Table 1. Pharmacokinetics and GI score with MMF in combination with PPI / HRB

	MMF	MMF+ R	MMF + E	p
AUC mean (95% CI)	67.97 (62.73, 73.20)	53.04 (44.80, 61.27)	45.69 (41.10, 50.28)	<0.001*
T- MAX mean (95% CI)	42.00 (33.60, 50.40)	46.50 (32.48, 60.52)	79.50 (58.99, 100.01)	<0.001*
C-MAX mean (95% CI)	29.61(26.74, 32.48)	15.14 (11.32, 18.97)	12.62 (10.58, 14.66)	<0.001*
Mean GI score mean (95% CI)	0.28 (0.15,0.40)	0.19 (0.09, 0.30)	0.14 (0.06,0.23)	0.009

AUC, area under curve Mycophenolic acid; C-MAX, maximum concentration of MPA in 12 hours following MMF; CI confidence interval;Mean GI score, UCLA Scleroderma Clinical Trial Consortium GIT 2.0 scoring; MMF, mycophenolate mofetil; MMF+E, mycophenolate mofetil + esomeprazole; MMF+R, mycophenolate mofetil+ ranitidine;*p value < 0.05 considered as significant

Conclusion: As co administration of PPI or HRB can significantly reduce the bio-availability of MMF in patients with systemic sclerosis. To avoid therapeutic failure of MMF drug level monitoring is essential when these agents re prescribed with MMF.

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POS0890 MACROVASCULAR DYSFUNCTION AND ITS CLINICAL IMPLICATION IN SYSTEMIC SCLEROSIS

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Background: Even though microvascular dysfunction has been implicated in pathogenesis of scleroderma (SSc), there is minimal evidence to suggest presence of macrovascular dysfunction. The clinical implication of macrovascular dysfunction in SSc is unknown. Moreover, data on the correlation between dysfunction in small and large blood vessel is inconclusive. [1-2]

Objectives: To study the correlation between macrovascular dysfunction as assessed by percent change in flow mediated vasodilation (FMD) of brachial artery and microvascular dysfunction as assessed by nail fold capillaroscopy (NFC) findings in SSc. To assess the clinical impact of macrovascular dysfunction.

Methods: This cross-sectional comparative study enrolled patients with SSc and age and gender matched healthy controls. FMD change was calculated using standard USG probe of 5 to 6 MHz in right brachial diameter from the average of 3 consecutive end diastolic frames. NFC was performed using portable nail fold capillary microscope at 800X magnification. Clinical features of SSc were compared between SSc patients with and without macrovascular dysfunction.

Results: This study enrolled 59 SSc patients including 29 (49.2%) diffuse, 20 (20.4%) limited, 08 (10.2%) sine SSc and 2 patients (3.4%) with myositis overlap. SSc patients had significantly (p-<0.0001) lower % FMD change compared to healthy controls. NFC showed significantly higher architecture distortion (p-<0.0001), loss of capillaries (p-<0.0001) and abnormal capillaries (p-<0.0001). There was no correlation between FMD change and capillary density (p-0.381), avascular area (p-0.266) and abnormal capillaries (p-0.899). None of the clinical features like pulmonary hypertension, digital ulcer burden, acro-osteolysis and auto amputation were different between SSc with and without macrovascular dysfunction.

Conclusion: Macrovascular dysfunction in SSc is substantial and it seems to be independent of the microvascular dysfunction. The clinical implications of macrovascular dysfunction are yet to be identified.

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Table 1. Comparison of various parameters between the SSc patients with healthy controls.

