FRI0376 DIFFERENCES IN RIGHT VENTRICULAR FUNCTION AND MORPHOLOGY IN SSC-PAH AND IPAHE ASSESSED BY RIGHT HEART CATHETERIZATION AND CARDIAC MRI

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Background: Systemic sclerosis (SSc) is a serious disorder with high mortality, mainly driven by cardiopulmonary pathologies including pulmonary arterial hypertension (PAH). Patients with SSc-PAH appear to have worse prognosis than idiopathic PAH (iPAH).

Objectives: (A)Compare cardiac magnetic resonance (CMR) of the right ventricle, hemodynamic parameters and immunological markers between patient cohorts with SSc-PAH, iPAH and SSc without PAH, respectively. (B)Evaluate the impact of these variables on PAH-related morbidity and mortality.

Methods: The study cohort included SSc-PAH (n=16), iPAH (n=15) and SSc without PAH (n=20). At baseline, all patients were examined by ventricular volumes by short axis summation of cine CMR, echocardiography and right heart catheterization (RHC). Blood samples were analysed for immune-related factors. At a median follow up of 3 years, clinical data, and new onset of PAH and vital status were registered. A composite outcome for PAH related events was created including: PAH progression, end-stage PAH, hospitalization for PAH worsening and all-cause mortality. Associations between parameters were assessed using ANOVA, Pearson Chi-square, Fishers exact, or independent sample t-test.

Results: Patients with SSc-PAH were significantly older at PAH onset, had lower 6MWD, DLCO% and Hb than the iPAH patients. RHC results are shown in Table 1. CMR showed that SSc-PAH patients had lower right ventricular mass index (RVMI), RV to left ventricular ratio and RV mass to volume ratio (Table 1). Multiplex immune assays demonstrated higher serum levels of IP-10, VEGF and, IL12 in SSc-PAH than in iPAH. At the end of the study, 12/15 SSc-PAH had developed a PAH-related event. Compared to event-free patients, they were marked by significant CMR changes including higher RVM (p=0.006) and RVMI (p=0.005). In the iPAH subgroup, 7/16 patients developed an event. These patients were characterized by younger age at onset (p=0.001), higher NT-proBNP (p=0.017), lower 6MWD (p=0.034), higher RVM (p=0.010), RVMI (p=0.005), RV-to-LV ratio (p=0.001) on CMR.

Table 1. Baseline right ventricle hemodynamic and cardiac magnetic resonance measurements

	SSc-PAH (n=15)	iPAH (n=16)	p-value
RHC			
Cardiac output	6.0 (2.9)	5.4 (1.4)	n.s.
Cardiac index	3.2 (1.5)	2.9 (0.6)	n.s.
RAP, mmHg	4.6 (3.1)	7.2 (3.4)	0.007
sPAP, mmHg	60 (19.8)	88 (23.3)	<0.001
mPAP, mmHg	35.5 (11.7)	55 (17.1)	<0.001
PCV, mmHg	6.2 (2.9)	7.4 (3.1)	n.s.
PA oxygen saturation%	81.3 (33.1)	93.2 (31)	n.s.
PVR (Wood)	5.4 (3.9)	9.7 (4.3)	<0.001
RV MRI			
RVS index, ml/m ²	40.9 (7.8)	40.4 (7.8)	n.s.
RVESV, ml	144.9 (80.3)	146.8 (46.4)	n.s.
RVEDV, ml	219.5 (84.2)	223.8 (52.8)	n.s.
RVEDV index, ml/m ²	120.8 (50.5)	120.8 (28.3)	n.s.
RV EF, %	37.1 (10.5)	34.5 (10.5)	n.s.
RV mass, g	50.1 (21.3)	72.9 (27.4)	<0.001
RV mass index, g/m ²	26.2 (10.8)	38.2 (14.9)	<0.001
RV-to-LV ratio	0.51 (0.14)	0.82 (0.32)	<0.001
RV mass-to-volume ratio, g/ml	0.22 (0.06)	0.31 (0.08)	<0.001

Conclusions: The CMR measures indicate that the RV adapts differently in iPAH and SSc-PAH; with more pronounced RV hypertrophy in iPAH patients. The mechanisms behind the differences in RV hypertrophy in SSc-PAH and iPAH are not known, but may involve microvascular changes and deregulated inflammatory cascades. This study indicates that CMR may predict PAH progression in SSc.

