**PSI12**

**ACTIVATION OF LIVER X RECEPTORS INHIBITS EXPERIMENTAL FIBROSIS BY INTERFERING WITH INTERLEUKIN-6 RELEASE FROM MACROPHAGES**

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**Background.** Liver X receptors (LXRs) are orphan nuclear receptors with emerging roles in metabolic and autoimmune diseases. Here, we investigated the role of LXRs in experimental skin fibrosis and evaluated their potential as anti-fibrotic targets for systemic sclerosis (SSc) and other fibrotic diseases.

**Methods.** We studied the role of LXRs in bleomycin-induced skin fibrosis and in the skin of patients within early stages of SSc. Objective: To correlate the prevalence of anti-type V collagen with different clinical manifestations of SSc, disease duration and positivity of anti-type V collagen.

**Summary of the results.** LXR activation by the LXR agonist T0901317 had potent anti-fibrotic effects in both bleomycin-induced skin fibrosis and Tsk-1 mice as assessed by skin thickness, hydroxyproline content, and the number of myofibroblasts. The anti-fibrotic activity of LXRs was particularly prominent in the inflammatory bleomycin-model in which LXR activation reduced skin thickening in a dose-dependent manner by up to 64%, the hydroxyproline content by up to 91% and the number of myofibroblasts by up to 91%.

**Conclusions.** We identified LXRs as novel therapeutic targets for SSc and other fibrotic diseases, a yet unknown aspect of these nuclear receptors. Note, fibroblasts were not the direct targets of the anti-fibrotic effects of LXRs. By contrast, LXR activation inhibited macrophage infiltration in fibrotic tissue and decreased the release of the pro-fibrotic cytokine interleukin-6 from macrophages, resulting in reduced fibroblast activation and collagen release.

**PSI13**

**CORRELATION BETWEEN SHORTER DURATION IN SYSTEMIC SCLEROSIS (SSC) AND ANTI-COLLAGEN TYPE V**

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**Introduction.** Collagen type V is a highly immunogenic molecule with preserved globular and telopeptide domains found inside heterotypic fibrils in the skin in association with collagen types I and III. Experimental studies have shown that rabbit’s immunization with human type V collagen triggers epitope spreading with activation of Th2 lymphocytes, increased release of cytokines, augmented B lymphocytes activation and production of high titters of anti-type V collagen. Therefore, an animal model of SSC where rabbits immunized with collagen type V developed a disease similar to human disease, with vasculopathy and tissue fibrosis. Studies in humans also have shown that type V collagen is overexpressed in the skin of patients within early stages of SSC. Objective: To correlate the prevalence of anti-type V collagen with different clinical manifestations of SSC, disease duration and severity.

**Results.** From 2005 to 2008, 100 patients with a definite diagnosis of SSc were included in the study; 3 age, gender, and smoking habits matched controls were selected for each patient. A committee of experts evaluated blindly occupational exposure to crystalline silica, white spirit, organic solvents, ketones, welding fumes, epoxy resins, pesticides; an occupational exposure score was calculated for all subjects.

**Conclusions.** Increased ORs for SSc was found for: crystalline silica (>0.0001), white spirit (p=0.0001), aromatic solvents (p=0.0002), chlorinated solvents (p=0.0014), trichlorethylene (p=0.044), ketones (p=0.002) and welding fumes (p=0.021). Elevated risk associated with high final cumulative score in SSc was observed for: crystalline silica, white spirit, chlorinated solvents, trichlorethylene, aromatic solvents, any type of solvents, ketones and welding fumes. A marked association between SSc and occupational exposure was further found for: 1) crystalline silica, chlorinated solvents, trichlorethylene, white spirit, ketones and welding fumes in male patients; and 2) white spirit, aromatic solvents, any type of solvent and ketones in female patients.

**Conclusion.** The results show the impact of occupational risk factors in the development of SSc for: crystalline silica, white spirit, aromatic solvents, chlorinated solvents, trichlorethylene, ketones and welding fumes. The risk associated with high cumulative exposure was markedly increased in SSc. Finally, our series shows that the association of SSc and occupational exposure was variable according to gender.

**PSI14**

**SYSTEMIC SCLEROSIS AND OCCUPATIONAL EXPOSURE: A CASE CONTROL STUDY OF 100 PATIENTS AND 300 CONTROLS**

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**Objective.** This case control study assessed: the relationship of systemic sclerosis to occupational exposure, the risk of SSc related to occupational exposure in male and female patients.

**Methods.** From 2005 to 2008, 100 patients with a definite diagnosis of SSc were included in the study; 3 age, gender, and smoking habits matched controls were selected for each patient. A committee of experts evaluated blindly occupational exposure to crystalline silica, white spirit, organic solvents, ketones, welding fumes, epoxy resins, pesticides; an occupational exposure score was calculated for all subjects.

**Results.** Increased ORs for SSc was found for: crystalline silica (>0.0001), white spirit (p=0.0001), aromatic solvents (p=0.0002), chlorinated solvents (p=0.0014), trichlorethylene (p=0.044), ketones (p=0.002) and welding fumes (p=0.021). Elevated risk associated with high final cumulative score in SSc was observed for: crystalline silica, white spirit, chlorinated solvents, trichlorethylene, aromatic solvents, any type of solvent, ketones and welding fumes. A marked association between SSc and occupational exposure was further found for: 1) crystalline silica, chlorinated solvents, trichlorethylene, white spirit, ketones and welding fumes in male patients; and 2) white spirit, aromatic solvents, any type of solvent and ketones in female patients.

**Conclusion.** The results show the impact of occupational risk factors in the development of SSc for: crystalline silica, white spirit, aromatic solvents, chlorinated solvents, trichlorethylene, ketones and welding fumes. The risk associated with high cumulative exposure was markedly increased in SSc. Finally, our series shows that the association of SSc and occupational exposure was variable according to gender.
PS115

A GENOME-WIDE ASSOCIATION STUDY FOLLOW-UP UPGRADE SUGGESTS A POSSIBLE ROLE FOR PPARG IN SYSTEMIC SCLEROSIS SUSCEPTIBILITY


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Introduction. A recent genome-wide association study (GWAS) comprising a French cohort of systemic sclerosis (SSc) reported several non-HLA single-nucleotide polymorphisms (SNPs) showing a nominal association in the discovery phase. We aimed to perform a follow-up strategy in order to identify previously overlooked susceptibility variants.

Methods. Sixty-six non-HLA GWAS-genotyped SNPs showing a p-value <10-4 in the discovery phase of the French SSc GWAS were analyzed in the first step of this study performing a meta-analysis which combined data from the two published SSc GWAS. A total of 2,921 SSc patients and 6,963 healthy controls were included in this first step. Two SNPs, PPARG rs310746 and CIRNRN9 rs6832151, were selected for genotyping in the replication cohort (1,068 SSc patients and 6,762 healthy controls) according to the results of the first step. Genotyping was performed using TaqMan SNP genotyping assays.

Results. In the first step of our study, we found nominal associations for both PPARG rs310746 (PMH = 1.90 x 10-6, OR= 1.28) and CIRNRN9 rs6832151 (PMH = 4.30 x 10-6, OR= 1.17) genetic variants with SSc. In the replication phase, we observed a trend of association for PPARG rs310746 (p-value = 0.066, OR = 1.17). The combined overall Mantel-Haenszel meta-analysis of all the cohorts included in the present study revealed that PPARG rs310746 remained associated with SSc with a nominal non-genome wide significant p-value (PMH = 5.00 x 10-7, OR= 1.25). No evidence of association was observed for CIRNRN9 rs6832151 either in the replication phase or in the overall pooled-analysis.

Conclusion. Our results suggest a role of PPARG gene in the development of SSc.

PS116

PREVALENCE OF ANTI-RNA POLYMERASE III ANTIBODIES IN SYSTEMIC SCLEROSIS: NEW DATA FROM A FRENCH COHORT, SYSTEMATIC REVIEW AND META-ANALYSIS

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Objectives. Studies assessing the prevalence of anti-RNA polymerase III antibodies (ARA) in systemic sclerosis (SSc) have yielded a wide range of results. One hundred and thirty-three French SSc patients were tested for ARA, reported several non-HLA single-nucleotide polymorphisms (SNPs) showing a nominal association in the discovery phase. We aimed to perform a follow-up strategy in order to identify previously overlooked susceptibility variants.

Methods. Sixty-six non-HLA GWAS-genotyped SNPs showing a p-value <10-4 in the discovery phase of the French SSc GWAS were analyzed in the first step of this study performing a meta-analysis which combined data from the two published SSc GWAS. A total of 2,921 SSc patients and 6,963 healthy controls were included in this first step. Two SNPs, PPARG rs310746 and CIRNRN9 rs6832151, were selected for genotyping in the replication cohort (1,068 SSc patients and 6,762 healthy controls) according to the results of the first step. Genotyping was performed using TaqMan SNP genotyping assays.

Results. In the first step of our study, we found nominal associations for both PPARG rs310746 (PMH = 1.90 x 10-6, OR= 1.28) and CIRNRN9 rs6832151 (PMH = 4.30 x 10-6, OR= 1.17) genetic variants with SSc. In the replication phase, we observed a trend of association for PPARG rs310746 (p-value = 0.066, OR = 1.17). The combined overall Mantel-Haenszel meta-analysis of all the cohorts included in the present study revealed that PPARG rs310746 remained associated with SSc with a nominal non-genome wide significant p-value (PMH = 5.00 x 10-7, OR= 1.25). No evidence of association was observed for CIRNRN9 rs6832151 either in the replication phase or in the overall pooled-analysis.

Conclusion. Our results suggest a role of PPARG gene in the development of SSc.

PS117

SEMAPHORIN 3A AS A POSSIBLE IMMUNOREGULATOR IN SYSTEMIC SCLEROSIS

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Background. Semaphorin 3A (sema 3A), is now recognized as a potent immunoregulator during all stages of the immune response, early initiation as well as late phases of inflammatory processes. Sema 3A expression has been recognized on T regulatory cells as a suppressive marker, contributing to the regulatory properties of these cells. Defective expression of sema 3A in CD4+ T cells derived from rheumatoid arthritis (RA) patients has been reported. T reg cells in Ssc were reported to be reduced in amount and function. The expression of semaphorin 3A hasn't been evaluated in systemic sclerosis (SSc) thus far.

Objective. To measure expression of semaphorin 3A in serum and on regulatory T-cells in SSc patients and normal controls and correlate it with demographic, clinical and laboratory parameters in SSc.

Methods. SSc patients were evaluated for demographics, clinical manifestations, routine laboratory results, serum autoantibodies, semaphorin 3A serum levels (measured by commercial ELISA kit) and expression on regulatory T cells CD4+ CD25+ (by flow cytometry), nailfold capillaroscopy patterns, pulmonary function tests, echocardiograms, high resolution lung CT scans, modified Rodnan skin score (mRSS), Medger disease severity scale and Valantiety activity index.

Results. 27 SSc patients were evaluated and compared with healthy controls. 10 SSc patients had diffuse disease with lung fibrosis and 17 had limited cutaneous disease. Sema 3A concentration in SSc was lower than healthy controls both as measured by ELISA 14.4±s 6 mg/ml vs. 27.1±4.8 mg/ml (p<0.001) and by flow cytometry on regulatory T cells 61.7±15.7 % vs. 88.7±3.6 % (p<0.001). Sema 3A levels negatively correlated with the disease duration B = 0.4, p-value=0.036 but not with disease severity.

Conclusion. This is the first study to demonstrate low serum levels of sema 3A in SSc patients. The reduced expression of sema 3A has specifically been demonstrated on regulatory T cells and was found to worsen with disease duration. These findings are in line with previous studies that described Treg deficit in SSC which is related to disease duration. Low level of sema 3A, a regulator of autoimmune activity, may play a role in the pathogenesis of SSc. Further studies are needed to further understand this novel relationship.

PS118

INFLUENCE OF ALPHA 2 DO COLLAGEN V OVEREXPRESSION IN PHYSIOPATHOLOGY OF FIBROSIS SYSTEMIC SCLEROSIS PATIENTS

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Background. Systemic sclerosis (SSc) is disease of unknown etiology its pathophysiology is thought to be based on vascular alterations as well as immunological and fibrotic processes. Collagen V assembles into diverse molecular forms and (1V/2V)2VX controls fibrosis. We have recently demonstrated increased mRNA o2(V) expression in early SSc correlated with disease activity (Autoimmun Rev, 11(11):827-35, 2012). We evaluate if the α1(V)2 and α2(V)-containing fibrils leads to ultrastructural modifications at dermis and in fibroblasts culture of skin biopsy and related the different subtypes with the fibrosis.

