Efficacy of rituximab in treatment naive PSS related ILD patients needs to be studied.

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AB0634 RITUXIMAB IN SYSTEMIC SCLEROSIS-INTERSTITIAL LUNG DISEASE, A CASE SERIES OF 18 PATIENTS

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Background: Interstitial lung disease (ILD) is a severe complication of systemic sclerosis (SSc). Immunosuppressives such as cyclophosphamide (CYC) and mycophenolate mofetil (MMF) are used in its treatment with no proven efficacy (1). Rituximab (RTX) appears to be an emerging agent according to case series.

Objectives: This retrospective study aims to evaluate the efficacy of RTX on SSc-ILD in a group of patients followed in our center.

Methods: A chart review revealed 18 patients (16 women, 2 men; mean age 50.3±12.1 SD years (range 30–72), mean disease duration 8.3±9.3 SD years) with SSc who have been diagnosed as having ILD (confirmed by high-resolution thorax computed tomography and pulmonary function tests) and have been treated with one or more cycles of RTX. Efficacy was evaluated according to the criteria of the American Thoracic Society: improvement= an increase in FVC≥10% or DLCO≥15%; worsening= a decrease in FVC≥10% or DLCO≥15%; stabilization= changes in FVC less than 10% or DLCO less than 15% (2).

Results:

Table 1 Demographic findings of the patients and their response to RTX treatment

	Group 1 (ILD with short duration and naive to treatment)	Group 2 (ILD with long duration and previous IS therapy)	All patients
Number of patients	4 (22.2%)	14 (77.7%)	18
Sex (F/M)	3/1	13/1	16/2
Mean disease duration	2±0.8 SD years	10.2±9.8 SD years	8.3±9.3 SD years
Follow-up time after initiation of RTX	12.2±6.8 SD months	21±12.4 SD months	19±11.8 SD months
Baseline FVC%	69.2±20.9	65.1±14	
Last FVC%	66.7±13	61.6±19.6	
Baseline DLCO%	57.7±24.1	43.5±12.2	
Last DLCO%	52±18	41.2±21.8	
Outcome: Stable/ Improvement (n)	2	7	9
Worsening (n)	2	5	7
Death	0	1	1
Unable to do PFT (n)	0	1	1

Four patients were treatment naive for ILD when they received RTX (Group 1). The mean duration between the diagnosis of ILD and RTX treatment in Group 1 was 3.5 months (range 0–14 months). The average RTX cycle in this group was 2 with 1 patient also receiving mycophenolate mofetil in combination with RTX. The mean follow-up time after the initiation of RTX in this group was 12.2±6.8 SD months (range 7–22 months). FVC/DLCO was stable or improved in 2/4 compared to baseline and worsened in 2/4 at the end of follow-up at group 1. Fourteen patients had a 10.2 years-history of SSc and have been treated with immunosuppressives (cyclophosphamide, azathioprine, methotrexate, MMF) for ILD before RTX (Group 2). The mean duration between the diagnosis of ILD and RTX treatment in Group 2 was 71.2 months (range 5–246 months). These patients received a mean of 3 cycles of RTX with 5 receiving MMF (n=3) or AZA (n=2) in addition to RTX. One patient died after 3 months following the first RTX cycle (unknown reason) and 1 was unsuitable for spirometry because of microstomia. Of the remaining 12 patients in Group 2, improvement or stabilisation was seen in 7 and worsening was seen in the remaining 5 patients.

Conclusions: RTX appears to be modestly effective for ILD of SSc. The duration

of ILD as well as the presence or absence of previous immunosuppressive therapy do not appear as playing a role in response.