Disclosure of Interest: None declared
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FRI0377 ABNORMAL NAILFOLD CAPILLAROSCOPY PATTERN IS COMMON IN PATIENTS WITH CONNECTIVE TISSUE DISEASE AND ASSOCIATED WITH ORGAN INVOLVEMENT

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Background: Nailfold capillary microscopy (NCM) has been shown to be associated with disease severity and internal organ involvement in non-consecutive systemic sclerosis (SSc) cohorts. NCM may help in early recognition of connective tissue disease (CTD) but it is unclear to which extent NCM abnormalities occur in several CTD and whether these are associated with organ involvement.

Objectives: To assess NCM in consecutive patients with Raynaud's phenomenon (RP) and whether these are associated with signs of organ involvement.

Methods: NCM was assessed in consecutive patients with RP (n=759) by wide-field videocapillaroscopy, according to standardized procedures at a dedicated vascular laboratory by trained and experienced technicians. The pattern was classified as normal (n=325), non-specific (n=188) or SSc pattern (early (n=106), active (n=140) or late (n=0) based on the Cutolo patterns). Potential pulmonary involvement was defined as forced vital capacity or diffusion capacity <70%. Gastro-intestinal involvement as scintigraphically (Tc-99m colloid) oesophagus dysmotility. Skin involvement as puffy fingers or sclerodactyly. Patients were classified as primary RP (normal NCM and negative serology, n=226) or secondary RP (abnormal NCM and/or serology) groups: early SSc (n=195), SSc (n=40), incomplete Sjögren's syndrome (iSS, n=5), primary SS (pSS, n=30), incomplete systemic lupus erythematoses (iSLE, n=42), SLE (n=30), mixed CTD (MCTD, n=7), rheumatoid arthritis (RA, n=15) or when not meeting criteria as other (n=169). None were diagnosed with polymyositis or dermatomyositis.

Results: SSc pattern was observed in 33% of patients with pSS, 17% SLE, 71% MCTD and 13% RA. Pulmonary, oesophageal and skin involvement was more frequent in secondary RP patients with an SSc pattern, even when analysing only those fulfilling definite criteria for CTD or after exclusion of early SSc and SSc patients. For secondary RP patients, absence of an SSc NCM pattern had a high negative predictive value for pulmonary (92%), oesophageal (91%) and skin (96%) involvement, while positive predictive values were low.

Table 1. Nailfold capillaroscopic pattern per patient diagnosis group in patients with Raynaud's phenomenon

NCM pattern	Primary Raynaud n=226	Secondary Raynaud									
		Definite diagnosis					No classifiable disease				
		SSc n=40	pSS n=30	SLE n=30	MCTD n=7	RA n=15	early SSc n=195	iSS n=5	iSLE n=42	Other n=169	
Normal	226 (100)	1 (3)	10 (33)	12 (40)	2 (29)	11 (73)	4 (2)	4 (80)	29 (69)	26 (15)	
Non-specific	0 (0)	4 (10)	10 (33)	13 (43)	0 (0)	2 (13)	2 (1)	1 (20)	13 (31)	143 (85)	
Early	0 (0)	7 (18)	4 (13)	2 (7)	1 (14)	1 (7)	91 (47)	0 (0)	0 (0)	0 (0)	
Active	0 (0)	28 (70)	6 (20)	3 (10)	4 (57)	1 (7)	98 (50)	0 (0)	0 (0)	0 (0)	

Data in number (percentage).

Organ involvement and nailfold capillaroscopy in secondary Raynaud's patients

Conclusions: SSc pattern on NCM is common in CTD patients and is associated with frequent prevalence of organ involvement, even in the absence of (early) SSc. Although this was a retrospective cohort, these data underline the importance of assessing NCM in RP patients to evaluate the risk for organ involvement in CTD other than SSc, already in early disease stages.

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FRI0378 CARDIAC INVOLVEMENT IN UNDIFFERENTIATED CONNECTIVE TISSUE DISEASE AT RISK FOR SYSTEMIC SCLEROSIS. A TISSUE DOPPLER IMAGING STUDY

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Background: Undifferentiated connective tissue disease at risk for Systemic Sclerosis (UCTD-risk-SSc), previously referred to as very early SSc, is a condition characterized by Raynaud's phenomenon (RP) with SSc marker autoantibodies and/or typical capillaroscopic findings and unsatisfying classification criteria for the disease (1). UCTD-risk-SSc patients have been reported to present, in about 40% of the cases, a preclinical vascular internal organ disease as detected by a diffusing lung capacity for CO <80% of the predicted value (lung involvement) and/or a low esophageal sphincter pressure <15 mmHg (oesophageal involvement) and/or a mitral E/A ratio <1 (heart involvement) (2, 3).