Methods. Biopsies from 5 early-SSc female patients (ACR criteria), with <2 years of diagnosis and treatment naive and 5 samples of normal skin from healthy individuals were studied. All biopsies were submitted for electron microscopy, immunofluorescence to identify α1(V)2 and α2(V) were evaluated and compared with normal skin. The expression of COLSA1 and COLSA2 expression and were detected by PCRseq and sequencing of COLSA1 and COLSA2 chains cDNA was performed.

Results. Ultrastructural level by transmission electron microscopy results showed a dense packing of collagen in epidermal-dermal interface, characteristic marks of extracellular matrix alterations, including highly dense packing
of collagen and vascular basement membrane thickening was frequently seen in superficial derm 3D-reconstruction revealed that α1(V)(2) and α2(V) exhibited dense fluorescence around dermal fibroblasts, along the small vessels and capillary walls. The α1(V)(2)/2 in fibroblasts displayed a granular intracytoplasmic and perinuclear pattern with higher intensity in SSc compared to controls. In contrast, a dense filamentous protrusion around the nucleus and pericellular pattern was found for α1(V)(2) in dermal fibroblasts from SSc patients. Morphometric analysis revealed that the expression of α2(V) was significantly higher than controls (p=0.05 and p=0.001, respectively) and was observed increased α2(V) expression when compared to α1(V)(2), but in the epidermal-dermal, near the basement membrane of papillary dermis, the α1(V)(2) expression was absent. Immunohistostaining confirming the increased production of this chain. The COLV A1/ COLVA2 gene indicate that in dermal fibroblasts from SSc patients was higher than that observed in normal fibroblasts (p<0.05), but no difference was found in polymorphic genes COL5A1 and COL5A2.

Conclusion. We conclude that overexpression of α2(V) and absence of chains α1(V)(2) alters the skin histoarchitecture, contributed by the disarrangement and thickness mainly in the early stage and may be related with cutaneous severity.

PS119

SERUM FREE LIGHT CHAINS OF IMMUNOGLOBULINS ARE ASSOCIATED WITH DISEASE ACTIVITY IN SYSTEMIC SCLEROSIS: A PROSPECTIVE AND CONTROLLED STUDY

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Introduction. There is a free light chains excess production over immunoglobulin heavy-chain synthesis by B lymphocytes. Serum free light chains (SFLC) are high in monoclonal gammapathy and can serve as a diagnosis tool for myeloma. Recent studies have suggested that SFLC could be interesting biomarkers for diagnosis and disease activity assessment in autoimmune diseases like Sjögren syndrome, lupus or rheumatoid arthritis. There are no data in systemic sclerosis (SSc).

Patients and Methods. 134 patients with SSc were prospectively enrolled. Following data were gathered: age at diagnosis, SSc subtypes, visceral involvement, biological manifestations including rheumatoid factor and beta2 microglobulin, SSc activity score and association with other autoimmune diseases. SFLC were assessed by Combylité® (The Binding Site, Birmingham, RU). SFLC were also assessed in a control group of 401 blood donors who were matched for age and sex.

Results. Mean and median SFLC values were significantly higher in SSc than in controls (median : 19.99 mg/L, mean 24.03 mg/L vs median 15.43 mg/L, mean 17.50 mg/L, respectively, p<0.05). In univariate analysis, there was a significant correlation between SFLC and the modified Rodnan score, past or current digital ulcers, systolic pulmonary arterial pressure, DLCO and EUSTAR as well as correlation between SFLC and the modified Rodnan score, past or current digital ulcers. The SFLC were also correlated with erythrocyte sedimentation rate, CRP and IgG, IgA, IgM levels. While there was a correlation with the presence of a particular autoantibody, we did not find a significant association with the presence of another autoimmune disease.

Conclusion. Our study is the first to assess SFLC in SSc. We show that SFLC are higher in SSc than in controls. Moreover SFLC is significantly correlate with activity and severity of the disease. Our results add an additional line of evidence that B cells activation plays probably a role in the pathophysiology of SSc.

PS120

COLLAGEN CROSS LINKING ENZYMES LOXL2 AND PLOD2 SHOW NO ASSOCIATION WITH SYSTEMIC SCLEROSIS

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Background. Scleroderma or systemic sclerosis (SSc) is a rare complex disease. The exact aetiology of SSc is not fully understood however genetic factors have shown to play a role in disease pathogenesis. SSc has shown evidence of dysregulated pruning of the microvascular and immune system. To date, a number of candidate gene studies and Genome-wide association studies (GWAS) have shown the replication of a number of key immunological loci. Here we genotyped polymorphisms across two collagen cross linking enzymes LOXL2 (Lysyl oxidase-like protein 2) and PLOD2 (Pro-collagen-lysine, 2-oxoglutarate 5-dioxygenase 2) to ascertain a potential pathological role in SSc.

Methods. 728 SSc cases and 260 healthy controls were genotyped for polymorphisms in LOXL2 and PLOD2 as part of a larger genotyping study. All patients and controls were of Caucasian decent and were categorised according to three mutually exclusive autoimmune status: anti-topoisomerase-1 (ATA), antici-
ntromere (ACA) and anti-RNA-polymerase (ARA). Patients were further clas-
sified into sub-phenotypes according to major organ involvement; pulmonary hypertension, pulmonary fibrosis and renal crisis. All genotyping was performed by the KASP system (allele specific PCR, KBioscience, UK). All genotype data and sub-phenotype analysis was performed using PLINK.

Results. Our cohort consisted of 274 (38%) patients with lung fibrosis, 112 (15%) with pulmonary hypertension and 63 (9%) with renal crisis. 255 (35%) pa-
tients were positive for ACA, 155 (21%) patients were positive for ATA, and 140 (19%) patients were positive for ARA. The SSc cases and the healthy controls were genotyped and all SNPs and individuals passed quality control checks for Hardy-Weinberg equilibrium (p=0.05) and missingness (p=0.1). A case-control sub-phenotype analysis were performed using PLINK, of which no association was found in any individual SNP or haplotype in either loci.

Conclusion. Here we show two loci LOXL2 and PLOD2 which show poten-
tial functional contribution to SSc pathogenesis, but which to not demonstrate a genetic association. As our study cohort was small we were hindered by the low numbers of each phenotype and therefore may lack statistical power, how-
ever our cohort is clearly defined and we would expect to find an association if present. Our data suggests it is unlikely SNPs in LOXL2 and PLOD2 contribute to the genetics of SSc pathogenesis however replication of these polymorphisms would confirm our findings. Although no genetic association was found, these loci may still contribute to the functional pathways of disease manifestations and warrant further investigation.
PS122

A LOSS OF TELOCYTES ACCOMPANIES FIBROSIS OF MULTIPLE ORGANS IN SYSTEMIC SCLEROSIS

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Objective. Telocytes are a distinct population of stromal (interstitial) cells recently identified in a variety of tissues and organs. By their extremely long cytoplasmic processes telocytes form a three-dimensional network that functions as a scaffold to define the correct organization of tissues/organisms during pre-natal life or their repair/renewal in post-natal life. According to their specific locations within different organs, telocytes may participate in intercellular signaling, either by cell-to-cell contacts or by secreting paracrine signaling molecules, immune surveillance, neurotransmission, and tissue regeneration by forming tandem cell structures with stem cell niches. Recently, we have shown that telocytes display severe ultrastructural damages suggestive of ischaemia-induced cell degeneration and are progressively lost from the clinically affected skin of systemic sclerosis (SSc) patients. On this basis, in the present study we investigated the presence and distribution of telocytes in the internal organs of SSc patients.

Methods. Archival paraffin-embedded samples of gastric wall, myocardium and lung were obtained from SSc patients and controls. Tissue sections were stained with Masson’s trichrome to detect fibrosis. Telocyte distribution was investigated on sections subjected to CD34 immunostaining and haematoxylin counterstain. CD34/CD31 double immunofluorescence was performed to unequivocally differentiate telocytes (CD34-positive/CD31-negative) from vascular endothelial cells (CD34-positive/CD31-positive).

Results. The histopathological examination of Masson’s trichrome-stained sections showed the typical fibrotic changes of SSc. A generalized fibrosis affected all SSc gastric wall layers, with most severe changes in the muscularis mucosae, submucosa and muscularis propia. Few telocytes entrapped in the fibrotic extracellular matrix were found in the muscularis mucosae and submucosa. In the muscularis propia, the network of telocytes was discontinuous or even almost completely absent around smooth muscle bundles and cells, and around ganglia and nerve strands at the myenteric plexus. Wide areas of fibrosis, hypertrophy of myocardi-ald fibers and macrophage infiltration were observed in SSc myocardium. Telocytes disappeared from these fibrotic areas. Lung sections from SSc patients displayed the typical features of non-specific interstitial pneumonia with both diffuse cellular inflammation and collagen deposition. Few or no telocytes could be observed in the thickened alveolar septa and in the interstitial space around terminal bronchioles.

Conclusions. In SSc, the loss of telocytes does not occur only in the skin, but it is a widespread process affecting also the internal organs targeted by the fibrotic process. Since telocytes are believed to be key players in the regulation of tissue/organ homeostasis, our data suggest that telocyte loss may have important pathological implications in SSc.

PS123

INCREASED FREQUENCY OF TH1 AND TC1 LYMPHOCYTES PRODUCING TUMOR NECROSIS FACTOR ALPHA IN PERIPHERAL BLOOD OF LATE-STAGE SYSTEMIC SCLEROSIS

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Background/Purpose. Substantial evidence supports the implication of immune-activated cells, cytokines and chemokines in the pathogenesis of systemic sclerosis (SSc). The frequency of T cells expressing activation markers is increased in the peripheral blood (PB) of SSc patients. Proinflammatory cytokines, such as IL-2, TNF-α and IFN-γ, seem to be mostly involved in immune responses at early stages of the disease. However, discrepancies exist between the results of several studies. We undertook the present study to investigate the pattern of expression of proinflammatory cytokines by PB Th1 and Tc1 populations and to explore associations with disease duration.

Methods. Forty SSc patients and 18 healthy controls (HC) were included. All SSc patients fulfilled the American College of Rheumatology Criteria for the classification of SSc (limited cutaneous SSc (lCSSc, n=29) or diffuse cutaneous SSc (dCSSc, n=11), according to LeRoy et al.). A further subdivision was made, based upon the duration of disease, as early- (n=11) and late-stage (n=30), and these groups were individually compared with HC. A thorough clinical evaluation was performed and registered.

All patients signed an informed consent and provided a PB sample, which was processed to separately analyze the intracellular expression of IL-2, TNF-α and IFN-γ in Th1 and Tc1 cell populations. Data was statistically analyzed using the SPSS® version 20.0. Mann-Whitney and Kruskal-Wallis tests were used to evaluate differences between groups. Correlations between continuous variables were assessed by Spearman’s correlation coefficient. P values <0.05 were considered statistically significant.

Results. The mean age was 56.0±11.9 and 51.7±9.9 years for SSc patients and HC, respectively. Females represented 77.5% of SSc and 83.3% of the control group. The mean disease duration was 9.6±8.55 years and the mean mRSS was 11.60±7.65. The frequency of Th1 and Tc1 circulating cells was not statistically different between SSc patients and HC. The percentage of Th1 and Tc1 cells producing TNF-α was significantly higher in late-stage than in early-stage SSc (p=0.034 and p=0.005, respectively). The percentage of Th1 cells producing IFN-γ was significantly lower in early-stage than in late-stage SSc (p=0.017). No statistically significant differences were observed between early and late-stage SSc, concerning IL-2 expression among Th1 and Tc1 cells and IFN-γ expression among Th1 cells.

Conclusion. The frequency of TNF-α-producing Tc1 cells was higher in late-stage SSc. The potential pathogenic relevance of these observations justifies further investigation, concerning the profile of proinflammatory cytokines and their potential involvement in different stages of the disease.