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AB0635 THE CLINICAL FEATURES AND PROGNOSIS OF PULMONARY ARTERIAL HYPERTENSION ASSOCIATED WITH SCLERODERMA AND OTHER CONNECTIVE TISSUE DISEASE DURING THE MODERN MEDICAL ERA IN JAPAN

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Background: Due to the recent progress of vasodilators for pulmonary arterial hypertension (PAH), the prognosis of PAH has been getting better for the past 10 years. Among them, idiopathic PAH (IPAH) well improved but PAH associated with connective tissue disease (CTD-PAH) especially scleroderma (SSc-PAH) have poorer prognosis than IPAH.

Objectives: This study intended to clarify the clinical features and prognosis of CTD-PAH in modern era when multiple PAH drugs are available, in addition, compare between SSc-PAH and PAH associated with other CTD-PAH (non SSc-PAH).

Methods: Fifty-seven consecutive CTD-PAH patients were enrolled to this study, who received hemodynamic examination with right heart catheterization between 2004 and 2016. Thirty of 57 patients were SSc-PAH patients and other 27 patients were non SSc-PAH patients (11 mixed connective tissue disease, 8 systemic lupus erythematosus, 5 primary sjogren syndrome, 1 polymyositis, 1 rheumatoid arthritis and 1 Still's disease were included). We retrospectively analyzed the relationship between clinical parameters at baseline and the prognosis of CTD-PAH patients.

Results: Mean age at entry were 65.3±10.3 and 48.3±15.5 years old each other (SSc-PAH vs non SSc-PAH P<0.001). Twenty-eight SSc-PAH (93%) and 26 non SSc-PAH patients (96%) took at least one vasodilator, among them, 18 SSc-PAH (60%) and 13 non-SSc-PAH (48%) patients took multiple vasodilators at the end of follow-up period. Comparing the baseline clinical parameters between two groups, vital capacity and diffusing capacity of the lung for carbon monoxide (DLCO) were significantly lower in SSc-PAH patients than non SSc-PAH patients and brain natriuretic peptide and creatinine level were higher in SSc-PAH patients than non SSc-PAH patients (P<0.05). However, there were no significant differences in hemodynamic indices between two groups. During a mean follow-up period of 42.5±31.5 months, 22 patients (18 SSc-PAH and 4 non SSc-PAH) died or received lung transplantation. The SSc-PAH patients had worse prognosis than non SSc-PAH patients (figure: P<0.001). Only 6 of 18 SSc-PAH patients and 1 of 4 non SSc-PAH patient died of PH related cardiovascular event and other principal causes of death included interstitial lung disease (ILD), neoplasm and infection. Applying multivariate Cox-proportional hazard regression, mean pulmonary arterial pressure, right atrial pressure, creatinine level and %DLCO were extracted as the independent risk for all-cause mortality.

(survival rate)

Conclusions: SSc-PAH patients had poor prognosis among CTD-PAH patients despite the progression of PAH drugs. As well as the report from REVEAL registry, not only PAH severity but also respiratory dysfunction may predict the prognosis of CTD-PAH patient. Scleroderma is multiorgan disease affected by complex pathology of vasoconstriction (ischemia), proliferation, inflammation, autoimmune disorder and fibrosis. Our data suggest that vasodilator alone is not enough to improve the prognosis of CTD-PAH patients. Comprehensive therapeutic strategy for scleroderma is needed.

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AB0636 A COMPARISON STUDY OF PREVALENCE OF TRADITIONAL CARDIOVASCULAR RISK FACTORS AND FRAMINGHAM RISK SCORE IN SYSTEMIC SCLEROSIS PATIENTS AND MATCHED CONTROLS

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Background: In Systemic Sclerosis (SSc), data on prevalence of traditional cardiovascular (CV) disease risk factors is scarce and conflicting (1). Therefore, SSc patients CV risk attributed to traditional CV risk factors remains an issue of debate.

Objectives: To evaluate if patients with SSc have a higher prevalence of traditional CV disease risk factors and a higher risk of long-term CV events based on the risk prediction tool of the Framingham risk score (FRS) in comparison with age, race and sex matched control subjects.

