world patients suggest that tocilizumab might be a valuable choice for difficult-to-treat SSc.

Table 1. Clinical and laboratory parameters and measures (mean ± SD) at baseline and after one year of treatment with tocilizumab in 20 patients with Systemic Sclerosis

	Baseline	1 st year	change	p
Modified activity index	4.9 ± 1.6	2.0 ± 1.2	-2.9 ± 1.8	<0.001
mRSS	21.5 ± 9.5	14.6 ± 6.6	-6.9 ± 5.9	<0.001
DAS28	5.3 ± 0.7	3.4 ± 0.6	-1.9 ± 0.8	<0.001
FVC (% of predicted)	82 ± 19.5	79 ± 19.1	-2.9 ± 12	0.389
DLCO (% of predicted)	60.4 ± 16.3	61.1 ± 18.4	0.7 ± 12.3	0.844
ESR (mm/1 st hr)	35.6 ± 17.2	12.9 ± 11.8	-22.8 ± 19.1	0.001
CRP (mg/l)	13.2 ± 12.5	1.2 ± 2.1	-12 ± 13.1	0.006
SHAQ	1.6 ± 0.8	1.0 ± 0.7	-0.6 ± 0.5	<0.001
VAS	37.8 ± 16.8	60.5 ± 15.4	22.7 ± 20.3	<0.001
VAS patient global score	33.4 ± 13.2	63.2 ± 13.9	29.8 ± 15.6	<0.001

mRSS: modified Rodnan skin score; DAS28: disease activity score 28; FVC: forced vital capacity; DLCO: diffusing lung capacity for carbon monoxide; ESR: erythrocyte sedimentation rate; CRP: c-reactive protein; SHAQ: scleroderma health assessment questionnaire; VAS: visual analogue scale

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