PS124

HELICOBACTER PYLORI AS A TRIGGER OF SYSTEMIC SCLEROSIS: IMMUNOLOGICAL ASPECTS

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Introduction. Helicobacter pylori infection has been considered a potential trigger of systemic sclerosis (SSc), possibly via a mechanism of molecular mimicry involving H. pylori heat shock 60 kDa (hsp60) and SSc-related autoantigens.

Aim. The aim of the study was to investigate the fine specificity of antigen-specific immune responses against the immunodominant H. pylori antigens in patients with SSc, and compare it with that seen in other rheumatic diseases. We also assessed the role of microbial/self molecular mimicry in the induction of H. pylori-related SSc autoantibody reactivity.

Methods. A total of 56 H. pylori-infected individuals were studied including 19 SSc patients, 23 patients with other rheumatic diseases (Sjögren’s syndrome, n=16, psoriatic arthritis, n=7) and 14 normal controls. Antibody reactivity to individual H. pylori antigens was assessed by immunoblotting and line dot assay (EUROMMUN, Germany). Autoantibody reactivity was investigated using ELISA (INOVA) and line dot assays (EUROMMUN). Inhibition studies were performed using recombinant hsp60 or purified H. pylori extracts (EUROMMUN). To assess the role of microbial/self molecular mimicry, serum samples from H. pylori-infected SSc pre-incubated with purified hsp60 or H. pylori antigens in order to see if they loose their autoantibody reactivity against Scl-70, centromere or other SSc-related autoantigens were made.

Results. Antibody reactivities to H. pylori antigens such as hsp60, VacA, CagA, BabA2, ompB, HopM, HopB, PEX, hopK, TonB, TPX, NapA, TsaA, UreA, UreB, UreG, FabG, HP0175, HP0318 did not differ between SSc patients and controls (pathological or healthy). Pre-incubation of serum samples from SSc patients with H. pylori extracts abolished reactivity to H. pylori antigens (60-95%) but did not alter reactivity to SSc-autoantigens, such as Scl-70 or centromere autoantibodies (less than 7% inhibition).

Conclusion. The fine specificity of antibody responses to H. pylori antigens in patients with SSc does not differ from other autoimmune rheumatic diseases. Molecular mimicry and immunological cross-reactivity involving H. pylori and SSc autoantigens does not appear to play a role in the induction of humoral autoimmune responses in SSc.
PS125

ROLE OF ANGIOSTATIN AND ENDOSTATIN IN SYSTEMIC SCLEROSIS

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Systemic Sclerosis (SSc) is a connective tissue disease characterized by vascular injury and widespread fibrosis involving the skin and various internal organs, which results from an imbalance between proangiogenic and antiangiogenic factors. Angiostatin and endostatin are proteolytic fragments of different extracellular proteins known for having antiangiogenic activity.

The aim of this study was to determine the concentrations of circulating endostatin and angiostatin in patients with SSc and to assess a relationship between these concentrations and disease subtypes (pre-scleroderma, limited SSc - lcSSc, and diffuse SSc - dcSSc), evolution phase (early, intermediate and late), different organ involvement (according to Medsger score) and nailfold capillaroscopic changes.

Sixty-one consecutive patients were selected from a 190-patients-population with SSc, at the Clinical Immunology Unit of a Portuguese hospital, with later exclusion of four patients. Forty-seven patients fulfilled the American College of Rheumatology criteria for SSc while the remaining ten were classified as pre-scleroderma patients.

Endostatin (p<0.001) and angiostatin (p=0.005) were found to be significantly higher in patients with SSc than in healthy controls. Also, it was shown that angiostatin levels were elevated in dcSSc (p=0.025) and lcSSc (p=0.014), while endostatin was increased in all SSc subtypes - pre-scleroderma, lcSSc and dcSSc (p<0.001). Likewise, analysis according to evolution phase found that endostatin was elevated in all stages (p<0.001) while angiostatin was only significantly higher in intermediate (p=0.037) and late phase of disease (p=0.015). Moreover, it was shown that endostatin was increased in keSSc, with or without CREST syndrome (p<0.001), and angiostatin was exclusively elevated in lcSSc patients with CREST (p=0.025). Analysis of endostatin and angiostatin concentrations in various stages of organ involvement and of nailfold capillaroscopic changes found no significant differences.

These results are in consonance with the ones found in previous studies, which also concluded that endostatin and angiostatin concentrations were elevated in SSc patients, although contradictory results were reported in regard to endostatin. Additionally, we recognised the important role that endostatin might play as an early marker of disease and that angiostatin becomes increasingly relevant as disease advances. At last, finding increased concentrations of angiostatin only in CREST patients made us wonder – could there be different pathogenic mechanisms in limited SSc?

PS126

ROLE OF CD8+ LYMPHOCYTES IN SYSTEMIC SCLEROSIS

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Introduction. Scleroderma (SSc) is a rare and heterogeneous disease involving the connective tissue and microvasculature but its complete pathogenesis remains unclear. The interrelationship between the vascular endothelium and cells of the immune system, highlighting the role of T lymphocytes, seems to be an important component. In fact, in early phases of SSc, before fibrosis occurs, the affected tissues exhibit mononuclear inflammatory infiltrate composed of macrophages, mast cells and lymphocytes, especially of T-cells. Most studies to date concerning the role of T lymphocytes in the pathogenesis of SSc have focused on CD4+ T-cells and evidence regarding the role of CD8+ T-cells is scarce and contradictory.

Objectives and methods. The present study aimed to analyze the changes of T lymphocytes in the peripheral blood of patients with SSc and its relation to the disease subtype (Medsger score) and nailfold capillaroscopic changes. Sixty-one consecutive patients were selected from a 190-patients population, with later exclusion of four patients.

Blood samples were analyzed by flow cytometry for T-cell subsets (CD4, CD8) and T-cell activation markers (HLA-DR, CD45RO) and compared with healthy controls.

Results. Fifty-five out of the 57 patients studied were women (97%); 10 patients presented pre-scleroderma, 34 limited (lcSSc) and 13 the diffuse (dcSSc) subtypes. Patients with limited and diffuse subtypes were classified in early (eSSc 7 patients), intermediate (iSSc 10 patients) and late (laSSc 30 patients) disease, according to Medsger classification. There was a statistically significant reduction in the number of total lymphocytes and T-cells in SSc patients comparing to controls. Both CD4+ and CD8+ T-cells were lower in patients comparing to controls, but differences were statistically significant only for CD8+ T-cells. CD8+ T-cells were decreased both in limited and diffuse subtypes, as in all stages of disease. Regarding cellular activation there was a decrease in the number of CD8+CD45RO+, but not of CD8+HLA-DR+, comparing to healthy controls. CD8+CD45RO+ was also decreased in limited and diffuse subtypes as in early and intermediate stages of the disease. No relation of CD8+ to organ involvement or nailfold capillaroscopic was found.

Discussion and conclusion. Our study indicates that T-cells may play a relevant role in the pathogenesis of scleroderma especially concerning the CD8+ T-cells and the disease subtype, in the initial phases.

PS127

PROPYLTHIOURACIL ATTENUATES AORTIC VASCULO-PATHY IN AN ANIMAL MODEL OF SYSTEMIC SCLEROSIS

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Background/Purpose. Systemic sclerosis (SSc) is a generalized connective tissue disorder of unknown etiology characterized by thickening and fibrosis of the skin and distinctive visceral involvement associated with vascular damage. Traditionally, the vasculopathy of SSc has been considered mainly to affect small arteries and capillaries but there is recent evidence showing that SSc is also associated with large vessel disease. Increased aortic augmentation index and pulse wave velocity in comparison to age and sex matched healthy controls indicate large-vessel involvement in patients with SSc. A second, and as yet poorly accounted for, endocrine feature of scleroderma is its overlap with thyroid abnormalities. Recent experimental data suggest that propylthiouracil (PTU) abrogates the development of cutaneous and pulmonary fibrosis in SSc murine model and reduces the development of plexiform lesions in an animal model of primary pulmonary hypertension. The aim of the study is therefore to evaluate the effect of propylthiouracil administration on intima-media (IM) thickness and ratio in a murine model of systemic sclerosis.

Methods. Chronic oxidant stress SSc was induced in BALB/c mice by daily subcutaneous injections of HOCl for 6 weeks, characterized in detail as the Cochin chronic oxidant stress model of SSc. Mice (n=25) were randomized in three arms: treatment with either propylthiouracil plus HOCl (n=10), HOCl (n=10), or vehicle alone (n=5). Propylthiouracil treatment (12 mg/kg) was initiated 30 minutes after HOCl subcutaneous injection and continued daily for the 6 weeks. Thoracic aorta was evaluated by histological methods. IM thickness and the disease subtype, in the initial phases.
PS128
THE RELATIONSHIP BETWEEN NAILFOLD CAPILLAROSCOPY AND TELANGIECTASIA SCORE WITH SEVERITY OF PERIPHERAL VASCULAR INVOLVEMENT IN SYSTEMIC SCLEROSIS

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Objectives. To determine the association of nailfold video-capillaroscopy (NVC) findings and telangiectasia score with digital ulcer (DU) history and severity of peripheral vascular involvement (PVI) in Systemic Sclerosis (SSc).

Methods. Fifty-nine SSc patients fulfilling Leroy and Medsger criteria were evaluated including Telangiectasia Score (TS) (Shah AA, et al. J Rheumatol 2010), Modiﬁe Rodnan Skin Score (MRSS), Vanity Activity Scale (VAS) and Medsger Severity Scale (SSS). Qualitative (early-active and late patterns) (Cuto M, et al. J Rheumatol 2000) and semiquantitative assessments [capillary number (CN), irregularly enlarged capillaries (ICC), giant capillaries, capillary ramifications, microhaemorrhages, capillary array disorganisation and microangiopathy evolution score (MES)] (Sulli A, et al. Ann Rheum Dis 2008) were performed by NVC.

Results. The mean age of patients was 45.6 and 91.5% were females. The mean duration of Raynaud’s, non-Raynaud symptoms, skin involvement (year) were 6.1±6.3, 3.1±2.0, 3.0±2.0 respectively. Of the patients 20(34%) had diffuse, 35(59%) had limited cutaneous involvement and 4(7%) had sine-scleroderma. 13(22%) were anti-centromere (+) and 29(49%) were anti-Scl70 (+). DU history (DU+) was present in 27(46%) and telangiectases were present in 34(58%). When we compare DU+ and DU- groups, the mean CN was 2.0±0.5 vs 1.4±0.7 (P<0.001), EIC was 1.8±0.6 vs 1.4±0.7 (P<0.05), MES was 2.5±1.5 vs 1.8±1.0 (P<0.05); early pattern was in 1 vs 9, active pattern was in 14 vs 16, late pattern was in 12 vs 7 patients. Current PV1 was grouped as severe (SSS-2-4) (n=16) or non-severe (SSS-0-1) (n=43). The frequency of severe PV1 was 22% in females (12/54) and 80% in males (4/5). When we compare severe and non-severe groups, the mean CN was 2.1±0.4 vs 1.5±0.7 (P<0.001), MES was 2.8±1.6 vs 1.8±1.1 (P<0.05); early pattern was in 0 vs 10, active pattern was in 9 vs 21, late pattern was in 7 vs 12 patients. The mean TS was 2.7±4.6 vs 1.9±2.1 in DU+ and DU- groups; 3.0±5.5 vs 2.0±2.4 in severe and non-severe groups. The mean values of TS, MRSS, VAS, SSS were similar between groups.

Conclusions. DU history and severe PV1 in SSc was associated with capillary loss and microangiopathy. ‘Early’ NVC pattern was very rare in patients with DU history and was not found in patients with severe PV1. Males had severe PV1 more frequent than females. Telangiectasia scores were not significantly different in patients with digital ulcer history or severe PV1. NVC may be a helpful method in the assessment of SSc patients with PV1, warranting prospective studies.

Table I. DU History, Current Severity of Peripheral Vascular Involvement and NVC Pattern.

