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SAT0319

SUBCLINICAL ATHEROSCLEROSIS IN INDIAN PATIENTS WITH SCLERODERMA – CLINICAL AND SEROLOGICAL ASSOCIATIONS

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Background: Scleroderma has been associated with increased risk of cardiovascular events, however, studies on this from India are sparse. We evaluated clinical and serological factors associated with subclinical atherosclerosis in Indian patients with scleroderma, in a cross-sectional design.

Objectives: To compare carotid intima-medial thickness (CIMT, mean value of both carotids) as a measure of subclinical atherosclerosis (SCA) between patients with scleroderma (n=61) fulfilling 2013 ACR/EULAR criteria, and healthy controls (n=41).

- To compare clinical (body mass index – BMI, waist-hip ratio – WHR, fasting lipid profile) and serological factors (microparticles, endothelial microparticles, inflammatory cytokines associated with increased cardiovascular risk) between patients with scleroderma and healthy controls.

- To identify factors associated with SCA in scleroderma patients.

Methods: Subclinical atherosclerosis (SCA) was defined by presence of carotid plaques, or increased CIMT >2 standard deviations compared with Indian reference standards for age and sex. Total microparticles (TMP) were measured of plasma after ultracentrifugation as per previously described protocol using microbeads of 3 µm size (TMP were of size 0.1-1 µm); of these, microparticles positive for CD31 and CD142 were endothelial microparticles (EMP). Serum cytokines (IL-1, IL-6, TNF-α, IL-17) were measured by ELISA using manufacturer instructions. Linear regression was used to identify the determinants of CIMT in scleroderma. Binomial logistic regression was used to identify factors associated with subclinical atherosclerosis in scleroderma.

Variable	Patients with scleroderma (n=61)	Healthy controls (n=41)	p value
Age	37.8 ± 11.92	35.37 ± 6.69	0.2375
Gender (M:F)	11:50	6:35	0.6516
Diabetes/Hypertension/Tobacco use	1/2/0	0/0/0	NS
Body mass index (kg/m ²)	20.11 ± 3.82	24.38 ± 4.45	<0.0001
Waist-hip ratio	0.86 ± 0.11	0.89 ± 0.07	0.1251
Total cholesterol (mg/dL)	142.5 ± 30.7	147.3 ± 39.5	0.4948
Triglycerides (mg/dL)	99.4 ± 37	121.4 ± 46	0.0087
HDL cholesterol (mg/dL)	46.9 ± 4.9	46.1 ± 4.2	0.4029
LDL cholesterol (mg/dL)	93.6 ± 10.5	93.3 ± 7.5	0.8520
VLDL cholesterol (mg/dL)	19.9 ± 7.4	24.7 ± 9.7	0.0057
Carotid intima-medial thickness (mm)	0.68 ± 0.10	0.53 ± 0.03	<0.0001
Total microparticles (per ±L)	12913 ± 2493	6272 ± 1533	<0.0001
Endothelial microparticles (per ±L)	2623 ± 1032	829 ± 439.5	<0.0001
Serum IL-1± (pg/mL)	38.19 ± 13.46	31.38 ± 18.29	0.0326
IL-6 (pg/mL)	176.6 ± 85.74	128.9 ± 53.61	0.0020
IL-17 (pg/mL)	56.3 ± 20.45	53.89 ± 20.51	0.5611
TNF± (pg/mL)	49.65 ± 26.71	42.09 ± 30.41	0.1879

Results: Despite lower BMI, triglycerides and VLDL cholesterol, CIMT was significantly higher in patients with scleroderma. Patients with scleroderma had significantly higher total microparticles and endothelial microparticles in plasma, and serum IL-1± and IL-6 (Table 1). On multivariable regression, age was the only significant determinant of CIMT. 28 (45.9%) patients had SCA; 13 (21.3%) had carotid plaques. Patients with SCA had higher proportion of males (9/28 in

those with SCA vs 2/33 in those without SCA). Binomial logistic regression did not identify any other significant predictors of SCA.

Table 1. Comparison between patients with scleroderma and healthy controls

Serum IL-1± (pg/mL)	38.19 ± 13.46	31.38 ± 18.29	0.0326
IL-6 (pg/mL)	176.6 ± 85.74	128.9 ± 53.61	0.0020
IL-17 (pg/mL)	56.3 ± 20.45	53.89 ± 20.51	0.5611
TNF± (pg/mL)	49.65 ± 26.71	42.09 ± 30.41	0.1879

Conclusion: Patients with scleroderma had significant burden of subclinical atherosclerosis, which could not be explained by traditional or novel cardiovascular risk factors.

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SAT0320

BONE MINERAL DENSITY AND FRACTURE RISK IN A COHORT OF PORTUGUESE SYSTEMIC SCLEROSIS PATIENTS

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Background: Although poorly understood, patients with Systemic Sclerosis (SSc) seem to have higher prevalence of low bone mineral density (BMD) and an increased spine fracture risk.