Methods: The study comprised patients diagnosed with SSc, fulfilling both the 1980 ACR and the 2013 ACR/EULAR criteria for the disease, and followed-up at our Rheumatology Department and a group of age, race and sex-matched controls. Inclusion criteria were age 30 to 74 and no history of CV events in order to calculate FRS. In total, 46 out of 62 patients were eligible for the study. Traditional CV disease risk factors (diabetes, arterial hypertension and smoking) were compared among the 46 patients with SSc and 51 matched controls. Systolic blood pressure (SBP) values and total and high-density lipoprotein (HDL) cholesterol levels were also collected. The 10-year risk for CV events according to FRS was calculated and means of patients and controls were compared. Subjects' distribution into 3 categories of risk – low (<10% risk), medium (10–20% risk) and high (>20% risk) was also compared. Parametric and nonparametric tests were used for comparison between groups. P value <0.05 was defined as statistically significant.

Results: Mean risk for CV events in 10-years assessed by FRS was 10.00%±8.61 for SSc patients and 7.76%±8.30 for matched controls. Differences were not statistically significant (p=0.196). Additionally, prevalence of diabetes, arterial hypertension and smoking did not differ significantly between the two groups (p=0.890, p=0.443, p=0.651, respectively). Total and HDL cholesterol levels were also similar between groups (p=0.963 and p=0.506, respectively). Only SBP values (mmHg) of SSc patients were significantly higher (128.50 mmHg [113.5 to 139.3]) (median [interquartile range]) compared with controls (120.00 [110 to 130]), p=0.031. Subjects' distribution into the 3 groups of risk defined was similar for both groups (p=0.205).

Conclusions: In our study, prevalence of traditional CV disease risk factors and 10-year risk for CV events based on FRS assessment tool did not differ significantly between SSc patients and age, sex and race matched controls.

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AB0637 SUBCLINICAL ATHEROMATOSIS AND VITAMIN D DEFICIENCY IN PATIENTS WITH SCLERODERMA

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Objectives:

To study whether patients with systemic sclerosis (SSc) have an increased cardiovascular risk (CVR), measured on the basis of analytical, angiodynamic and/or vascular lesions on carotid ultrasound.

The carotid IMT is a marker of cardiovascular morbidity and mortality, allowing measurement and monitoring of atherosclerosis in asymptomatic individuals, being surrogate markers of future coronary disease, stroke and general death in the general population and in inflammatory rheumatologic diseases.

Methods: Epidemiological and analytical data were collected, including the determination of the RCV SCORE index.

Vascular ultrasound protocol included assessment of carotid intima-media thickness (IMT), presence of atheromatous plaques, and exploration of peripheral arteriopathy using the ankle arm index (ABI).

Results: Seventy adult patients with ES diagnosis (ACR-EULAT 2013 criteria) were included.

94% of the women had a mean age of 50.2±12.5 years, and an average evolution time of 3.0±4.4 years.

The distribution by subgroups was: limited SSc (48%), diffuse SSc (34%), pre-SSc (4.2%), sine SSc (2.8%), MCTD (5.7%) and overlap syndrome 4.2%). The mean SSRm was 9.3±7.0 (range 0–42).

The ANA were positive in 91.4%, ACA (51.4%), ATA (10%), RNA polymerase (4.2%).

4% were DM, 7% were obese, 11% were active smokers, 13% were HTN, and 28% were ex-smokers.

28% had hypercholesterolemia with a mean total cholesterol of 192.5 (SD ± 31.9) and LDL of 102.4 (SD ± 29.4 mg/dL).

57% received vasodilators, most of them ARA-II. 10% bosentan, 4.2% sildenafil, and a 2.8% combination therapy.

The percentage of immunosuppressive drugs was corticoid (50%), MTX (34%), mycophenolate (3%), AZA (11%), HCQ (14%), CP (%).

