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SURVIVAL AND PROGNOSIS IN SYSTEMIC SCLEROSIS: RESULTS FROM A SINGLE-CENTER COHORT

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Objectives: To analyze survival, causes of death, and risk factors associated with mortality in a cohort of patients with Systemic Sclerosis (SSc) at a single center

Methods: We performed a retrospective observational study of a cohort of patients with SSc undergoing follow-up during 2012 and until August 2020. We used the Kaplan-Meier method to estimate survival from onset of symptoms and multivariate Cox regression analysis to obtain independent risk factors associated with mortality

Results: The study population included 85 patients (women, 85.8%; mean age at diagnosis, 64.4 ± 12.7 years). A total of 19 patients (22.6%) died (table 1). Of these 11 (57.9%) died of a cause related to the disease itself (interstitial lung disease [ILD], 5 (26.3%); pulmonary hypertension, 2 (10.5%); or a combination of both, 3 (15.8%). The main cause of non-SSc-related death was cancer (21.1%). Survival rates at 5, 10, and 20 years were 98%, 92%, and 75%, respectively. Survival was statistically significantly poorer for the absence of ACA, the presence of antitopoisomerase I antibodies, proximal skin thickening, pulmonary hypertension, ILD, cancer and the diffuse subtype. The multivariate analysis performed to determine which factors were independently associated with mortality confirmed that older age at diagnosis of the disease, lower FVC in spirometry at diagnosis of ILD, and proximal skin thickening were associated with greater mortality

Table 1. Clinical and immunological characteristics of patients who died and patients who lived

	Dead (n=19)	Alive (n=66)	p-value
Female sex, n (%)	17 (89.5)	55 (83.3)	0.594
Age at diagnosis (years), mean (SD)	56.9 (13.7)	50.4 (13.6)	0.076
Time since diagnosis (years), mean (SD)	11.6 (7.3)	14.2 (9.2)	0.215
lcSSc, n (%)	6 (33.3)	50 (75.7)	< 0.001
dcSSc, n (%)	12 (66.7)	10 (15.1)	< 0.001
Digital ulcers, n (%)	9 (47.4)	33 (50)	0.748
Calcinosis, n (%)	1 (5.3)	16 (24.2)	0.061
Telangiectasias, n (%)	15 (78.9)	56 (84.8)	0.184
ILD, n (%)	15 (78.9)	32 (48.5)	0.021
FEV ₁ at diagnosis of ILD, mean (SD)	78.3 (19.3)	78.7 (17.7)	0.955
FVC at diagnosis of ILD, mean (SD)	65.2 (13.1)	78.1 (20.7)	0.043
DLCO at diagnosis of ILD, mean (SD)	56.9 (17.5)	63.9 (16.7)	0.301
Pulmonary hypertension, n (%)	11 (57.9)	14 (21.9)	0.002
sPAP (mmHg), mean (SD)	49.2 (24.7)	30.2 (8.2)	0.009
Gastrointestinal involvement, n (%)	13 (68.4)	30 (45.4)	0.125
Cardiac involvement, n (%)	3 (15.8)	11 (16.7)	0.907
Muscle involvement, n (%)	1 (5.3)	2 (3.03)	0.851
Arthritis or arthralgia, n (%)	5 (26.3)	23 (34.8)	0.436
Renal crisis, n (%)	0	2 (3.03)	<0.001
Cancer, n (%)	5 (26.3)	2 (3.03)	0.001
Positive ACA, n (%)	5 (26.3)	35 (53.03)	0.034
Positive ATA, n (%)	10 (52.6)	9 (13.6)	< 0.001

Abbreviations: ILD: diffuse interstitial lung disease, SSc: systemic sclerosis, FEV₁: forced expiratory volume in the first second, FVC: forced vital capacity, DLCO: diffusing capacity for carbon monoxide, sPAP: systolic pulmonary artery pressure, ACA: anticentromere antibody, ATA: antitopoisomerase I antibody.