Objectives: We aim to determine, by conventional densitometry (DXA) and using the fracture risk assessment tool (FRAX), the prevalence of low BMD and the fracture risk, respectively, in our SSc cohort and its potential determinants.

Methods: Observational transversal study was performed including consecutive patients with the diagnosis of SSc. We collected data regarding demographics, BMD (lumbar spine and femoral neck) and occurrence of fracture. Ten-year risk of osteoporotic fracture was estimated using FRAX v4.1 with the Portuguese population reference. Statistical analysis was performed using SPSS 23.0; p<0.01 was considered statistically significant.

Results: Median age of patients (n=97) was 62 years old [56, 70], 88.7% females (n=86). Seventy-eight patients (80.4%) had limited cutaneous form, 5 (5.2%) presented a diffuse cutaneous form and 13 (13.4%) an overlap syndrome. Regarding clinical features: digital ulcers in 30 patients (30.9%), interstitial lung disease (ILD) in 16 (6.5%), gastrointestinal involvement in 16 (16.5%), myositis in 4 (4.1%) and pulmonary arterial hypertension in 3 (3.1%). Anti-topoisomerase I antibody (anti-Scl70) positivity was present in 15 patients (15.5%) and anti-centromere antibody (ACA) positivity in 63 (64.9%). Nine patients (9.3%) were smokers and 6 (6.2%) reported an alcohol consumption of 3 or more units/day. Median body mass index (BMI) was 25.4 Kg/m² [21.4, 29.1], with 5 patients (5.2%) being underweight. Vitamin D insufficiency was reported in 19 patients (19.6%). Twenty-one patients (21.6%) have been exposed to oral glucocorticoids (GCT) for more than 3 months at a dose of 5mg daily or more. Eleven patients (11.3%) had previous low impact fractures: 10 of which were vertebral and 1 wrist fracture. Regarding the prescribed anti-osteoporotic treatment (AOP), we found: alendronate (n=7, 7.2%), zoledronic acid (n=7, 7.2%), denosumab (n=2, 2.1%) and teriparatide (n=1, 1%).

Low BMD was present in 45 patients (46.4%); median femoral neck BMD (FN-BMD) was 0.827 [0.709, 0.893]. Ten-year probability of fracture (%) was: median risk for major fracture was 5.1 [3.5, 9.7] and 3.8 [2.5, 8], with and without FN-BMD, respectively; for hip fracture the estimated risk was 1.2 [0.6, 3.1] and 1.0 [0.4, 2.5], with and without FN-BMD, respectively. According to FRAX thresholds for the Portuguese population, 25 patients (25.8%) met criteria to start AOP treatment. Among them, only 10 patients (40%) started it, as the agreement between the indication to treat by FRAX and the onset of treatment was weak (k=0.338). A strong agreement was found between FRAX risk threshold with DXA and World Health Organization (WHO) threshold for starting AOP (k=0.814) and no agreement was found between FRAX risk without DXA and WHO threshold. FN-BMD presented a weak correlation with BMI (r = 0.393), a moderate inverse correlation with major fracture risk with and without FN-BMD (r = -0.704,

$r = -0.412$, respectively) and with hip fracture risk with and without FN-BMD ($r = -0.799$, $r = -0.412$, respectively). Major fracture risk with and without FN-BMD presented a moderate correlation with spine fractures ($r = 0.350$; $r = 0.397$, respectively).

No correlation was found between WHO threshold and spine fractures. No correlations were found between FN-BMD or fracture risk estimated by FRAX and disease manifestations, anti-Scl70 or ACA positivity, vitamin D insufficiency, smoking or GCT use.

Conclusion: In our cohort, low BMD was prevalent and had correlation with BMI. FRAX appears to be an useful instrument as it correlated with spine fractures, contrary to what was verified when we used the WHO threshold. Early monitoring of BMD and estimating fracture risk using FRAX appear to be useful tools for the prevention of fractures in this population.

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SAT0321

CURRENT PATIENT REPORTED OUTCOMES (PROS) POORLY REFLECT CHANGES IN LUNG FUNCTION IN PATIENTS WITH SYSTEMIC SCLEROSIS

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Background: Lung involvement is very common in systemic sclerosis (SSc). Approximately one quarter of patients develops pulmonary problems within the first 3 years of diagnosis and still represents the leading cause of death in these patients. In a recent clinical trial, the reduction of FVC was not accompanied by a benefit with respect to health-related quality of life and patient-reported outcomes (PROs).

Objectives: To assess how the change in Pulmonary Function Test (PFTs) parameters correlates with the Patient Reported Outcomes (PROs) in an observational cohort of patients with Systemic Sclerosis (SSc).

