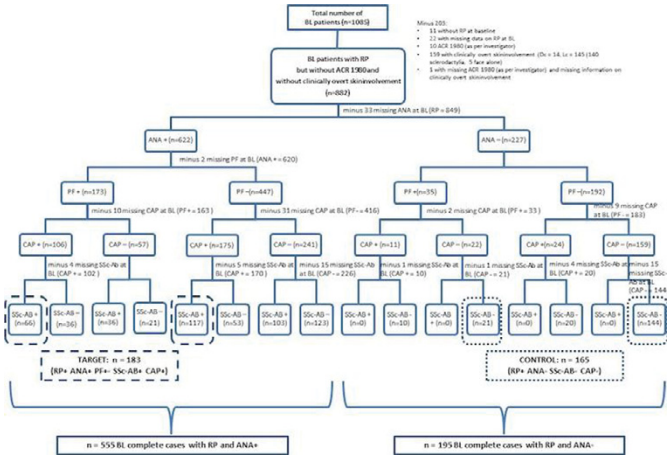

Conclusions: The VEDOSS cohort presents predominantly an "Early" NVC SSc pattern. Notably the prevalence of NVC SSc patterns was higher in the ANA+ than ANA- stratum. This evidence further reflects the pivotal role of NVC in the very early diagnosis of SSc.
Disclosure of Interest: None declared
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OP0036 SEROLOGICAL BIOMARKERS OF ECM TURNOVER ARE ASSOCIATED WITH SKIN FIBROSIS AND LUNG INVOLVEMENT IN SYSTEMIC SCLEROSIS

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Background: Extracellular matrix (ECM) unbalance of the skin is a hallmark of systemic sclerosis (SSc). However, currently there is no objective tool to monitor the ECM unbalance in SSc patients allowing for better understanding of the disease stage and activity.
Objectives: We investigated the potential of serological biomarkers of ECM turnover (collagen formation and degradation) as biomarkers of skin fibrosis and internal organ involvement in SSc patients.
Methods: Peripheral blood obtained from 79 SSc patients and 19 healthy subjects was included in the study. Type I, III, IV, V and VI collagen formation (P1NP, PRO-C3, P4NP7S, PRO-C5, PRO-C6) and degradation (C3M, C4M2, C5M, C6M) biomarkers were detected by ELISA in serum. Modified Rodnan skin score (mRSS) and extent of internal organ involvement (renal, lung, vasculopathy and gastrointestinal) were recorded for SSc patients with a scoring between 0 and 4, with 0 being no involvement and 4 being severe involvement. Mann-Whitney t-test was used to test difference in the biomarker levels between the patient groups and in groups with and without internal organ involvement. Spearman's correlation coefficient investigated the association between biomarkers and clinical manifestations.
Results: SSc patients had a mean age of 63.0 years, mean disease duration of 98.3 months and a mean mRSS of 11.1. SSc patients compared to healthy individuals had higher levels of C5M, C6M and PRO-C6 ($p=0.0001$, $p<0.0001$, $p<0.0001$, respectively). The levels of type VI collagen formation and degradation (PRO-C6 and C6M) were twice as that of healthy controls (12.6 vs. 5.4 and 26.0 vs 16.7 ng/ml, respectively). C4M2, PRO-C3 and PRO-C6 was associated with skin fibrosis assessed by mRSS (Spearman's rho=0.24, 0.39 and 0.29, respectively). Patients with signs and manifestation of lower gastrointestinal lesion compared to patients without lesion had higher levels of C3M (median 10.7 vs 13.8ng/mL, $p=0.017$; figure). PRO-C6 was higher in patients with pulmonary hypertension compared to patients without any signs of pulmonary hypertension (median 9.6 vs 14.3ng/mL, $p=0.006$) with a Spearman's correlation coefficient of 0.31. C6M was higher in patients with definite pulmonary hypertension (>1) compared to patients with signs of or no pulmonary hypertension (median 22.1 vs 29.9ng/mL, $p=0.026$). P1NP was lower in patients with interstitial pneumonia, whereas C6M was higher. There was no difference in the biomarker levels with and without upper gastrointestinal lesions, renal dysfunction or vasculopathy.