<table>
<thead>
<tr>
<th>NVC Pattern</th>
<th>Early</th>
<th>Active</th>
<th>Late</th>
<th>Total (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Du history -</td>
<td>9</td>
<td>16</td>
<td>7</td>
<td>32</td>
</tr>
<tr>
<td>Du history +</td>
<td>1</td>
<td>14</td>
<td>12</td>
<td>27</td>
</tr>
<tr>
<td>PV1 Non-Severe</td>
<td>10</td>
<td>21</td>
<td>12</td>
<td>43</td>
</tr>
<tr>
<td>Severe</td>
<td>0</td>
<td>9</td>
<td>7</td>
<td>16</td>
</tr>
</tbody>
</table>

PS129
EFFICACY OF BOSENTAN IN THE TREATMENT OF RAYNAUD’S PHENOMENON: ANALYSIS OF THREE COHORTS OF PATIENTS

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Systemic sclerosis (SSc) is a chronic autoimmune inflammatory pathogenic disease of the connective tissue, characterized by progressive fibrosis thickening of skin and internal organs. The first vascular event is Raynaud’s phenomenon (RP). In our study we evaluated the efficacy of the endothelin receptor antagonist, bosentan, in patients with Raynaud’s Phenomenon secondary to Systemic Sclerosis in treatment with prostanoids (Iloprost), with Bosentan or with both drugs. We evaluated a sample of 78 patients with SSc divided in 3 groups. Group ILO: 25 patients in treatment with ACE inhibitors and prostanoids; Group BOS: 31 patients treated with Bosentan 125mg bid, never undergone prostanoid therapy (For personal reasons or specific contraindications); and Group BOS+ILO: 22 Patients in treatment with ACE inhibitors, prostanoids and Bosentan 125mg bid. All patients were aged between 46 and 69 years (mean 57.3 ± SD 11.70), with SSc according to ACR criteria. Follow up was performed every 4 weeks for 12 months and each patient kept a diary where reported: - Onset data of Raynaud’s Phenomenon - Duration: minutes - Raynaud’s Condition Score (RCS): Limitation of daily activity on a scale of 1 to 10 (meaning 10 as a total inability to do the activity) - Pain VAS (1-10): 1 meaning the least pain and 10 as the maximum pain - Number of daily attacks - Ulcers onset (date)

Results. The reduction of RP attacks at week 48 from the baseline was statistically significant in group BOS and BOS+ILO (respectively delta-2.1 p=0.007, delta-2.5 p=0.009). There was decrease of duration in RP attacks in all groups and the Raynaud’s Condition Score showed a statistically significant improvement (-0.5 p=0.007, -0.5 p=0.007), while VAS Pain showed an improvement in Group BOS and BOS+ILO (delta-2.5 p=0.003, delta-1.6 p=0.007) at the 48th week. SF-36 showed improvements, in particular physical activity and mental health showed same results in patients of Group BOS and BOS+ILO (p<0.04) Six patients of Group ILO and only one patient of Group BOS showed the onset of new digital ulcers, while none of the patients of Group BOS+ILO has presented a new digital ulcer.

Conclusion. Bosentan seems to be effective and may be a valid alternative for the treatment of severe Raynaud’s Phenomenon for patients where prostanoids therapy is contraindicated or refused, moreover seems to have a synergic effect with prostanoids treatment.

PS130
CORRELATIONS BETWEEN PERIPHERAL MICROVASCULAR DISEASE SEVERITY AND VITAMIN D SERUM LEVELS IN SYSTEMIC SCLEROSIS PATIENTS

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Background. Low 25-hydroxy-vitamin D [25(OH)D3] serum concentrations correlate with disease activity in several autoimmune connective tissue diseases (CTD), such as rheumatoid arthritis, systemic lupus erythematosus, and undifferentiated connective tissue disease (1). Systemic sclerosis (SSc) is an autoimmune CTD characterized by a progressive sequence of microvascular, immune-related and fibrotic alterations in several organs.

Objective. The aim of the study was to assess possible associations between 25(OH)D3 serum levels and both microvascular damage severity and clinical features in SSc patients.
Methods. 120 SSc patients were enrolled (mean age 66±11SD years; 84% female; mean disease duration calculated from onset of Raynaud’s phenomenon 13±12 years), 58 from the Academic Division of Clinical Rheumatology, University of Genova, Italy and 62 from the Department of Rheumathogy, Ghent University Hospital, Belgium. All patients were evaluated by nailfold videocapillaroscopy (NVC) to classify and to score the severity of the microangiopathy (identification of early, active and late NVC patterns, and calculation of microangiopathies evolution score [MESA], as previously reported (2,3). 25(OH)D3 serum levels were evaluated by radioimmunoassay: vitamin D concentrations were classified as normal (>30 ng/ml), insufficient (30 <25(OH)D3 <10 ng/ml) or deficient (<10 ng/ml) (4). Clinical features of the disease were assessed using Medger’s severity scale (score 0-4) (5). Statistical analysis was performed by nonparametric tests.

Results. 25(OH)D3 was found insufficient or deficient in 61% and 26% of SSc patients, respectively. 25(OH)D3 resulted significantly lower in patients with “late” NVC pattern of microangiopathy in comparison with either “active” or “early” patterns (17±12 vs 18±13 vs 20±7, p<0.005). Negative statistically significant correlations were found between 25(OH)D3 concentrations and both MES (r=-0.49, p<0.003) and peripheral vascular disease according to Medger scale (r=-0.24, p<0.01). There was no significant relationship between serum 25(OH)D3 and other clinical features of SSc, including skin, lung, gastrointestinal, renal, heart and joint involvement, assessed using the Medger's severity scale. No statistical significant differences were found between skin subsets or gender.

Conclusion. This study demonstrates a negative correlation between 25(OH)D3 serum concentrations and progressive severity of peripheral microvascular/vascular clinical involvement in SSc patients.

References

PS131
SCLERODERMA DIGITAL ULCER HEALING: BENEFICIAL ROLE OF BOSENTAN AND OPPOSITIVE ROLE OF SKIN DIGITAL FIBROSIS
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Aim of Study. The most recent guidelines for the management of digital ulcers (DU) in systemic sclerosis (SSc) indicate the use of iloprost to induce wound healing and bosentan to prevent the onset of new DU. The aim of our study was to evaluate whether the combination treatment may overcome the effect of the individual drugs.

Materials and Methods. From 2009 to 2012, we recruited 34 patients (31 F/3 M, mean age 43.8 years) with SSc according to the 1988 LeRoy criteria and with DU persistent despite intravenous iloprost at least 6 months. The population enrolled was selected, relative to the skin fibrosis digital, for its complete absence or its presence with modified Rodnan skin score (mRSS).

Patients were subjected for 6 months combination therapy with iloprost (1 infusion per month, for 6 hours/day) and bosentan (62.5 mg bid 1 month and 125 mg bid the remaining 5 months).

Results. Patients had initially 69 DU (58 hands and 11 toes). After 6 months of treatment with iloprost and bosentan 34 (50%) DU were healed (R), 18 (32.4%) were in remission (PR), 17 (17.6%) did not respond (NR) and no new UD was recorded (0%).

With regard to the hands, 34 DU were R (58.7%), 15 were PR and 9 were NR. The number of DU went from 58 to 24 (PR + NR) (p=0.004). The mean of DU went from 1.7 to 0.7 (p=0.00003).

The 11 patients with skin fibrosis (Rodnan skin score grade 3) had initially 22 DU and at the end of study only 4 R (18%), 9 PR and 9 NR (NR + PR 82%).

Overall, 57.8% of digital ulcers treated with both iloprost and bosentan healed completely. In particular, patients with mRSS grade 1 showed a recovery of 83.4% compared to 18% of patients with mRSS grade 3.

We conclude that the association iloprost more bosentan proves more effective than iloprost alone in determining the healing of DU and that the skin fibrosis strongly influences the healing process of DU.
PS133
CORRELATIONS BETWEEN VIRTUAL TOUCH IMAGING AND QUANTIFICATION ABSOLUTE SKIN STIFFNESS, NAILFOLD CAPILLAROSCOPY PATTERN AND DIGITAL ULCERS IN SYSTEMIC SCLEROSIS PATIENTS

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Background/Purpose: Microvascular damage as assessed by nailfold capillaroscopy is one of the best evaluable predictors of the systemic sclerosis (SSc) development and progression. The modified Rodnan skin score (mRSS) is employed to clinically evaluate the severity of skin involvement in SSc. However, this method lacks sensitivity to slight alterations in skin stiffness, and has high intraobserver and interobserver variability.

Recent studies have suggested that shear-wave elastography, namely Virtual Touch Imaging and Quantification (VTIQTM), may increase the sensitivity and validity of skin involvement evaluation in SSc.

The aim of this study was to explore possible associations between finger skin stiffness and different patterns of nailfold capillaroscopy and digital ulcers (DUs) in SSc patients.

Methods: The study included twenty-six consecutive SSc patients (23 females and 3 males, mean age 55.3 ±12.1 SD years), according to the ACR criteria for SSc, or the le Roy’s criteria for classification of early SSc. A complete medical history and clinical examination were carried out for all the patients. All patients were evaluated by nailfold capillaroscopy and classified into three major patterns “early”, “active”, and “late” pattern, as previously reported (1). Both mRSS and VTIQTM absolute skin stiffness were determined at the dorsum of the middle phalanx of the third finger bilaterally. An ACUSON S3000TM (Siemens) ultrasound system equipped with a 9 MHz probe was used for VTIQTM. The significance of differences between groups was calculated with Mann–Whitney test or Kruskal–Wallis test, as appropriate. p values <0.05 were considered statistically significant.

Results: The skin was statistically significant stiffer at the level of the dorsum of the middle phalanx of the third right finger (p=0.027) and left finger (p=0.025), in the group with DUs (See Table I).

No differences in finger absolute skin stiffness were found in association with the different capillaroscopy patterns (See Table II).

Conclusions: Measurements of skin stiffness by VTIQTM may improve the objective evaluation of skin stiffness in SSc patients and add a new dimension to the assessment of DUs. Further studies are warranted to validate and refine this non-invasive method to evaluate skin involvement in SSC clinical practice.

Table I. Clinical findings in 26 SSc patients.

<table>
<thead>
<tr>
<th>Digital ulcers</th>
<th>Differences between the group (p value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes (n=11)</td>
<td>No (n=15)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>52.6 (10.8)</td>
</tr>
<tr>
<td>RP duration (years)</td>
<td>15.9 (10.2)</td>
</tr>
<tr>
<td>SSc duration (years)</td>
<td>14.1 (9.3)</td>
</tr>
<tr>
<td>mRSS, at the left finger</td>
<td>2.4 (0.8)</td>
</tr>
<tr>
<td>mRSS, at the right finger</td>
<td>2.4 (0.8)</td>
</tr>
<tr>
<td>SWV, at the right finger</td>
<td>5.3 (2.6)</td>
</tr>
<tr>
<td>SWV, at the left finger</td>
<td>5.4 (2.2)</td>
</tr>
</tbody>
</table>

RP: Raynaud’s phenomenon; SWV: shear wave velocity in m/s. Results are shown in mean (SD).

Table II. Shear-wave velocity values (m/s) according nailfold capillaroscopy pattern in 26 SSc patients.

<table>
<thead>
<tr>
<th>Early</th>
<th>Active</th>
<th>Late</th>
<th>Non-specific</th>
<th>Differences between the groups (p value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>n=4</td>
<td>n=6</td>
<td>n=9</td>
<td>n=7</td>
<td></td>
</tr>
<tr>
<td>SWV, at the right finger</td>
<td>3.7 (0.8)</td>
<td>3.1 (0.9)</td>
<td>3.7 (2.0)</td>
<td>6.0 (3.0)</td>
</tr>
<tr>
<td>SWV, at the left finger</td>
<td>4.0 (1.7)</td>
<td>3.0 (1.0)</td>
<td>4.2 (2.2)</td>
<td>5.9 (2.4)</td>
</tr>
</tbody>
</table>

SWV, shear-wave velocity in m/s. Results are shown in mean (SD).

PS134
GINKGO BILOBA REDUCES THE DURATION AND SEVERITY OF RAYNAUD'S ATTACKS OF PATIENTS WITH SYSTEMIC SCLEROSIS

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Introduction: Systemic sclerosis (SSc) is a connective tissue disease with unknown etiology which causes remarkable morbidity and mortality. Raynaud’s phenomenon (RP) is a complication of SSc leading to ischemia of extremities and digital gangrene. Treatment of RP is a clinical problem and often remains ineffective. Gingko biloba is derived from the leaf of the Maidenhair tree. Its extract is leaded to improve tissue circulation; this study was designed to evaluate the efficacy of ginkgo biloba in the treatment of RP in systemic sclerosis.