Methods: We conducted a retrospective study of 330 clinic episodes from 121 unselected patients diagnosed with systemic sclerosis according to EULAR/ACR 2013 criteria, in annual follow-up (for a total of 165 patients/year) with PFTs, Health Assessment Questionnaire Disability Index (HAQ-DI), Scleroderma Health Assessment Questionnaire (sHAQ), Modified Borg Dyspnea Scale (Borg) and Cochin Hand Function Score (CHFS). We assessed the correlation between the HAQ and the Visual Analogical Scale 1-7 at baseline (VAS1 pain, VAS2 disease severity, VAS3 arthritis activity, VAS4 intestinal problems, VAS5 dyspnea, VAS6 Raynaud's phenomenon, VAS7 digital ulcers). We evaluated the correlation of PFTs with PROs at every time period and the correlation between the change of PFTs parameters (δ FVC, δ DLCO) with the change of the PROs over a year of follow-up. Following analysis of distribution, Spearman or Pearson Test were used to determine correlation coefficients, as appropriate (Prism 7).

Results: The median disease duration was 5 years (IQR 3-10). The median of 12 months δ FVC% and δ DLCO% were 0 (IQR -5.81 to 3.28) and -2.439 (IQR -8.76 to 5.98), respectively. The analysis evidenced a strong positive correlation between VAS1-7 and HAQ. We observed also significant correlation between FVC%, DLCO% and HAQ-DI ($r = -0.355$ and -0.266 , respectively; $p < 0.0001$ for both), Borg ($r = -0.403$ and -0.379 , respectively; $p < 0.0001$) and CHFS ($r = -0.355$ and -0.256 , respectively; $p < 0.0001$). Nevertheless, in longitudinal setting there was no significant correlation between δ PROs and changes lung function, as continuous variables, neither there was any significant PROs difference in patients that did or did not lose more than 10% of FVC and DLCO over a year of follow-up.

Conclusion: This analysis of a monocentric non-selected population evidenced that the current commonly used PROs in SSc while showing a good correlation with lung function are poorly sensitive to change or to reflect changes in lung function over 12 months. In this sense, prudent interpretation of the lack of correlation between FVC and patient-reported outcomes in studies of phase 3 is warranted.

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SAT0322

PREVALENCE AND RISK FACTORS FOR LEFT VENTRICULAR DIASTOLIC DYSFUNCTION IN SYSTEMIC SCLEROSIS: RESULTS FROM RESCLE REGISTRY

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Background: Left ventricular diastolic dysfunction (LVDD) is a very common finding in heart involvement in Systemic Sclerosis (SSc).

Objectives: To determine the prevalence, risk factors and mortality associated with LVDD in a cohort of patients with SSc.

Methods: A retrospective study was conducted with data from the multicentre Spanish Scleroderma Registry (RESCLE). A case-control study was performed to identify factors associated with LVDD.

Results: Out of 1517 cases of SSc, 319 (21%) developed LVDD. Basal characteristics are shown in Table 1. In multivariate analysis, LVDD was associated to older age at diagnosis of SSc [54 vs 44 years, OR 1.05 (1.04-1.06)], presence of telangiectasia [67 vs 59%, OR 1.42 (1.88-1.08)], and treatment with calcium channel blockers [50 vs. 45%, OR 1.55 (1.16-1.96)], and inversely correlated to treatment with ACE inhibitors [74 vs. 83%, OR 0.59 (0.44-0.8)]. Mortality was increased in patients with LVDD (24 vs 17%, OR 1.4, $p = 0.01$). Kaplan-Meier cumulative survival for the SSc cohort, according to the presence or absence of LVDD showed significant differences in 30 years from the first SSc symptom (59 vs. 70%, $p = 0.04$).

Table 1.

Number of patients	1517	319 (21%)	1198 (79%)	P
Limited SSc	923 (61%)	201 (63%)	722 (60%)	0.438
Diffuse SSc	304 (20%)	51 (16%)	253 (21%)	0.041
Sine Scleroderma SSc	174 (11%)	47 (15%)	127 (11%)	0.048
Age at disease onset (years) med±SD	46.4±16.5	54.1±15.9	44.5±16.1	<0.001
Arterial hypertension	491 (33%)	148 (48%)	343 (30%)	<0.001
Digital ulcers	615 (41%)	108 (34%)	507 (42%)	0.006
Telangiectasia	918 (61%)	212 (67%)	706 (59%)	0.011
Interstitial lung disease	645 (43%)	153 (48%)	492 (41%)	0.021
Pulmonary hypertension	139 (9.2%)	34 (11%)	105 (8.8%)	0.325
Capillaroscopy Slow pattern	673 (51%)	130 (46%)	543 (53%)	0.038
Centromere Antibodies	679 (49%)	154 (55%)	525 (48%)	0.032

Conclusion: In our cohort, LVDD is relative common in SSc patients, and it is associated with older age at diagnosis, treatment with calcium channel blockers and telangiectasia. ACE inhibitors could play a protective role against the development of LVDD. Mortality is higher in SSc patients with LVDD, and is more significative over time.

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