The IMT presented pathological values (>0.9 mm) in 39% of the sample, 23% had atheroma plaques (being bilateral in 40%). Subclinical atheromatosis affected 41.4% (patients without cardiovascular events, pathological IMT and/or atheroma plaques). The ABI had pathological values (<0.9) in 17% of the patients.

In the bivariate analysis, the pathological GIM was related to the presence of ACA antibodies (OR =3.80, 95% CI: 1.15–12.52, p=0.028) and with the SCORE index of CVR (OR =2.93, 95% CI: 1.12–7.64, p=0.028); And the presence of atherosclerotic plaques was associated with increased SSRm score (OR 1.09, 95% CI 1.00–1.19, p=0.046), and the highest CVR SCORE index (OR 3.90, 95% CI: 1.31–11.56, p=0.014).

In the multivariate analysis, the serum vitamin D concentration showed a protective effect on IMT (OR =0.94, 95% CI 0.89–0.99, p value =0.025); And the main determinant of atheromatous plaques is the SCORE index, since the increase of one unit in SCORE index multiplies by 4 the probability of presenting plaques (OR =4.06, 95% CI: 1.31–12.60; P=0.015), once the effect of SSRm was controlled.

Conclusions:

- 40% of the patients had pathological IMT values, showing association with the presence of positive AAC and the SCORE risk index.
- The serum concentration of 25-OH-vitamin D showed a protective effect on IMT. Sixty percent of the sample had vitamin D deficiency.
- The presence of atheromatous plaques (23% of patients) was associated with higher SSRm indexes and SCORE cardiovascular risk.

Disclosure of Interest: None declared

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AB0638 CARDIAC TRANSPLANT IN SYSTEMIC SCLEROSIS-ASSOCIATED CARDIOMYOPATHY: MONOCENTRIC EXPERIENCE OF 3 CASES

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Background: Cardiac involvement in systemic sclerosis (SSc) is a frequent complication, but end-stage cardiac failure remains uncommon and represents a poor prognosis. Heart-lung and lung transplant is an established treatment option for SSc-related pulmonary disease. Due to the limited published data, no recommendations exist for cardiac transplant in the context of SSc.

Objectives: We present our monocentric experience of 3 patients with SSc who underwent cardiac transplant for SSc-related end-stage heart disease (multiple hospitalisations due to failure of medical therapy and life-threatening complications).

Results: Case 1 is a 59-year-old male with limited cutaneous SSc. Antinuclear antibody (ANA) was negative. He had vascular (digital ulcers) and cardiac (heart failure (left ventricular ejection fraction (LVEF) 20%, NYHA class IV)) involvement, without major gastrointestinal or pulmonary involvement (no interstitial lung disease (ILD) or pulmonary arterial hypertension (PAH: assessed by right heart catheterization (RHC))). He underwent a cardiac transplant at the age of 51, after a disease duration of 6 years. Post-transplantation immunosuppressant therapy consists of tacrolimus and mycophenolic acid, initially associated with methylprednisolone, which is the standard immunosuppression protocol at our institution.

Case 2 is a 55-year-old male with limited cutaneous SSc. ANA was positive,

	Case 1	Case 2	Case 3
Sex, age	Male, 59 years	Male, 55 years	Male, 50 years
Type of SSc	Limited	Limited	Diffuse
Disease duration at Tx	6 years	7 years	4 years
ANA	Negative	1/320, speckled, no SSc-specific antibody	Negative
Pre-Tx			
NYHA class	IV	III	III
LVEF	20%	40%	40%
RHC: mPAP in mmHg	26	20	31
RHC: PCWP in mmHg	20	14	28
Post-Tx			
NYHA class	I	I	I
LVEF	60%	55%	60%
RHC: mPAP in mmHg	19	13	21
RHC: PCWP in mmHg	12	8	12

Tx: Transplant; mPAP: Mean pulmonary artery pressure; PCWP: Pulmonary capillary wedge pressure.