Conclusion: Survival at 10 years was greater than 90% in the study cohort. The main causes of death were ILD, pulmonary hypertension and cancer. The main factors associated with mortality were proximal skin thickening, older age at diagnosis, and lower forced vital capacity

Disclosure of Interests: None declared

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STUDY DESIGN FOR THE RANDOMISED CONTROLLED PHASE II ReSSCUE TRIAL: SAFETY AND EFFICACY OF FAECAL MICROBIOTA TRANSPLANTATION BY ANAEROBIC CULTIVATED HUMAN INTESTINAL MICROBIOME (ACHIM) IN PATIENTS WITH SYSTEMIC SCLEROSIS

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Background: Gastro-intestinal tract (GIT) symptoms is highly prevalent in patients with systemic sclerosis (SSc). The GIT-symptoms impact on the quality of life is significant, and available treatment alternatives are limited. Recently published articles show associations between gut microbiota changes and GIT-symptoms in SSc. We, therefore, performed a successful feasibility trial on faecal microbiota transplantation (FMT) in SSc patients using the single-donor bacterial culture "Anaerobic Cultivated Human Intestinal Microbiome (ACHIM)". Based on the promising results from the feasibility trial, we aim to evaluate the safety and efficacy of FMT by ACHIM in SSc patients. (NCT04300426)

Objectives: To design a clinical trial that explores the safety and efficacy of FMT in SSc patients.

Methods: The ReSScUE trial is a phase II, placebo-controlled, randomised 20-week, multicentre trial. The trial comprises three parts. In the induction phase (A1) lasting from week 0 to week 12, participants are randomised 1:1 to repeat infusions of 30 ml ACHIM or placebo at week 0 and 2 by gastro-duodenoscopy. In the maintenance phase (A2), all study participants will receive 30 ml ACHIM at week 12 and are followed continued blinded until week 20.

For longer-term data on intervention effects and safety, the participant will be followed for a maximum extended monitoring period of 16 weeks (part B).

The primary endpoint is change from baseline to week 12 in UCLA GIT scores on bloating or diarrhoea, depending on the worst symptom at baseline evaluated separately for each patient. Secondary endpoints are changes in UCLA GIT scores (bloating, diarrhoea and total) and safety measures.

Results: We aim to enrol 70 SSc patients based on the power calculations for the primary endpoint "change in worst symptom from baseline to week 12", with a considered drop out rate of 10%. This number of patients is expected to give a power of 80% of detecting a change in mean (p=0.05, two-sided) of -5.0 (or higher) if the relating standard deviation is 0.70 or lower. The patient screening started in September 2020, and we expect the study to be completed in May 2022.

Conclusion: The ReSScUE-study is to our knowledge the first FMT-study in SSc. This trial will assess the safety and efficacy of FMT in SSc patients with lower GI-symptoms, possibly leading to a novel treatment approach in SSc patients.

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AB0434 VITAMIN D IN SYSTEMIC SCLEROSIS PATIENTS

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Background: Systemic Sclerosis (SSc) is a generalized and systemic autoimmune disease that affects the connective tissue of the skin and internal organs, especially kidneys, heart and lungs [1].

Objectives: Numerous data from recent literature confirm the regulatory action of vitamin D on the immune system and, therefore, how a deficit of this micronutrient can lead to alterations in the immune response, as is known to happen in many allergic and autoimmune diseases [2]. We studied the association between vitamin D levels and SSc, evaluating their correlation with the characteristic manifestations of the pathology.

Methods: We dosed the serum levels of 25 hydroxy-vitamin D in 42 patients with SSc (average age 64.63 $\pm$ 7.33) and 40 healthy controls comparable for sex and age. The diagnosis of SSc was formulated in accordance to 2013 ACR/EULAR criteria. None of the subjects involved in the study took vitamin D products.

Results: Patients' vitamin D levels (26.22 $\pm$ 9.82 ng/ml), although they tended to be lower than controls (27.80 $\pm$ 16.53 ng/ml), showed no significant decrease. In patients with pulmonary fibrosis, vitamin D levels were 23.28 $\pm$ 12.30 lower than in patients with trophic ulcers and compared to patients without complications 26.07 $\pm$ 9.92, although with not statistically significant values. No statistically significant difference was found between vitamin D levels in patients with trophic ulcers compared to controls without complications.

Conclusion: According to the studies in the literature, in our sample, vitamin D deficiency was therefore greater in patients with SSc, especially with pulmonary fibrosis, than in controls [3,4]. Vitamin D levels in diffused-type SSc patients were significantly lower than those in limited-type SSc patients. Further studies are needed to clarify the role that vitamin D deficiency plays in SSc, but lower vitamin D levels in these patients may suggest the need to monitor blood levels of vitamin D and supplement it appropriately.