Parameter	Frequency (percentage)/median (interquartile range)	
	SSc patients (n=59)	Healthy controls (n=64)
Demographic details		
Age in years	38 (27-46)	36.5 (28.25-42)
Gender		
Male	03 (5.1%)	03 (4.7%)
Female	56 (95.1%)	61 (95.3%)
FMD findings		
FMD % change*	4.54 (3.13-8.82)	10.30 (8.33-13.16)
NFC findings		
Number of capillaries*	51 (38-63)	121 (113-128)
Average capillary density*	3.19 (2.38-3.94)	7.56 (7.06-8)
Disorganized architecture (%)*	37.5 (12.5-37.5)	0
U shape (%)*	50 (36.59-68.09)	85.51 (82.97 – 88.53)
Abnormal (%)*	36.11 (14.03-55.26)	0
Enlarged (%)*	10.63 (2.94-23.68)	0
Giant (%)*	21.05 (0-45.45)	0
Microhemorrhages (%)*	6.25 (0-12.5)	0
Neoangiogenesis (%)*	3.85 (0-20)	0
Avascular area (%)*	50 (31.25- 75)	0

*parameters with statistically significant (p value< 0.0001) difference among two groups. SSc; Systemic Sclerosis, FMD; flow mediated vasodilatation, NFC; nail fold capillaroscopy

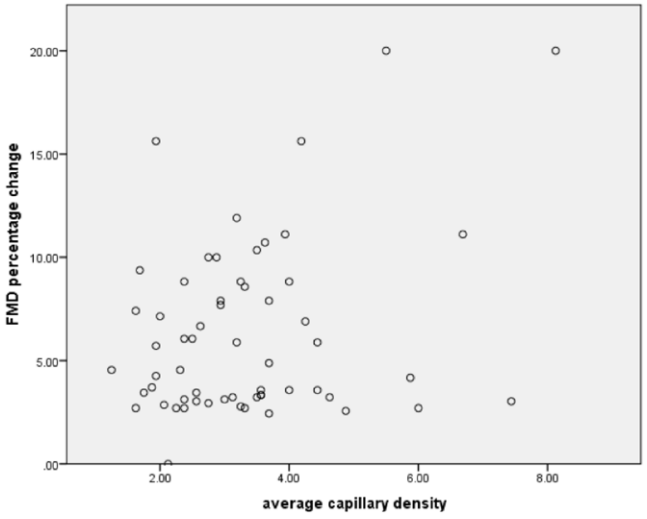

Figure 1. Scatter plot showing correlation between FMD percentage change and average capillary density. (r= 0.116) (P-value - 0.381)

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POS0891 IMPROVED SURVIVAL IN SYSTEMIC SCLEROSIS PATIENTS DURING LAST DECADE: CURRENT FINDINGS AND COMPARISON WITH DIFFERENT PREVIOUS ITALIAN COHORTS

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Background: Systemic Sclerosis (SSc) is a chronic rheumatic disease characterized by an autoimmune disorder with vasculopathy that leads to an excess in collagen and other extracellular matrix proteins deposition. This process results in progressive fibrotic and vascular damage of skin and visceral organs.

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.macrotrends.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 extractible 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.

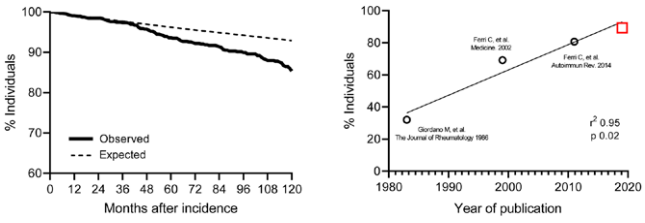

Figure 1. Ten-years survival in SSc patients since 2009 (left); comparison of survival across different Italian SSc cohorts (box: current analysis) (right).

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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<-920 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

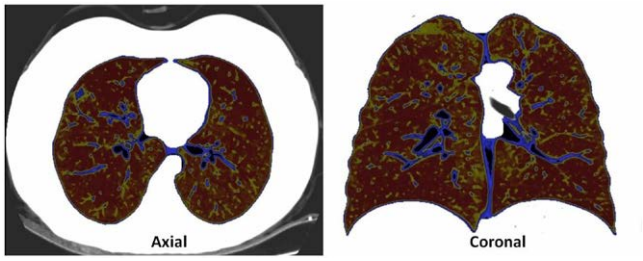

Figure 1. Segmentation of lung parenchyma

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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,