Materials and Methods: A total of Seventeen patients with SSc and RP were received either Ginkgo biloba pills (40 mg three times per day) or placebo for 3 months in a randomized, double blind, controlled trial. A two-week assessment period before treatment was done during which patients were asked to record the frequency, duration, and severity [using 10-point Raynaud’s Condition Score (RCS)] of attacks in a diary form before intervention. They continued to record the same data in their diary forms after intervention and were visited at the end of each month.

Results: The mean duration of attacks and the RCSs were significantly decreased in Ginkgo group compared with the baseline (p<0.05), whilst no significant reduction was observed in the mean number of attacks (p=0.147). In the placebo group no significant reduction was shown in the mean duration or number of attacks, and RCS.

Conclusion: Ginkgo biloba reduces the duration and severity of Raynaud’s attacks of patients with systemic sclerosis.

Keyword: Ginkgo biloba, Raynaud’s phenomenon, Scleroderma, Systemic sclerosis.
ACUPRESSURE FOR THE TREATMENT OF RAYNAUD’S PHENOMENON: A PILOT RANDOMIZED CONTROLLED TRIAL

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Background/Purpose. Raynaud’s phenomenon (RP) affects approximately 10% of the US population. The high cost, lack of efficacy, and side effects of conventional medical therapies necessitates the need for complementary or alternative options.

Methods. A pilot single-center RCT of vasodilation acupressure, relaxation acupressure vs. RP education obtained from the Raynaud’s Association (control). Patients with either primary (N = 15) or secondary (N = 8) RP were randomized from January through April by block randomization to the 3 groups for an 8 week period. Patients randomized to acupressure were instructed on how to self-perform at home by a single investigator and a DVD was provided with instructions. The primary endpoint was a decrease in the severity, frequency and duration of RP. All patients kept a daily Raynaud’s diary, (recording the number and duration of attacks, pain, tingling and numbness on a 0-100 scale), and daily Raynaud’s condition score. At baseline and 8 weeks, EndoPAT was performed to determine endothelial function, and serum was collected for biomarker analysis (VEGF, tPA, sE-Selectin, BFGF, VCAM-1, ICAM). Data analysis was conducted using the last observation carried forward and paired statistical analyses were used to assess difference.

Results. 23 patients were randomized and 7 discontinued prematurely (5 patients withdrew due to time restraints, 1 each for unrelated medical problems and lost to follow-up). Since there was no statistical difference between acupressure groups, they were combined and compared to the education group. 78% of patients were female, 96% were Caucasian, the mean age was 49.8 (SD=16) yrs; 5/16 patients in the acupressure group had secondary RP and 1/7 in the control group had secondary RP. There was no statistical difference in the baseline characteristics between the acupressure groups vs. the control group. At the end of study, there were no statistical differences between the acupressure vs. education groups. However, there were trends in the patient reported severity of RP favoring acupressure groups (Table). In addition there were no significant differences in EndoPAT measurements or serum markers of vasculopathy. Sensitivity analysis using the completers showed similar results.

Conclusion. Our pilot RCT showed that acupressure groups showed trends in improvement in symptoms associated with RP. However, there were no differences in the endothelial function and serum markers of vasculopathy. The parameters used to evaluate patients with RP have marked variability and supports the need for a composite measure to be developed for RP trials.

Table. Change from week 1 compared to week 8*

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group A-B</th>
<th>Control</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No of attacks</td>
<td>N: 12</td>
<td>N: 6</td>
<td>1.0</td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>-8.3 (3.0)</td>
<td>-7.2 (12.8)</td>
<td></td>
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<tr>
<td>Pain</td>
<td>N12</td>
<td>N6</td>
<td>0.12</td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>-13.6 (30.1)</td>
<td>0.6 (27.6)</td>
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<tr>
<td>Tingling</td>
<td>N: 12</td>
<td>N: 6</td>
<td>0.64</td>
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<tr>
<td>Mean (SD)</td>
<td>-5.4 (13.9)</td>
<td>-1.2 (7.5)</td>
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<tr>
<td>Numbness</td>
<td>N: 12</td>
<td>N: 6</td>
<td>0.80</td>
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<tr>
<td>Mean (SD)</td>
<td>-10.5 (37.0)</td>
<td>1.1 (22.1)</td>
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<td>N: 12</td>
<td>N: 6</td>
<td>0.09</td>
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<tr>
<td>Mean (SD)</td>
<td>-0.2 (18.7)</td>
<td>0.8 (11.2)</td>
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<td>RCS average for difficulty</td>
<td>N: 12</td>
<td>N: 5</td>
<td>0.72</td>
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<tr>
<td>Mean (SD)</td>
<td>-2.0 (2.4)</td>
<td>-0.6 (2.9)</td>
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<tr>
<td>RCS average for pain</td>
<td>N: 12</td>
<td>N: 5</td>
<td>0.63</td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>1.4 (2.0)</td>
<td>0.1 (3.0)</td>
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<td>Endopat</td>
<td>N: 14</td>
<td>N: 7</td>
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<td>Mean (SD)</td>
<td>0.1 (0.4)</td>
<td>0.2 (0.8)</td>
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<td>Patient VAS</td>
<td>N: 16</td>
<td>N: 7</td>
<td>0.39</td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>-1.6 (2.2)</td>
<td>-0.7 (2.0)</td>
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<td>MD VAS</td>
<td>N: 16</td>
<td>N: 7</td>
<td>1.0</td>
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<tr>
<td>Mean (SD)</td>
<td>-2.1 (2.0)</td>
<td>-1.9 (1.3)</td>
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</table>

*Using ??????
PS137
COMPARISON OF POSTOCCLUSIVE HYPEREMIA IN SYSTEMIC SCLEROSIS AND PRIMARY RAYNAUD'S PHENOMENON
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Cutaneous postocclusive reactive hyperemia (PORH) is mediated by sensory nerves and endothelial derived hyperpolarizing factors. Such a response is abnormal in the finger pad of patients with systemic sclerosis (SSc). However, the regional variation of the response remains undetermined. The primary objective of this study was to compare the PORH on several locations of the dorsum of the hand of patients with SSc, matched primary Raynaud phenomenon (PRP) and controls. Methods. Fifteen patients with SSc, 15 sex and age-matched patients with PRP, and 15 matched healthy controls underwent a post occlusive hyperemia test following a 5 min ischemia, recorded using laser speckle contrast imaging (LSCI). Results. PORH was altered under late NVC pattern in patients with PRP and SSc compared with controls, excepted the thumb where PORH was normal. In contrast, the kinetic of the response was altered only in patients with SSc. Conclusions. PORH is abnormal in terms of amplitude in all finger excepted the thumb in patients with PRP and SSc, whereas altered kinetic of the response is a specificity of SSc.

PS138
NAILFOLD VIDEOCAPILLAROSCOPY AND SERUM VEGF AS BIOMARKERS OF SEVERITY IN SYSTEMIC SCLEROSIS?
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Introduction. Nailfold videocapillaroscopy (NVC) identifies the microvascular hallmarks of systemic sclerosis (SSc) for diagnosis and monitoring the progression and severity of SSc. The vascular endothelial growth factor (VEGF) is the hallmark of angiogenesis and high levels are found in serum and skin of SSc patients with diffuse disease, late NVC pattern, or long-term disease. The aim of our study is to investigate NVC findings and serum VEGF levels in different subsets of SSc patients with variable internal organ involvement, disease activity and severity. Patients and Methods. Newly diagnosed SSc patients (n=44) fulfilling the ACR criteria were consecutively enrolled at our center in 2001-2012. Twenty healthy subjects were used as controls. NVC images of right and left II-V fingers, clinical, immunologic, clinimetric, and instrumental evaluations and serum samples for VEGF determination by ELISA commercial kit were used for analyses (statistical significance p<0.05).

Results. The number of VVC giant capillaries was significantly lower in SSc with DLC<50% (p=0.03) and gastrointestinal involvement (p=0.02), while avascular areas negatively correlated with Valentini-Medsger severity index (r=0.016, r=0.38) and were significantly lower in ACA (+) SSc patients (p=0.02). Neoungiogenesi was less frequent in SSc with signs of early disease (p=0.045) and without gastrointestinal involvement (p=0.045). The mean capillary density was significantly higher in ACA (+) SSc (p=0.02) than in other patients. No correlation was observed between CSU index and the presence or number of skin ulcers. CSUindex<2.94 was significantly less frequent in ACA (+) patients (OR 0.15 (95% CI 0.03-0.84). SSc with early NVC pattern had significantly shorter disease duration (p=0.02), higher DLC (p=0.049) than SSc patients with late NVC pattern. The early NVC pattern was significantly more frequent in ACA (+) SSc patients (OR 30; IC95% 4-22). VEGF level in SSc sera was significantly higher compared to healthy controls (0.49ng/ml (0.02-3.2) vs. 0.36ng/ml (0.11-0.73), p=0.05). It was inversely correlated to DLO (p=0.05, r=-0.4) and directly to ground glass and interstitial score at HRTC (p=0.05, r=+0.4). No association was identified between VEGF levels and gastro-esophageal involvement, pulmonary arterial hypertension, early-active-late capillaroscopy pattern, CSU index score, capillary density, number of giant capillaries, avascular and neoungiogenesi areas, and digital ulcers. Conclusions. Our data confirm the importance of NVC for the diagnosis of SSc and also for prediction of disease severity and organ involvement since the SSC onset. Of note, serum VEGF levels play an additional role as biomarker of SSc pulmonary interstitial involvement.

PS139
SCLERODERMA AND DIGITALS ULCERS TREATMENT ACCESS
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Background. Scleroderma (SD) is an Infrequent disease. The incidence is 2.3 to 22.8 cases per 1 million populations per year and the prevalence is 50-300 cases per 1 million populations over the word. Argentina lacks Epidemiological data but it is estimated between 40.000-42.000 cases of scleroderma. This study shows that more than 50 % of the patients with SSC had digital ulcers (DU). From July 2011 to August 2013 167 patients with SD and UD have been included in the study (contact by phone and web) Most of them had varying degrees of loss of function of the hand and access to treatments dependent on the health system.

Objective. Understand the buying process to access to the specific medication for patients with SD and UD in Argentina during the period July 2011 to August 2013.

Method. Analyzed 167 patients with active digital ulcers in scleroderma, which were contacted by phone and web with AADERYR, to receive information about health coverage.

Results. In a sample of 167 patients, 68% had medical coverage through a private system and social work (National Provincial Trade and prepaid), corresponding to the remaining 32% had access to medicines by the Public Health System. In the case of the private system is excluded patients with certified disabilities to achieve 100% coverage, otherwise, had a refund ranging from 40% to 70% of the drug cost. However, 80% of patients in the private sector and the state, with or without certificate of disability also experienced some delays in access to medicines for two months or more, depending on the type of health coverage.

Conclusions. The heterogeneity of the health coverage and the administrative bureaucracy that characterizes Argentina’s health system goes against the efficient use of resources and achievement of acceptable levels of equity. While the Certificate of disability allows 100% refund, no guarantees quick access to prescribed medications. Most patients ignore the possibility of obtaining this certificate and how to proceed. Therefore it becomes essential to inform to patients population about their rights to access the health system thereby ensuring adherence to drug treatments.

Bibliography

PS140
DIGITAL ULCERS IN SYSTEMIC SCLEROSIS
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1Ben Aknoun Hospital-Department Of Rheumatology, Algiers, ALGERIA; 2Beni Messous Hospital-Laboratory Of Immunology, Algiers, ALGERIA.

Objective. To assess the prevalence of digital ulcers in systemic sclerosis (SSc) and their association with clinical and serological features.

Patients and Methods. One hundred fifty (150) patients attending the rheumatology department at Ben Aknoun Hospital, as part of a prospective study and fulfilling the ACR and/or Lenyo and Medger criteria for systemic sclerosis were evaluated. The analysis of results was performed by the Epidata analysis. Data were expressed as the median and range or mean ± standard deviation (SD) and 95% confidence interval (95% CI), when appropriate. The statistical significance for the various associations was calculated using the Khi 2 test. The difference was significant when p value <0.05.