Objectives: Aim of the present study was to assess the prevalence of right (RV) or left ventricle (LV) systolic and/or diastolic dysfunction by standard echocardiography and tissue Doppler imaging (TDI).

Methods: Thirty patients with UCTD-risk-SSc (28 female, aged 47±13 years, range 21–70) and 30 age- and sex-matched controls underwent cardiac assessment by standard echocardiography and TDI.

Results: UCTD-risk-SSc patients and controls did not show any difference at standard echocardiographic evaluation. In particular, an inverted E/A ratio was pointed out in 10/30 patients and 7/30 controls (p=ns). TDI showed a mild impairment of LV and RV diastolic (E_m 15±4 vs 19±5, $p<0.0001$; E/E_a 6.1±1.7 vs 4.8±1.2, $p=0.001$; E_r 14±3 vs 16±2, $p=0.02$; E_r/A_r 0.9±0.4 vs 1.3±0.3, $p<0.002$; increased pulmonary artery wedge pressure 9±2 vs 8±1, $p=0.001$) and systolic function (S_m 13±3 vs 15±2 cm/sec, $p<0.0003$; S_r 14±2 vs 16±3 cm/sec, $p<0.0001$) in UCTD-risk-SSc patients in comparison to controls.

Conclusions: Our study shows that UCTD-risk-SSc patients present a previously unrecognized, mild biventricular systolic and diastolic dysfunction as compared to controls. The pathophysiologic meaning (i.e. intramyocardial artery disease and/or patchy fibrosis) as well the predictive value of developing overt SSc in the short time await to be elucidated.

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FRI0379 PREVALENCE OF FAM111 B GENE MUTATIONS IN SYSTEMIC SCLEROSIS

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Background: Systemic sclerosis (SSc) is a prototypic systemic fibrotic disease with unclearly characterized genetic basis. Implicated genes have been associated with autoimmune dysregulation with relatively few variants associated with fibrosis [1]. We have discovered that mutations in *FAM111B* gene cause hereditary fibrosing poikiloderma with tendon contractures, myopathy, and pulmonary fibrosis (POIKTMP)[2], a multisystem fibrotic condition with clinical aspects of SSc [3]. This observation has established *FAM111B* as a candidate gene for SSc.

Objectives:

The objective is to investigate whether *FAM111B* gene mutations are present in SSc patients and further explore relationships between *FAM111B* mutations and clinical expression of SSc.

Methods: Patients with a definite diagnosis of SSc attending the Rheumatology outpatient departments at Groote Schuur Hospital, Cape Town, and Chris Hani Baragwanath Hospital, Johannesburg, were enrolled into the study. Physical examination assessing the extent of disease was done in all patients and the modified Rodnan skin score (mRSS) was used to determine the extent of the skin involvement. Blood samples were collected for DNA extraction and mutation screening using the high-resolution melt technique. Samples with abnormal electropherograms were selected for Sanger sequencing to identify mutations. Public databases were used to verify the frequency of variants in *FAM111B*.

Results: 131 patients were genotyped, 13 men and 118 women, with a mean age of 26.6 years and mean age of symptom onset at 25.3 years. The majority of patients were black (59.5%). 72% of patients had diffuse systemic sclerosis (DSSc) with a median mRSS of 11. Genetic analysis revealed seven rare genetic variants (C832G>A; C855G>T; C917A>G; C937G>A; C988C>T; C995A>C and C1006G>C) in eight patients (five patients from Johannesburg and three patients from Cape Town) [Table 1]. These variants were missense mutations of unknown significance with a minor allele frequency <0.01. No *FAM111B* mutations that cause POIKTMP were found in patients with SSc.

Conclusions: Rare genetic variants of unknown significance (GVUS) in *FAM111B* gene were found in patients with SSc. It is possible that the GVUS may modify the function of *FAM111B*, and influence the pathogenesis of SSc or are rare polymorphisms with no functional impact.

