FRI0451

CONTINUOUS PRESENCE OF IGM ANTI-TOPOISOMERASE I ANTIBODIES INDICATES AN ONGOING IMMUNE RESPONSE IN SYSTEMIC SCLEROSIS

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Background: Small case-series of anti-topoisomerase I antibodies (ATA) in Systemic Sclerosis (SSc) show a highly varying immune response over time. IgA and IgG levels were shown to correlate with skin scores. One small study showed that increasing IgG levels can precede increasing skin scores. Thus far, detailed analysis of ATA characteristics with disease features in larger cohorts have not been performed.

Objectives: By taking advantage of our well described SSc cohort with annual follow-up data, we aimed to evaluate whether clinical heterogeneity within ATA +patients can be explained by ATA characteristics.

Methods: ATA IgG, IgM and IgA levels were assessed in consecutive serum samples of baseline ATA-IgG +patients from the Leiden SSc cohort. Disease progression during the first year of follow-up was defined as increase of modified Rodnan Skin Score (mRSS) with ≥ 5 points, progression of pulmonary involvement ($<10\%$ of predicted forced vital capacity [FVC] or diffusion capacity of the lung [DLCO]), development of digital ulcers, renal crisis, pulmonary arterial hypertension and/or mortality. Here, we present data on the association between the presence of ATA-IgM and disease progression.

Results: In total 344 samples of 102 ATA +patients were measured. Baseline and follow-up samples were available from 70 patients. Median follow-up was 3.7 years (range 0.9–7.4 years). At baseline 42/70 patients were positive for ATA IgM and 69/70 patients for ATA IgA (table 1). Strikingly, while clinical characteristics did not differ, mean ATA-IgM at baseline was higher in disease progressors (table 2). The possible relevance of an ATA-IgM response for disease progression was confirmed by the observation that those patients positive for ATA-IgM both at baseline and at FU, 59% of cases showed disease progression, as compared to 15% of patients negative for ATA IgM at both time points ($p=0.02$).

Abstract FRI0451 – Table 1. Changes in presence and levels of ATA isotypes in paired serum samples

	ATA isotype status at baseline/ follow-up				median ATA level (aU/mL[IQR])		p
	+/+	±	-/-	-/+	baseline	follow-up	
IgG	66	4	-	-	454 (193–876)	283 (79–647)	<0.01
IgM	29	13	25	3	627 (271–2081)	348 (167–1315)	0.06
IgA	65	4	1	0	2832 (812–8069)	2210 (645–7593)	0.01

Abstract FRI0451 – Table 2. Baseline characteristics of SSc patients with and without disease progression during the first year of follow-up

	progressors (n=25)	non- progressors (n=36)	p
female, n(%)	18 (72)	28 (78)	0.61
age, mean[yr.]±SD	55±16	50±15	0.15
time since onset first non-Raynaud symptom, median [yr.] (IQR)	4 (1–8)	3 (1–12)	0.75
mRSS, median (IQR)	4 (3–8)	5 (2–13)	0.94
DLCO, mean [% of predicted]±SD	69 (56–81)	63 (49–75)	0.17
ATA IgG level, median [aU/mL](IQR)	636 (301–1127)	312 (111–900)	0.09
ATA IgM level, median [aU/mL](IQR)	933 (533–3122)	447 (215–1293)	0.03
ATA IgA level, median [aU/mL](IQR)	5217 (2003–14187)	2202 (513–6240)	0.07

Conclusions: The presence of ATA-IgM at baseline and at follow-up and its association with disease course suggests that the ATA response in SSc patients is an ongoing process that possibly explains the heterogenic disease course of ATA +patients over time.