Results. 139 women and 11 men with a median age of 45.1±13.59 years and a disease duration (first non-Raynaud symptom) of 9.7 years. 42 patients had a diffuse scleroderma, 108 patients had a limited scleroderma. 93 (62%) patients had digital ulcers. Digital ulcers were associated with the extent of skin involvement (p=0.0008), intestinal lung disease (p=0.003), telangiectasia (p=0.01) and anti topoisomerase-I antibodies (p=0.0005). The Disability Index of the Health Assessment Questionnaire (HAQ-DI) and the Cochin Hand Function Scale (CFHS) score were higher in the patients with digital ulcers (p=0.003).

Conclusion Digital ulcers are frequent. They are disabling and associated with a severe disease.
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1Hospital General, Valencia, SPAIN; 2Hospital La Fe, Valencia, SPAIN; 3Hospital Dr. Peset, Valencia, SPAIN.

Raynoud phenomenon (RP) may precede to the diagnosis of systemic sclerosis (SSc) by years. The purpose of this study was to evaluate patients with RP for the early diagnosis of SS and other connective tissue diseases (CTD).

Methods. This study was developed under conditions of routine clinical practice in two stages. Stage I inclusion and screening; Stage II prospective 24-month follow-up. The study population included patients from 17 primary care units.

Results. 158 patients, 130 women and 28 men, with a mean age of 47±17 years were evaluated. The mean age of women was 45±16 years and the mean age of men was 53±19 years. Mean time of evolution of RP was 93 months. A presumptive diagnosis of the RP was made by consultation with the rheumatologist and the definitive diagnosis was achieved by blood test results and capillaroscopy pattern. The presumptive diagnosis of Primary Raynaud phenomenon (PRP) was given to 44.30% (n=70) patients and the presumptive diagnosis of Secondary Raynaud Phenomenon (SRP) to 48.10% (n=76) patients. The definitive diagnosis of PRP was given to 37.3% (n=59) patients and the definitive diagnosis of SRP to 33.3% (n=53) patients. The treatment was based on a presumptive diagnosis of PRP, 84.3% (n=59) had definitive diagnosis whereas 15.7% (n=11) changed to definitive diagnosis of SRP. The definitive diagnosis was distributed as follows: 1.4% (n=1) early SS, 1.4% (n=1) parapleptic RP, 10.0% (n=7) undifferentiated CTD, 1.4% (n=1) mixed CTD and 1.4% (n=1) cervical rib. All patients with definite diagnosis of PRP had ANA negative. All patients with SS and 95% of patients with early SS had ANA positive. Ninety-six percent of patients with early SS had centromere positive. Ninety percent of patients with RP showed a normal pattern in the nailfold capillaroscopy and 97% (n = 30) of patients with positive ANA and anti-centromere showed a characteristic SS capillaroscopy pattern. The total of 21 patients with diagnosis of SS and 93% (n=13) patients with early SS showed a characteristic SS capillaroscopy pattern. Ninety-five percent (n=73) of patients with negative ANA showed a normal capillaroscopy pattern and 10% showed a nonspecific pattern. The presumptive diagnosis of Secondary Raynaud Phenomenon was distributed as follows: 1.4% (n=2) early SS and 1.4% (n=2) parapleptic RP.

Conclusions. This study showed significantly more patients with secondary vs primary RP. There was a good agreement between the presumptive diagnosis and the definitive diagnosis. The most common diagnoses associated with SRP are SS (13%), followed by early-SS (9%) and lupus (8%).

97% (n=30) of patients with positive ANA and anti-centromere showed a characteristic SS capillaroscopy pattern. Ninety-five percent (n=73) of patients with negative ANA showed a normal capillaroscopy pattern and 10% showed a nonspecific pattern. The total of 21 patients with diagnosis of SS and 93% (n=13) patients with early SS showed a characteristic SS capillaroscopy pattern. Ninety-five percent (n=73) of patients with negative ANA showed a normal capillaroscopy pattern and 10% showed a nonspecific pattern. The total of 21 patients with diagnosis of SS and 93% (n=13) patients with early SS showed a characteristic SS capillaroscopy pattern. Ninety-five percent (n=73) of patients with negative ANA showed a normal capillaroscopy pattern and 10% showed a nonspecific pattern. The total of 21 patients with diagnosis of SS and 93% (n=13) patients with early SS showed a characteristic SS capillaroscopy pattern. Ninety-five percent (n=73) of patients with negative ANA showed a normal capillaroscopy pattern and 10% showed a nonspecific pattern. The total of 21 patients with diagnosis of SS and 93% (n=13) patients with early SS showed a characteristic SS capillaroscopy pattern.
NAILFOLD CAPILLAROSCOPY BY DIGITAL USB-MICROSCOPE: AN INEXPENSIVE AND EASY METHOD FOR IDENTIFYING SCLERODERMA PATTERN

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Background. Nailfold capillaroscopy (NFC) is a well established method for identifying microvasculopathy in scleroderma patients (1, 2). NFC has gained an important role as a tool to differentiate between primary and secondary Raynaud phenomenon (RP). The classification criteria for systemic sclerosis (SSc) are currently under revision, and NFC may become crucial for the early diagnosis of SSc (3).

Videocapillaroscopy is the current gold standard for screening patients with possible scleroderma pattern (1, 4). The digital USB-microscope is similar to the Videocapillaroscope. The price is less than 1500 $, software included.

The aim of our project was to identify scleroderma-pattern in patients formerly classified as Undifferentiated connective tissue disease (UCTD) by using a digital USB-microscope.

Method Our rheumatology outpatient clinic in Southern Norway serves a population of 300 000. We reviewed the electronic medical records from 2003 to 2013 of all adult patients initially diagnosed as UCTD (n=228). Patients who had been re-diagnosed with other diseases were excluded (n=110). UCTD-patients without anti-centremeter/anti-SCL-70 and RP were also excluded (n=75).

Eventually we classified 3 subgroups for NFC investigation (n=43):
1. Patients who already had been re-diagnosed as CREST or SSc (n=11).
2. UCTD-Patients with positive anti-centremeter/anti-SCL-70 antibodies and RP (n=18).
3. UCTD-Patients with positive anti-centremeter/anti-SCL-70 antibodies, without RP (n=14).

A digital USB-microscope (Dino-Lite AM-413HNT with high magnification (200x) was used. This small handheld device, with an inbuilt camera is connected to a computer with an USB-port. As standard we evaluated capillary density, capillary architecture, number of giant capillaries, microhemorrhages and signs of neoangiogenesis. We registered the specific scleroderma pattern (i.e. early-active-late) (4). All investigations were performed by one investigator (HB). Time spent per patient (8 fingers): 10-15 min.

Results. Our final studygroup contained 43 patients. In the first subgroup, scleroderma-pattern was identified in 11/11 patients (100%).

In the second subgroup, scleroderma pattern was identified in 13/18 patients (72.2%) and registered as early-5, active-5, late-3, respectively. As expected, scleroderma pattern was not identified in any of the 14 patients in the third subgroup.

Conclusion. Nailfold capillaroscopy by digital USB-microscope camera is a simple, fast to perform and inexpensive method. The pictures are provided with a good resolution and are easy to interpret. We find this method suitable for identifying vasculopathy in assessing patients diagnosed with UCTD.

Our findings support recent reports [5], though further investigations are needed. We encourage other colleagues to make use of this method in daily clinical practice.
PS147
SURGICAL TREATMENT OF SCLERODERMA – RE-THINKING THE ROLE AND TIMING OF PERIPHERAL SYMPATHECTOMY IN THE HAND

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While a multitude of therapeutic options exist for ischemic ulcers in scleroderma, peripheral sympathectomy surgery is frequently offered late in the disease process. The purpose of the present study was to critically analyze the results of peripheral sympathectomy in patients with a confirmed diagnosis of scleroderma. A retrospective analysis of all scleroderma patients who underwent peripheral sympathectomy between January 1, 2003 and December 31, 2012 at Stanford University Medical Center was performed. These patients underwent stripping of the adventitia to the radial and ulnar arteries in the wrist, the radial artery in the dorsal hand, and the superficial arch and common digital arteries in the hand. Vascular bypass was performed as indicated. Parameters included patient age, gender, length of follow-up, presence of preoperative pain and/or digital ulceration, number of digits affected, duration of symptoms prior to surgical intervention, number and type of surgical procedures after peripheral sympathectomy, rate of symptomatic (pain) improvement, rate of ulcer healing, and rate of postoperative complications.

A total of 15 patients (one male and 14 females) with a mean age of 49.5 years (range, 33 to 68 years) were included in the study. Peripheral sympathectomy was performed in all patients (23 hands). Pain improvement/resolution was seen in 21/23 hands (91.3 percent). Digital ulcers healed in all patients with only 2 patients (2 hands; 12.5 percent) requiring surgical intervention for ulcer recurrence. Minor complications were seen in 6 hands (26.1 percent); none of which required surgical intervention. Peripheral sympathectomy is a well-tolerated procedure in scleroderma patients and is associated with a favorable outcome with predictable pain relief and ulcer healing in the majority of patients. The notion to offer peripheral sympathectomy only after failed conservative treatment should be re-considered, as early surgical intervention may not only improve symptoms such as pain but may also delay the deleterious soft tissue findings seen in scleroderma by improving perfusion to the hands.

Results. Mean age of patients who received treatment is 43.9±12.9 years. Nausea is observed in 4 patients (13.7%), vomiting in 3 patients (10.3%), headache in 6 patients (20.6%), and hypotension in 4 patients (13.7%). Two patients’ treatments are stopped because of the side effects. In one patient the side effect was serious vomiting and in the second one it was hypotension and headache that required the treatment to be stopped.

Conclusion. Although side effects of intravenous iloprost treatment in patients with digital ulcers due to systemic sclerosis is very common, most of the patients continued their treatment

Fig. 1.

PS148
INTRA VE NROUS ILO PRO ST TREATMENT SIDE EFFECT PROFILE IN PATIENTS WITH DIGITALULCERS DUE TO SYSTEMIC SCLEROSIS

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Objectives. Digital ulcers due to systemic sclerosis is an important cause of morbidity. This condition is treated with intravenous iloprost. But with this treatment side effects are commonly seen. In this study we wanted to report side effects occurring during iloprost use in our clinic.

Methods. 29 patients (7 Male / 22 Female) with ischemic digital ulcer due to systemic sclerosis are included in the study. All of the patients are given intravenous iloprost. Side effects occurring during the treatment are recorded in their patients files. Data is evaluated retrospectively.

Results. Mean age of patients who received treatment is 43.9±12.9 years. Nausea is observed in 4 patients (13.7%), vomiting in 3 patients (10.3%), headache in 6 patients (20.6%), and hypotension in 4 patients (13.7%). Two patients’ treatments are stopped because of the side effects. In one patient the side effect was serious vomiting and in the second one it was hypotension and headache that required the treatment to be stopped.

Conclusion. Although side effects of intravenous iloprost treatment in patients with digital ulcers due to systemic sclerosis is very common, most of the patients continued their treatment

PS149
DEVELOPMENT OF A NEW SCORING SYSTEM TO ASSESS DIGITAL ULCERS IN PATIENTS SUFFERING FROM SYSTEMIC SCLEROSIS

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Introduction. Digital ulcers are a common complication in patients suffering from systemic sclerosis. Whereas pain and impairment of the hand function can be judged using standardized questionnaires, no validated tool exists to assess the severity of the digital ulcers. The aim of our study is the development of a new scoring system to assess the severity of digital ulcers in patients suffering from systemic sclerosis.

Methods. In an interdisciplinary collaboration between dermatologists and rheumatologists, we developed a scoring system to assess the severity of digital ulcers in standardized manner. The assessment includes several clinical features (medical history, current therapy, fingertip rewarming time, photographic assessment) and the localization and extension of digital ulcers. Size and depth of digital ulcers were assigned to a defined value. Altogether the sum of the parameters results in a final score.

Results. Initially 10 patients (8 female, 2 male, mean age 54 years) with systemic sclerosis suffering from digital ulcers were assessed with an exploratory score. The average number of digital ulcers was 3 per patient with a mean digital ulcer score of 4.1. The mean completing time for the score was 7 minutes.

Conclusion. The data show that it is possible to develop a digital ulcer score which considers clinical patient data supporting an improved measurement of the severity of digital ulcers. Feasibility needs consideration, therefore the assessment of the ulcers and the calculation of the score requires a system which is fast and easy to perform in a standardised manner.