	Healthy	SSc	P-value	Spearman's correlation to mRSS Rho (p-value)
C3M	12.8	13.4	–	0.21 (0.06)
C4M2	31.1	34.0	–	0.24 (0.03)
C5M	2.6	3.9	0.0001	0.03 (0.81)
C6M	16.7	26.0	<0.0001	0.18 (0.11)
P1NP	136.9	130.4	–	0.03 (0.80)
PRO-C3	14.2	20.8	–	0.39 (<0.001)
P4NP7S	286.8	290.3	–	0.19 (0.10)
PRO-C5	525.2	484.4	–	0.07 (0.52)
PRO-C6	5.4	12.6	<0.0001	0.29 (0.01)

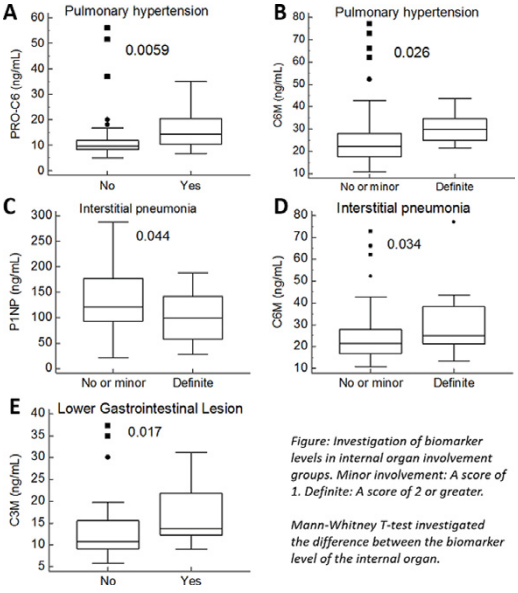

Figure: Investigation of biomarker levels in internal organ involvement groups. Minor involvement: A score of 1. Definite: A score of 2 or greater.

Mann-Whitney T-test investigated the difference between the biomarker level of the internal organ.

Conclusions: Serological biomarkers of type V and VI turnover (C5M, C6M, PRO-C6) were associated with SSc, but not serological biomarkers of type I, III and IV collagen. Especially, turnover of type VI collagen was associated with skin sclerosis, pulmonary hypertension, interstitial pneumonia and renal dysfunction. This study indicates that biomarkers of collagen turnover have a potential as new objective tool of skin fibrosis and internal organ involvement in SSc.
Disclosure of Interest: S. Kubo Speakers bureau: Bristol-Myers, A. S. Siebuhr Employee of: Nordic Bioscience, A.-C. Bay-Jensen Employee of: Nordic Bioscience, P. Juhl Employee of: Nordic Bioscience, M. A. Karsdal Employee of: Nordic Bioscience, K. Nakano: None declared, S. Nakayamada: None declared, Y. Tanaka Grant/research support from: Mitsubishi-Tanabe, Takeda, Daiichi-Sankyo, Chugai, Bristol-Myers, MSD, Astellas, Abbvie, Eisai, Speakers bureau: Abbvie, Chugai, Daiichi-Sankyo, Bristol-Myers, MitsubishiTanabe, Astellas, Takeda, Pfizer, Teijin, Asahi-kasei, YL Biologics, Sanofi, Janssen, Eli Lilly, GlaxoSmithKline
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OP0037 EVALUATION OF SKIN INVOLVEMENT IN SYSTEMIC SCLEROSIS PATIENTS BY USING TWO ULTRASOUND TRANSDUCERS WITH DIFFERENT FREQUENCY