Disclosure of Interest: None declared

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FRI0452

NAILFOLD CAPILLAROSCOPY IN ANTISYNTHEASE SYNDROME (NASCAR): RESULTS OF A MULTICENTER, INTERNATIONAL STUDY OF THE AMERICAN AND EUROPEAN NETWORK OF ANTISYNTHEASE SYNDROME (AENEAS)

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Background: Antisynthetase syndrome (ASSD) is an autoimmune disease characterised by the clinical triad arthritis, myositis, and interstitial lung disease (ILD). Despite Raynaud's phenomenon (RP) is another typical feature of ASSD, nailfold videocapillaroscopy (NVC) assessment of these patients has been only sporadically described, without the elucidating data for clinicians.

Objectives: To describe NVC features of ASSD patients and to investigate possible correlations with clinical and serological features of the disease.

Methods: We retrospectively analysed NVC images of 190 ASSD patients (females/males 3.76, mean age 49.7±12.8 years, mean disease duration 51.2±71.4 months, 133 anti-Jo-1 and 57 non-anti-Jo-1 positive patients). For each patient, we examined number of capillaries, giant capillaries, micro-haemorrhages, avascular areas, ramified capillaries, and the presence of scleroderma (SSc) patterns. Finally, we correlated NVC features with clinical and serological findings of ASSD patients.

Results: NVC abnormalities were observed in 62.1% of ASSD patients compared with 29.3% of a group of 75 patients with primary Raynaud's phenomenon ($p<0.001$). A SSc-like pattern was detected in 67 (35.3%) patients and it was associated with anti-Jo-1 antibodies ($p=0.002$) and also with a longer disease duration ($p=0.004$). Interestingly, there was no significant correlation between the presence of SSc-like pattern and RP, and only 47% of patients with SSc-like pattern had RP.

Conclusions: NVC abnormalities are commonly observed in ASSD, independently to the occurrence of RP. The presence of a SSc-like pattern should let to identify a more defined ASSD subtype and prospective studies could confirm the association with clinical and serological features of ASSD.

Disclosure of Interest: None declared

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FRI0453

HOSPITALISATION AND SURVIVAL ANALYSIS IN SYSTEMIC SCLEROSIS PATIENTS WITH CONCOMITANT OR ISOLATED PULMONARY HYPERTENSION AND INTERSTITIAL LUNG DISEASE IN THE MULTIETHNIC SCLERODERMA COHORT SINGAPORE

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Background: Concomitant pulmonary hypertension and interstitial lung disease in systemic sclerosis (SSc-PH-ILD) represents a distinct subpopulation of SSc with poorer prognosis in Western studies. In Asian patients, characterisation of SSc-PH-ILD is still lacking.

Objectives: To analyse hospital admissions, survival and prognostic markers among SSc patients with PH, ILD or concomitant PH-ILD in the Scleroderma Cohort Singapore.

Methods: In this study involving 3 tertiary Rheumatology institutions Jan 2008 to , Oct 2016 SSc patients with significant pulmonary involvement were included. ILD was based on high resolution computed tomography and predicted FVC <70%. PH was based on either echocardiographic systolic pulmonary arterial pressure (sPAP) ≥50 mmHg, or right heart catheterization (RHC) findings of mean PAP≥25 mmHg. Hospitalisation rates and survival of SSc patients with PH, ILD or PH-ILD were compared. Risk factors of poor outcomes were identified by multivariate stepwise Cox regression analysis.

Results: Among 490 patients, 92 had ILD, 50 PH and 43 PH-ILD (table 1). Of 93 patients with PH or PH-ILD, 56 were based on echocardiography and 37 on RHC. The 5 year survival was 79%, 87% and 90% in PH, PH-ILD and ILD subgroup, respectively (figure 1). In multivariable analysis, PH was significantly associated with 2.8-fold increased risk of death. Male gender, malabsorption, digital ulcerations and renal crisis were also significantly associated with mortality (table 2). No significant difference in hospital admissions/year among different subgroups. Increased hospital admissions were associated with renal crisis, right heart failure and use of PH medications.