PS150
QUANTITATIVE ANALYSIS OF NAILFOLD CAPILLARY MORPHOLOGY AND CORRELATION WITH RAYNAUD’S PHENOMENON IN PATIENTS WITH FIBROMYALGIA

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Background. Nailfold capillaroscopy (NFC) has been used to examine morphological and functional changes of microcirculation in connective tissue diseases. It has been demonstrated that NFC patterns reflect the abnormal microvascular dynamics that may play a role in fibromyalgia syndrome (FM).

Objectives. The aim of this study was to determine the NFC pattern in FM and its association with clinical features as like Raynaud’s phenomenon of FM.

Methods. Sixty four patients with FM and 31 age and sex-matched healthy controls were included for this study. Nailfold capillary patterns were quantitatively analyzed using computerized NFC. Other NFC parameters consisted of capillary number within central 3 mm, deletion score, apical limb width, capillary width, and capillary dimension. Capillary dimension was determined by calculating the number of pixel with Adobe Photoshop. Clinical parameters included tender point count, fibromyalgia Impact Questionnaire (FIQ), arthralgia, headache, raynaud’s phenomenon as like numbness or coldness sensation, irritable bowel syndrome, dry eye, and dry mouth.

Results. FM patients had lower capillary number but higher deletion score than health controls on NFC (21.8±2.9 versus 17.3±1.7, p<0.05, 0.7±0.6 versus 1.8±1.5, p<0.05). Other parameters were similar between the groups.

Conclusion. NFC scores reflect the capillary morphology changes in FM and are easy to perform in a standardised manner.
Poster Session

3rd Systemic Sclerosis World Congress

PS151

OBSERVATION PATIENTS WITH RAYNAUD SYNDROME IN SLOVAK POPULATION INCLUDE CAPILLAROSCOPY FINDINGS, USING CAPILLAROSCOPY FOR SEARCHING PATIENTS WITH EARLY STAGE OF SCLERODERMA

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Introduction. Systemic sclerosis (SSc) is a connective tissue disease characterized by excessive collagen deposition and by vascular hyperactivity and obliteration of microvasculopathy. Raynaud phenomenon appears years before other scleroderma patterns. The capillaroscopy findings and their changes could help us to define the diagnosis of scleroderma in early stages or decide of therapy. The modified Scleroderma Health Assessment Questionnaire (SHAQ) could be important to monitoring activity of disease.

Methods. We evaluate 97 patients with systemic sclerosis, 80.4% of patients with limited SSc (lSSc), 10.3% of patients with CREST syndrome, 7.2% of patients with diffuse SSc (dSSc) and 2.1% of patient with overlap syndrome with SSc. We monitoring skin score by nRodnan, presence of organ involve- ment, presence of antibodies include Scl70 and anticientromeric antibodies. We observed HAQ-DI and SHAQ and capillaroscopy examination.

We apply capillaroscopy to 97 patients with SSc and 25 pat. with only episodic Raynaud phenomenon too.

Results. In observation patients with dSSc has higher frequency of pulmonary hypertension (28.6% vs. 12.8% in lSSc patients and vs. 10% in CREST), lung involvement control by DLCO - 85.7% in dSSc vs. to 67.1% in lSSc, although fibrosis detected by CT was similar. Activity score was higher in patients with dSSc (4.41), vs. 2.33 in patients with lSSc. Skin score modifying by Rodnan was higher than 14 in 87.5% in patients with dSSc, to 16.7% in patients with lSSc and 40% in patients with CREST. SHAQ score was a little bit higher in patients with dSSc (1.6) and CREST (1.67) to lSSc (1.43).

In all patients with SSc we find picture of SSc in different stages. In 7 patients with episode of Raynaud phenomenon only during winter we found early SSc changes (in number of cases dilatation, megacapillary and some haemorrhages).

Conclusion. Monitoring clinical findings, organ involvement is important in patients with SSc, for therapy and prognosis. Observation of skin score, activity score, HAQ-DI and SHAQ score could help to control of activity and prognosis of patients with SSc. Capillaroscopy findings could help us to define stage of scleroderma and to find early stages of disease.

PS152

COMPUTERIZED NAIL-FOLD VIDEO CAPILLAROSCOPY AND SYSTEMIC SCLEROSIS

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Introduction. The computerized nail-fold video capillaroscopy (CNVC) is the gold standard in the exploration of Raynaud phenomenon (RP). It permits to determine with a tall sensitivity a large specificity systemic sclerosis (SSc) not yet identified showing morphological abnormalities of capillaries and rheologi- cal disorders. CNVC aimed diagnostic is a non-invasive examination that must be realized not in all unexplained RP but also in all unidentified arthralgias, unexplained pulmonary hypertension (PH), undetermined vasculitic leg ulcers, Intestinal lung diseases, aperistaltic esophagus etc.

Aims. To review the main manifestations justifying the CNVC and to appreciate its rentability in the SSc diagnosis.

Patients and Methods. We have studied through 200 requests for CNVC the main symptoms which have oriented the physician to SSc suspicion (arthralgia, myalgia, scleroderma, RP…).

Results. A 200 requests retrospectively analyzed. Most requests are established to determine the characteristic organic or not of RP (80%). The other requests (asociated or isolated) are digital ulcers (10), digital ischemia (5), familial study of SSc (2), unexplained pulmonary hypertension (5), severe malabsorption syndrome (3), kidney failure (4), primary biliary cirrhosis (5), puritus (5), syndrome erectile dysfunction (2) and young woman myocaridal infraction (1). The common motivations associated are arthralgia (15), myalgias(5), dental alterations (4), muscle weakness (10), erosive esophagitis (5), sever reflex esophagi is (10), dysphagia (14), leg ulcers (1) and morphea (2). The CNVC oriented to the SSc diagnosis in 70% showed typical aspect (mega capillaries, hemorrhage, or rarefaction of capillaries) and was more performed in cutaneous and musculoskeletal symptoms. Nerveless we have identified some cases of SSc thought gastrointestinal (5), ischemic heart disease (1) and PH (1) requests.

Conclusion. CNVC is a no invasive examination, which must be realized not only in all unexplained RP but also- as reported in this work- in arthralgias and any others symptoms suggesting SSc. We recommend the CNVC investigation in each item recognized as potential symptom in SSc. The rentability of CNVC is operator dependant and the multidisciplinary confrontation improve its rentability.
Digital ulcers (DUs) are among the most frequent recurrent vascular complications in patients with systemic sclerosis (SSc). Ischemia in the context of SSc-related vasculopathy is the main pathogenetic mechanism for the development of fingertip DUs. Epidermal thinning, mechanical friction and inflammation contribute for appearance of DUs over bony prominences and in the regions of calcification, e.g., calcium channel blockers (CCBs), intravenous prostanoïd, phosphodiesterase inhibitors, endothelin receptor antagonists and antiplatelet drugs should be administered. In addition local antiseptic care should be provided. In some cases angiectasies and antioxidants are required. Impaired hand function and quality of life are major consequences of DUs. In a part of the cases infection of soft tissue or ostomyelitis develop or digit amputation may be indicated. The therapeutic efficacy of CCBs, intravenous prostanoïds and endothelin receptor blockers for the treatment of DUs in SSc is proved in randomized clinical trials. The others above mentioned medications such as antiplatelet drugs, antibiotics and local treatment as well as combination therapies are also recommended in these case and are used in the leading scleroderma centers as complex approach is necessary for successful outcome.

Background. Systemic sclerosis (SSc), characterized by cutaneous and visceral fibrosis with diffuse vascular pathology, is a complex autoimmune disease and may be complicated by digital ulcers (DU) in up to 50% of cases. Leading to pain, superposed chronic infections, autoamputation, and eventually impairment in hand function, these ulcers pose not only medical problems but psychological and social concerns also become apparent. Although the etiopathogenesis of the disease is not clear, increased endothelin-1 (ET-1) activity is thought to be involved in the pathogenesis of the vascular component. Bosentan, a dual ET-1 antagonist, by binding to ET-A and B receptors, competitively inhibit ET-1 and proved to be an effective treatment option in preventing new DUs in 2 large, multicenter, placebo-controlled studies and in treating current DUs in relatively small series. It also has beneficial effects on micro- and macrovascular hemodynamics and severity of digital fibrosis documented by improvement in venous occlusion plethysmography, flow mediated dilation and modified Rodnan skin score, respectively. Controversies exist in its use in Raynaud’s phenomenon secondary to SSc.

Aim. We conducted a retrospective study to investigate the effect of bosentan on DU prevention and healing.

Methods. Between the years 2010-2013, in Ankara University Department of Rheumatology, a total of 26 patients who were diagnosed as SSc, having DUs and using bosentan were included in the study. Diagnosis of SSc was based on subcommittee for scleroderma 1980 criteria of American Rheumatism Association (ARA) and patients were classified as limited or diffuse cutaneous SSc according to LeRoy’s classification. Frequencies (%) for categoric variables and means (± standard deviations) for continuous variables were used in descriptive statistics.

Health Assessment Questionnaire - Disability Index (HAQ-DI) scores for SSc were used for functional assessment.

Results. 4(15.4%) of patients were male and 22(84.6%) were female. Mean age was 49.46(±14.79) years. Mean disease duration was 8.98(±8.7) years and mean duration of DUs was 2.85(±2.8) years. At the start of treatment 12(46.2%) patients were classified as limited and 18(69.2%) as diffuse cutaneous SSc. Under bosentan treatment 7(26.9%) patients had new DUs and all of these patients had diffuse cutaneous SSc. Overall response rate, designated as no new DUs was 73.1%. 12(46.2%) patients needed additional i.v. iloprost under bosentan treatment.

Conclusion. The major limitation of this study was the absence of a control group and a relatively small number of patients. Also the number of DUs was not measured limiting the ability to see whether a reduction in the number of new DUs did or did not occur under bosentan treatment, which was the primary endpoint in RAPIDS-2 trial. In this trial there were no difference in bosentan and placebo arms in terms of development of new DUs and also no difference in two arms in DU healing was found although some smaller series indicate. As a result, bosentan, by inhibiting endothelin-1 in endothelium and subendothelial smooth muscle has a favorable effect on micro- and macrovascular hemodynamics resulting in a decrease in development of new DUs and on fibrosis, which also may be aggravated by endothelin-1. Further preclinical studies shedding light on etiopathogenesis of SSc and larger clinical trials are needed for more definitive treatment strategies.
PS158

COMBINED PULMONARY FIBROSIS AND EMPHYSEMA (CPFÉ) IN SYSTEMIC SCLEROSIS

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Background. Combined pulmonary fibrosis and emphysema (CPFÉ) is a recently described syndrome, in which emphysema in upper lung zones coexist with pulmonary fibrosis in lower lobes in the same individual. These patients have a characteristic lung function profile, with unexpected subnormal dynamic and static lung volumes, contrasting with a significant reduction of carbon monoxide diffusing capacity (DLCO) and exercise hypoxemia. CPFÉ has recently been described in association with connective tissue disease

Objectives. The aim of this study was to describe the recently individualized syndrome of CPFÉ in a population of patients with systemic sclerosis (SSc).

Methods. In this multicenter case-control study, we retrospectively investigated data from patients with SSc who also had CPFÉ. The demographic characteristics of the patients, the results of pulmonary function testing, and treatment, and the outcomes of the patients were analyzed. For each patient with CPFÉ and SSc, two patients with SSc and pulmonary fibrosis without emphysema were included.

Results. 31 SSc patients with CPFÉ were identified and paired with 62 controls exhibiting only pulmonary interstitial lung disease. In the Cochin hospital cohort, CPFÉ prevalence was 3.5% of SSc patients, and 8.2% of those with interstitial lung disease. CPFÉ patients with SSc were more likely to be male (77% vs 68%, p=0.0001), smokers (84% vs 37%, p=0.0001), and to have a limited SSc (52 vs 21% p=0.01) than control SSc patients. At diagnosis, pulmonary function testing revealed a marked decrease in DLCO (39% vs 50% of theoretical value, p<0.0001) in CPFÉ patients compared to controls, despite similar lung volumes (total lung capacity 78 vs 80%, forced vital capacity 77% vs 78%). Autopsy profiles did not differ significantly between SSc patients with or without CPFÉ. Over follow up, CPFÉ patients with SSc more frequently developed pulmonary hypertension (52 vs 10%, p<0.0001), had more frequent unscheduled hospitalisation (45% vs 11%, p<0.01) and showed decreased survival (p=0.02 by Log rank test analysis) as compared to those with SSc without CPFÉ.