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Background: The modified Rodnan skin score (mRSS) is the validated method to evaluate the extension of skin involvement in systemic sclerosis (SSc) and to distinguish between patients with limited cutaneous skin involvement (lcSSc, skin involvement is confined to the extremities) or diffuse (dcSSc) (1,2). Recently several studies have demonstrated that skin high frequency ultrasound (US) is a valid and reproducible technique to measure dermal thickness (DT) in patients with SSc (3–6).
Objectives: To compare the values of DT obtained by two ultrasound transducers with different frequency (18 MHz and 22 MHz) in evaluating the DT in lcSSc patients and healthy controls.
Methods: Thirty-seven lcSSc patients (mean age 62±13SD years, mean disease duration 5±5SD years) and 37 healthy controls (CNT) sex and age matched were enrolled after informed consent. Both US transducers of 18 and 22 MHz (Esaote, Genova) were used to evaluate DT in the seventeen areas of the skin (zygoma, fingers, dorsum of hands, forearms, arms, chest, abdomen, thighs, legs, feet) of SSc patients where Rodnan skin score (mRSS) is usually assessed. Skin US was also performed in the same seventeen areas of CNT, looking for DT differences in comparison with lcSSc patients. Statistical analysis was carried out by non parametric tests.
Results: DT evaluated with the 22 MHz probe was found significantly higher in all body areas in comparison with the 18 MHz transducer, both in lcSSc patients ($p<0.01$) and in CNT ($p=0.05$). The median difference of DT values between the two probes was of 0.11 millimetres in lcSSc patients (minimum 0.0023, maximum 0.28 mm) and 0.01 millimetres in CNT (minimum 0.0029, maximum 0.03 mm). Of interest, in lcSSc DT evaluated by 18 MHz transducer was recognized significantly higher ($p<0.001$) also in four out of six skin areas where the mRSS was found normal (score=0) (upper-arms, chest and abdomen), with exclusion of thighs ($p=0.08$), in contrast with the classification of lcSSc. However, by using the 22

MHz transducer a statistically significantly higher median DT was showed in all skin areas, included thighs ($p<0.01$). Finally, a positive statistically significant correlation was observed between the two transducers in the evaluation of DT ($p<0.0001$), as well as between both probes and mRSS ($p<0.0001$ for both).
Conclusions: This study suggests that subclinical dermal involvement may be detectable by skin high frequency US already in patients with limited cutaneous SSc. This study confirms that DT can be better assessed in SSc patients by using a 22 MHz US probe, and suggests that DT might be underestimated by using US probes of lower frequency (18 MHz). However, the DT values obtained using both probes resulted significantly correlated together and with the mRSS.
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OP0038 MYOSITIS AUTOANTIBODIES OUTPERFORM CLINICAL SUBGROUP CLASSIFICATION IN PREDICTING MUSCLE WEAKNESS IN MYOSITIS PATIENTS

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Background: Myositis patients may be classified as belonging to one of four clinical groups: dermatomyositis (DM), polymyositis (PM), clinically amyopathic dermatomyositis (CADM) or necrotizing myositis (NM). Alternatively, myositis patients may be classified according to myositis autoantibody status.
Objectives: The aim of this study was to determine whether clinical groups or myositis autoantibodies provide better prognostic categories with regard to muscle involvement in these patients.
Methods: All Johns Hopkins Myositis Center patients from 2002 to 2015 with a myositis specific autoantibody confirmed by two different immunologic techniques were included. Autoantibody groups accounting for less than 2% of the final sample size were excluded. Strength (analyzed as the average of deltoid and hip flexor strength using Kendall's scale) and log transformed CK levels were compared between the different autoantibody groups using multilevel regression models adjusted for age, time from disease onset, sex, race and treatments. Models with different combinations of key variables were compared using the likelihood ratio test to ascertain if autoantibody groups and clinical subgroups provided the same amount of information regarding muscle weakness and CK levels over time.
Results: 483 patients with 4181 visits were included and 10 different autoantibody groups were identified. Muscle weakness and CK levels followed a gradient among both antibody and clinical groups. Anti-SRP patients had the greatest weakness, followed by anti-HMGCR, anti-Mi2 and anti-NXP2, and then anti-Jo1. CK levels were highest in anti-HMGCR patients, followed by anti-SRP, anti-PL7, anti-Jo1 and anti-Mi2. Interestingly, strength and CK levels were dissociated in two groups: anti-NXP2 patients had significant weakness with low CK levels and anti-PL7 patients were relatively strong despite high CK levels. Multilevel regression models showed autoantibody groups explained the strength and the CK variability better than the clinical groups (AIC difference>20). Indeed, adding clinical groups to a model using only autoantibodies did not improve the model's ability to predict strength (p=0.2) and only mildly improved its ability to predict CK (p=0.01). In comparison, adding the autoantibodies to a model using the clinical groups resulted in a marked improvement in predicting both CK and strength (both $p<0.001$).
Conclusions: In patients with myositis, autoantibody status predicts strength and CK levels better than clinical grouping.
Disclosure of Interest: None declared
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WEDNESDAY, 14 JUNE 2017