Abstract FRI0453 – Table 1. Clinical characteristics

	PH (n=50)	ILD (n=92)	PH-ILD (n=43)	No PH/ILD (n=305)
Female, n	44	76	38	270
Follow up duration (months)	53.46	101.5	88.71±65.53	64.66±36.27
±SD)	±55.76	±80.04		
Age at SSc diagnosis (years)	51.08	46.87	53.84±15.17	46.44±14.59
±SD)	±16.44	±12.4		
Duration of SSc at entry (years)	5.85±6.95	6.93±7.45	6.14±7.98	5.20±8.24
±SD)				
Dc-SSc, n	13	45	11	100
PH specific treatments*, n	28	N/A	26	N/A
Immunosuppressants**, n	25	64	27	176

*Prostacyclin, phosphodiesterase type 5 inhibitors, endothelin receptor antagonist;

**Methotrexate, cyclophosphamide, mycophenolate mofetil.

Abstract FRI0453 – Table 2. Survival analysis

	Hazard Ratio (95% CI)	P Value
Male gender	2.85 (1.53–5.33)	0.0010
Malabsorption	2.89 (1.67–5.01)	0.0002
Renal crisis	2.00 (1.00–3.99)	0.0490
Digital ulcerations	2.06 (1.21–3.50)	0.0076

Abstract FRI0453 – Figure 1. Adjusted survival curve comparing survival of SSc patients with PH, ILD, and concomitant PH-ILD. X-axis shows years of survival from diagnosis of PH or ILD.

Conclusions: Compared to those with ILD or PH-ILD, SSc-PH patients had increased mortality, but not hospitalisation rates. This could be due to small sample size or short follow up duration. We identified risk factors associated with worse outcomes in SSc patients with significant pulmonary involvement.

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FRI0454

ARTERIAL STIFFNESS OF THE FOREARM IS ASSOCIATED WITH NAIL-FOLD CAPILLARY COUNT IN SSC: A NOVEL MARKER OF EARLY VASCULOPATHY?

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Background: Microvascular disease, characterised by rarefaction of capillaries, is the hallmark of systemic sclerosis. Remarkably, obliteration of the ulnar and radial artery is regularly observed, implicating involvement of the larger forearm arteries. Pulse wave velocity (PWV) is a widely accepted non-invasive measure for arterial stiffness and may serve as an early biomarker of forearm artery involvement, before the occurrence of irreversible arterial obliteration.

Objectives: The aim of the current study was to investigate arterial stiffness of the aorta and of the upper extremities in SSc patients compared to healthy controls and to correlate these findings with nail-fold capillary count, skin involvement, and extent of disease.

Methods: In total, 19 SSc patients (median age 51 years, 68% female) and 19 age and gender matched healthy controls (median age 53 years, 68% female) were included. Patients characteristics were obtained and blood was drawn. Measurements of arterial stiffness were carried out by using the SphygmoCor System (AtCor Medical, Sydney, Australia) and pressure waveforms were measured at four sites, i.e. carotid, femoral, brachial, and radial. Aortic PWV was defined as carotid-femoral (cf) PWV. Upper extremity PWV was measured as carotid-brachial (cb) and carotid-radial (cr) PWV, and the ratio between cbPWV/crPWV was used as an indication of the relative change in PWV in the forearm. Capillary count was defined as the mean capillary count per 3 mm of 8 fingers. Skin involvement was assessed by the modified rodnan skin score. The number of ACR/EULAR 2013 criteria points was used as a surrogate for extent of disease.

Results: Upper extremity PWV measures were significantly higher compared to aortic PWV in patients and in controls (SSc: p<0.001; HC: p=0.03), but did not significantly differ between both groups (table 1). CbPWV/crPWV ratio correlated strongly with capillary count (r=-0.55, p=0.022, figure 1) in SSc patients with a borderline significant trend in regards to its relation with the extent of disease (r=0.48, p=0.053) and skin involvement (r=0.41, p=0.10).