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AB0435 CAPILAROSCOPY DOES NOT PREDICT CARDIOVASCULAR EVENTS IN PATIENTS WITH SYSTEMIC SCLEROSIS: A RETROSPECTIVE STUDY

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Background: Systemic sclerosis is associated with increased risk of cardiovascular disease (CVD) (1) and studies using MRI suggest that microvascular disease has an important role (2). Capillaroscopy is a non invasive and safe technique that assesses peripheral microvascular damage (3).

Objectives: The objective of this study was to evaluate the predictive value of the capillaroscopy in relation to major adverse cardiovascular events (MACE).

Methods: Retrospective study with three timepoints (at baseline, at 5 and 10 years) including patients with scleroderma from EUSTAR center 096. Data were collected from the registry and observation papers. We performed capillaroscopy to all patients at the time of inclusion in the EUSTAR registry (2004) and at baseline (2009). Also, CV risk scores were calculated at baseline and were reassessed at 5 and at 10 years using the SCORE calculator. Risk score was considered low if was between 0 and 2, moderate 3-9 and high >10. The relation between capillaroscopy and MACE was tested in using bivariate regression.

Results: Of 22 patients, mean (standard deviation (SD)) age was 43.1 (11.5), all patients were females, mean (SD) disease duration was 5.4 (4.5). During the 10 years of follow up, 5 (22.7) patients had been lost of follow up and 8 (36.4) patients had died. Only 9 (40.9) patients completed the 10 year follow up.

At the time of inclusion in the EUSTAR, one patient showed early scleroderma pattern at capillaroscopy, 15 had active pattern and 6 patients had late pattern. Capillaroscopic scoring showed 2 (9.1) patients with disarranged (<50%) aspect, 5 (22.7) patients with disarranged (>50%) aspect, 4 (18.2) patients with local paucity, 10 (45.5) patients with enlarged loop bordering local paucity and 1 patient (4.5) with complete paucity.

Capillaroscopy at baseline showed active pattern in 4 patients and late pattern in 18 patients. Thus, 13 (59.1) of patients had a progression of the disease at capillaroscopy before follow up.

At baseline, 14 (63.6) patients had traditional CV risk factors. Cardiovascular risk scores found 21 (95.5) patients with a low risk score and 1 (4.5) patient with a moderate risk score. At 5 years 11 (0.5) patients had a low risk score and 1 (4.5) patient had moderate risk score and at 10 years, 5 (22.7) and 2 (9) patients had low and moderate risk scores, respectively. We found 6.2 MACE/100 patient-year and 5.5 deaths/100 patient-year.

Capillaroscopy (p=0.684), disease progression on capillaroscopy (p=0.781), capillaroscopic scoring (p=0.92) and CV risk score (p=0.98) were not predictive factors of MACE.

Conclusion: Patients with systemic sclerosis are at high risk of MACE and traditional CV risk scores underestimate this risk. Changes/progression on capillaroscopy is not predictive for MACE. However, this hypothesis needs to be tested on a bigger cohort.

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AB0436 OUTCOMES OF DOSE-REDUCTION OR DISCONTINUATION OF TOCILIZUMAB IN PATIENTS WITH EARLY DIFFUSE CUTANEOUS SYSTEMIC SCLEROSIS

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Background: Potential efficacy and favorable safety profiles of tocilizumab (TCZ) have been demonstrated in patients with diffuse cutaneous systemic sclerosis (dcSSc) [1, 2]. However, clinical outcomes after dose-reduction or discontinuation of TCZ due to an improvement of skin thickness remain unclear.

Objectives: To investigate the clinical outcomes after dose-reduction or discontinuation of TCZ in patients with dcSSc in a real-world setting.

Methods: This is a single-center, retrospective, observational study using a database of consecutive SSc patients who visited our center between April 2014 and October 2020. For this study, we selected eligible patients from the database based on the following criteria: patients who (i) fulfilled the ACR/EULAR classification criteria, (ii) were classified as having dcSSc, (iii) had been treated with TCZ for at least 6 months, and (iv) were follow-up >6 months after TCZ introduction. Clinical information including demographic and clinical characteristics at TCZ introduction; dosing, administration route, and adherence of TCZ; and serial clinical parameters