SLE, Sjögren's and APS - clinical aspects

OP0039 A POPULATION-BASED STUDY ON MORTALITY AND THE INFLUENCE OF MEDICATION USE IN 4356 PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS AND 21845 MATCHED CONTROLS FROM THE UNITED KINGDOM

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Background: Systemic lupus erythematosus (SLE) has been associated with an increased mortality rate. However, population-based data on all-cause, age-specific and sex-specific mortality risk are limited and data on the influence of medication exposure on mortality risk in SLE are scarce.
Objectives: To estimate the magnitude of the risk from all-cause, age-specific, and sex-specific mortality in patients with SLE and relative risks compared with matched controls, and to evaluate the influence of medication exposure on mortality risk in SLE.
Methods: We conducted a population-based cohort study using the Clinical Practice Research Datalink (from 1987 to 2012). Each SLE patient (n=4356) was matched with up to 6 controls (n=21845) by age and sex. Multivariate Cox regression analysis estimated adjusted relative rates (RR) of mortality, and time interaction terms to evaluate mortality timing patterns. Time-dependent Cox models were used to evaluate the association of glucocorticoid use and hydroxychloroquine use on mortality and were adjusted for age, sex, lifestyle parameters, comorbidities and comedication.
Results: A total of 442 out of 4356 SLE patients died during the study period. Patients with SLE had an increased mortality rate for all-cause mortality compared with age- and sex-matched subjects, after adjustment for confounders (adjusted RR 1.80, 95% CI 1.57–2.08). Glucocorticoid use in the previous six months raised the mortality rate while the adjusted RR was 45% decreased with low dose hydroxychloroquine use. The RR was highest in patients aged 18–39 years (adjusted RR 4.87, 95% CI 1.93–12.3) and slightly higher in females (adjusted RR 1.82, 95% CI 1.56–2.13) compared to male patients (adjusted RR 1.68, 95% CI 1.19–2.39). The mortality rate was significantly increased for patients with a history of dementia, seizures, diabetes, cancer, and renal disease (Table 1).

Table 1. Risk of all-cause mortality within SLE patients (n=4356), stratified according to organ damage (reference = no risk factor)

	Person years (x1000)	Deaths	IR (/1000)	Adjusted RR* (95% CI)
Dementia	0.1	14	140.0	2.99 (1.74–5.14)
Seizures	1.4	37	26.4	2.33 (1.66–3.28)
Cerebrovascular event	1.9	73	38.4	1.28 (0.99–1.65
Renal disease	2.0	86	43.0	1.40 (1.09–1.78)
Osteoporotic fracture	5.1	110	21.6	1.06 (0.85–1.32)
Diabetes mellitus	0.9	45	50.0	1.90 (1.39–2.59)
Malignancy	2.0	95	47.5	1.90 (1.50–2.40)

*Adjusted for: recent use of corticosteroids, recent use of antimalarials, recent use of benzodiazepines.

Conclusions: Patients with SLE have a 1.8-fold increased mortality rate compared with the general population. Glucocorticoid use, female sex and young age are associated with an increased mortality risk while low dose hydroxychloroquine use significantly reduces the mortality rate. In addition, special attention should be paid to lupus patients with neuropsychiatric complications, diabetes, malignancy or renal disease since these subgroups of patients are at high risk of death.
Disclosure of Interest: I. Bultink Grant/research support from: Lilly Netherlands, MSD, Amgen, UCB, A. Lalmohamed: None declared, F. de Vries: None declared
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OP0040 INTEGRATION OF SALIVARY-GLAND ULTRASONOGRAPHY IN CLASSIFICATION CRITERIA FOR PRIMARY SJÖGREN'S SYNDROME: AN INTERNATIONAL VIGNETTE-BASED STUDY

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Background: The recent classification criteria sets for primary Sjögren's syn-