References:

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FRI0380 PATIENT PREFERENCES AND DIFFICULTIES CONCERNING THE HOME TREATMENT OPTIONS IN SYSTEMIC SCLEROSIS (SSC)

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Background: SSc patients suffer from Raynaud's phenomenon, hand skin hardening and scarring, digital ulcers, esophagus/gastric dysmotility, dysphagia and mucosal dryness. These symptoms significantly reduce patient's life autonomy and impair the capacity to handle their therapy usually made by different modalities of administration: oral, topical, inhalation, intramuscular, subcutaneous, intravenous, and rectal.

Objectives: to investigate the methods of administration used by SSc patients, their preferred methods, their compliance to pharmacological therapy, and the difficulties that are encountered by the patients during pharmacotherapy.

Methods: 2 questionnaires were prepared on an ad hoc basis. The first given to patients, the second to be filled out by the patient's physician. The first questionnaire comprised 25 questions to investigate the problems encountered by patients when taking their medications by correlating these with two validated activities indices: SHAQ-DI (activities of daily living) and the COCHIN scale (hand activities). The second questionnaire collected demographic and important SSc-related clinical information (eg. age, sex, disease duration, symptoms). 80 SSc patients completed the questionnaires, maintaining anonymity. A "difficulty index" was also filled out, where: 0 = no difficulty to 4 = impossible to use or too difficult to use.

Results:

Table 1. Patient use of pharmacological therapies

	% Using	% Users preferring this method	Difficult index [†]	Comment
Oral	100	91,25	0,83	Most preferred
Eye drops	52,5	2,5	1,07	Least preferred
Topicals	33,75	3,75	0,77	Cannot open the top (safety lock)
Injections	28,25	2,5	2,17	Cannot apply to skin
Inhaler	16,25	0	1,07	Cannot spray
Vaginal/rectal	6,25	0	1,03	

Table 2. Most frequent problems encountered

	% Using	Most frequent problems	Users have these problems	Difficult index [†]
Oral	100	Blister: pushing out pills	73,75	2,22
Eye drops	52,5	Open thin stoppers	78,75	1,51
Topicals	33,75	Cannot open the top (safety lock)	70,5	1,4
Inhaler	16,25	Cannot spray/push the inhaler	85	1,71

[†]4 = most difficult.

In particular, the dimension of the pills is problematic, and has identified a paradoxical situation because large pills are difficult to swallow (41,25% patients who use pills) but at the same time small pills are difficult to pinch with the fingers (62,25% patients who use pills).

Conclusions: SSc patients experience significant problems in maintaining adherence to treatments due to difficulties in the use of blisters and bottles with children proof stoppers. Pills still remain the most preferred method of treatment. In conclusion, patients unanimously wished to avoid the use of blisters, definitely preferring bottles without the children proof stopper to make the treatment easier and provide a more independent life.

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FRI0381 INCREASED RISK OF OSTEOPOROTIC FRACTURES IN ADULT PATIENTS WITH POLYMYOSITIS AND DERMATOMYOSITIS: A NATIONWIDE POPULATION-BASED COHORT STUDY

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Background: Patients with polymyositis and dermatomyositis (PM/DM) are characterized by chronic muscle weakness due to autoimmune-mediated myositis and are usually treated with corticosteroids initially. PM/DM patients prone to develop osteoporosis and subsequent fractures but are rarely investigated.

Objectives: To explore the incidence rate (IR) and risk factors of osteoporotic fractures (OFs) among adult PM/DM patients.

Methods: We conducted a cohort study by utilizing the Taiwan National Health Insurance database. PM/DM patients and respective age- and gender-matched cohort without PM/DM were enrolled. The primary endpoint was the initial event of OFs. We used the Cox proportional hazard model to study the risk factors of OFs in the PM/DM cohort.

Results: Among 2391 PM/DM patients (67.8% female, mean age: 49.5 years) followed for a mean (SD) of 6.1 (5.0) years, 116 developed vertebral fractures, 32 had hip fractures, and 14 experienced radius fractures (IR: 8.18, 2.20, and 0.96 per 1000 person-years, respectively, Table 1). Compared with the matched cohort, the PM/DM patients had higher IR ratios (IRRs) (95% CIs) of OFs at all age groups at enrollment: 3.27 (2.19 to 4.81, $p<0.0001$) for people <50 years and 2.29 (1.85 to 2.82, $p<0.0001$) for those ≥50 years. The IRRs were 2.39 (1.92