Conclusion. CPFÉ is a distinct pulmonary manifestation within the spectrum of lung diseases occurring in patients with SSc. SSc patients with CPFÉ more frequently develop pulmonary hypertension and show increased morbidity and decreased survival as compared to those with pulmonary fibrosis without emphysema.

PS159

DYNAMICS OF DISEASE SEVERITY INDEX AND ESCSG ACTIVITY INDEX IN SSC-ASSOCIATED ILD DURING LONG-TERM FOLLOW UP

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Background. The course of SSc-ILD is not well estimated in prospective long-term study.

Objectives. To evaluate alterations total index severity of disease and ESCG activity index in patients with SSc-ILD during 5-year follow up.

Methods. It was a prospective longitudinal study involving 77 pts (4 were men) with SSc-ILD. The mean age was 46±13 years. The mean time between two evaluations was 56±12 months. Pts. were divided into 3 groups based on the dynamics of ILD by HRCT: 1 group – pts with improvement of ILD (n=16), 2 – pts with no change and 3 – pts with progressive of ILD (n=22).

We examined the total severity index of disease (scores of organ systems are combined in one score) and European Scleroderma Study Group (ESGSG) activity index at baseline (point 1, P1) and through the 5 years (point 2 (P2) in all pts.

Results. The mean scores of ESGSG activity index in all pts and in the groups 1.2 were normal and hadn’t got any changes, however increased in group 3 (G4±0 vs 52 ± 3.5±1.97) in follow-up (p=0.05) respectively. We found a statistically significant difference the mean scores of ESGSG activity index between the group 3 and groups 1,2 in the P2 (p=0.004 and p=0.03 respectively). The mean score of total severity index in all pts and in the groups 1.2 didn’t change and were: 6.5±2.5 vs 6.9±2.3; 5.7±3.1 vs 5.5±2.2; 6.7±2.3 vs 6.3±2.1 but increased in group 3 (6.7±2.7 vs 8.1±4.2,3) (p=0.05) in P1 and P2 respectively. Total severity index in group 3 was significantly higher than in group 1 (p=0.002) in P2. The mean score of ESGSG index correlated with total severity index in the P1 and P2 as all pts as in the group 1 and 2 (0.57 and 0.53; 0.51 and 0.37; 0.67 and 0.71 p<0.05 respectively). However we didn’t find any correlation between them in the group 3 (0.64 and 0.18 p<0.05) in follow-up.

Conclusion. After five-years follow up the ESGSG activity index and total severity index of disease in pts with progressive of ILD were higher than in pts without progression of ILD.

PS160

THE PREVALENCE AND CLINICAL RELEVANCE OF INTERSTITIAL LUNG DISEASE ON THE HIGH-RESOLUTION COMPUTED TOMOGRAPHY (HRCT) IN EARLY SYSTEMIC SCLEROSIS PATIENTS

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Purpose. To determine the prevalence of interstitial lung disease (ILD) in early SSc patients and to compare the clinical differences between those SSc patients with and without ILD.

Methods. 103 SSc patients from an inception SSc cohort of newly diagnosed SSc (disease duration from NRP to study entry were within 36 months) seen at the dermatology clinic, Chiang Mai University Hospital from January 2010 to June 2013 were identified. 83 (80.6%) had HRCT performed within 3 months of the study entry were included. Data abstracted include baseline clinical characteristics, laboratory investigations and HRCT findings. The HRCTs were read by one experienced chest radiologist. Comparing between patients with and without ILD were made using Chi-square test, Fisher’s exact test, Student’s t test and Mann-Whitney U test, as appropriate.

Results. Of the 83, mean (SD) age was 52.8 years (7.8), and median disease duration was 8 months (8-36). Median (range) duration from HRCT performed to study entry was 0 month (0-3); 47 (56.6%) were female and 63 (75.9%) were classified as diffuse cutaneous SSc (dCSSc). There were patients with dyspnea, cough, NYHA class II, GERD symptoms, and positive anti Scl-70 of 43.4%, 24.1%, 62.6%, 37.3%, and 80.7% respectively. Mean (SD) values were: Modified Rodnan’s skin score [MRSS] 20.5 (11.0), Hb 12.5 (1.7), Cr 0.9 (0.3), % LVEF 67.6 (8.8), estimated systolic pulmonary artery pressure [sPAP] 31.9 (9.6). Median (range) values were: ESR 33 (11-161), CK 236 (32-5251). Current medications were: 38.6% low dose prednisolone, 27.7% colchicine, 24.1% chloroquine, 19.3% cyclophosphamide, 12% methotrexate, and 7.2% azathioprine. 62 (74.7%) were classified as having ILD determined by HRCT including 49 (59%) NSIP and 13 (15.7%) UIP. 7 (8.4%) had sPAP>45 mmHg determined by echocardiography. There were no significant differences between early SSc patients with and without ILD with respect to age, gender, disease duration, cough, NYHA class, GERD, ESR, CK and positive anti Scl-70. However, early SSc with ILD had higher proportion of dCSSc (82.2% vs. 57.7%, p=0.02), dyspnea (51.6% vs. 19%, p=0.009), and less methotrexate used (6% vs 28% p=0.014).

Conclusions. ILD is a common finding in our early SSc populations which is more prevalent in dCSSc patients with dyspnea. However, more than half of ILD patients were asymptomatic. Therefore, baseline HRCT of chest should be performed in SSc patients as early as possible to determine and promptly treat lung complication.

PS161

PROGNOSTIC FACTORS OF FUNCTIONAL OUTCOME IN SYSTEMIC SCLEROSIS-ASSOCIATED INTERSTITIAL LUNG DISEASE

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Introduction. Interstitial lung disease (ILD) is a frequent complication of systemic sclerosis (SSc). It is one of the first causes of mortality in this disease. ILD screening is mandatory at the initial evaluation and a close follow-up is necessary. However, the outcome and the factors influencing the evolution of ILD are still a matter of debate in SSc.

Patients and Methods. We retrospectively collected all pulmonary function tests (PFT) performed in 75 SSc patients with ILD with a mean follow up of 5 years and a median number of 5 PFT. FVC and DLCO evolution was modelled
using a linear mixed model with random coefficients. Clinical, biological and HRCT data at baseline were collected. HRCT were analyzed using the Wells score and the Goh staging system.

**Results.** Seventy-five SSc patients (57 females; 23 diffuse cutaneous SSc) with ILD (18 extensive forms according to Goh) were included. The linear mixed model with random coefficients showed that DLCO significantly decreased of 1.45±0.34%/yr while FVC remained stable. Multivariate analysis, patients with NYHA III/IV dyspnea, age<56yrs and/or less than 50% of ground glass opacities had a lower initial FVC. CRP<10 mg/L was the sole significant and independent parameter associated with a higher decrease in FVC over time. For DLCO, presence or past history of digital ulcer, grade 1 ILD and initial DLCO>70% were significantly associated with a higher decrease of DLCO over time. SSc subtypes and ILD extension had no influence on the FVC and DLCO outcomes.

**Conclusion.** Modeling PFT outcome in SSc-associated ILD is interesting to find prognostic factors. Initial CRP, reflecting IL-6 production, appears as an important prognostic factor for FVC evolution over time. Conversely, SSc subtypes and ILD extension were not prognostic factor for PFT evolution in our study.

**PS162**

**INTERSTITIAL LUNG DISEASE IN SOUTH AFRICANS WITH SYSTEMIC SCLEROSIS**

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**Background.** Interstitial lung disease (ILD) is one of the leading causes of death in systemic sclerosis (SSc). It has been poorly characterized in SSc patients in Sub-Saharan Africa. The aim of the study was to describe the associations of ILD in SSc patients with baseline demographic, clinical and laboratory features.

**Methods.** A retrospective review of case records, from 1992 until 2012, of patients with SSc attending a tertiary Connective Tissue Diseases Clinic. SSc ILD was defined based on features of ILD on high-resolution computed tomography (HRCT), with/without restrictive pulmonary function tests. Comparisons between ILD and non-ILD groups at presentation were performed using Fisher’s exact test and Student’s t-test where appropriate. A p-value <0.05 was considered significant.

**Results.** Of 151 patients evaluated, 60 (40%) had ILD. The female:male ratio was 9:1 in the non-ILD group and 5:1 in the ILD group (p=0.222). The majority of patients were Black in both groups (>85%). The mean (SD) age at diagnosis was 42.7 (12.1) years and 45.0 (13.4) years for patients with ILD and non-ILD, respectively (p=0.142). Univariate analysis is displayed in the table below.

<table>
<thead>
<tr>
<th>Variable</th>
<th>ILD (n=60)</th>
<th>Non-ILD (n=91)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean duration (range)</td>
<td>6.13 years (0-20)</td>
<td>3.95 years (0-20)</td>
<td>0.009</td>
</tr>
<tr>
<td>Diffuse limited disease</td>
<td>6.7</td>
<td>1.2</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Gold mining history (%)</td>
<td>5 (8.3)</td>
<td>1 (1.1)</td>
<td>0.073</td>
</tr>
<tr>
<td>Cough (%)</td>
<td>23 (35.0)</td>
<td>15 (16.5)</td>
<td>0.005</td>
</tr>
<tr>
<td>Dyspnea (%)</td>
<td>27 (45.0)</td>
<td>24 (26.4)</td>
<td>0.009</td>
</tr>
<tr>
<td>Bibasal crackles (%)</td>
<td>28 (46.7)</td>
<td>10 (11.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Positive ANA (%)</td>
<td>57 (95.0)</td>
<td>77 (83.5)</td>
<td>0.039</td>
</tr>
<tr>
<td>Scl-70 antibodies (%)</td>
<td>13 (22.8)</td>
<td>12 (15.6)</td>
<td>0.002</td>
</tr>
<tr>
<td>Anti-centromere antibodies (ACA) (%)</td>
<td>0 (0.0)</td>
<td>10 (13.0)</td>
<td>0.002</td>
</tr>
<tr>
<td>Nuclear ANA pattern (%)</td>
<td>13 (22.8)</td>
<td>28 (36.4)</td>
<td>0.002</td>
</tr>
</tbody>
</table>

On multivariate analysis the independent predictors of ILD were: disease duration (p=0.007); diffuse disease (p=0.0001); gold mining history (p=0.026); dyspnea (p=0.01); and bibasal crackles (p=0.001).

**Conclusion.** ILD in South African SSc patients is common. There should be a high index of suspicion for ILD in SSc patients presenting with a gold mining history, dyspnea, cough and bibasal crackles. Disease process appears to be driven by the diffuse subtype and anti-Scl-70 antibodies. Limited subtype, ACA and nuclear anti-nuclear antibody (ANA) patterns may have a protective effect.

**PS163**

**COMPARISON OF INTERSTITIAL LUNG DISEASE CT INDEXES AND PULMONARY FUNCTION VALUES IN SISTEMIC SCLEROSIS PATIENTS**

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**Background.** Pulmonary fibrosis is the main death cause in systemic sclerosis (SSc). Lung involvement is assessed with spirometry (which evaluates pulmonary function) and chest Computed Tomography (CT) scan (that identifies interstitial fibrosis). FVC <70% and DLCO <75% are considered pulmonary functional values associated with a remarkable interstitial lung disease (ILD) and, therefore, they are adverse prognostic indicators. Both qualitative and semiquantitative radiologic ILD assessment have a considerable interobserver variability. To overcome this problem quantitative scores (called CT indexes) correlating with ILD extent detectable on chest CT have been proposed.

The aims of this work are to find: a) whether there is a correlation between pulmonary functional tests and CT indexes, b) which CT indexes have the best performance in discriminating patients with a pulmonary functional indicative of an extensive ILD.

**Methods.** Chest TC and spirometry of 90 SSc patients (31 from Parma, 30 from Turin, 29 from Piacenza) meeting ACR criteria were performed. Digital Imaging and COmmunications in Medicine (DICOM) images of chest CT were processed with OsiriX (a free and user-friendly DICOM-viewer) in order to obtain patients’ CT indexes. The Spearman rank test was used to verify the correlations between CT indexes and spirometrical measures. CT indexes discriminative ability was verified using ROC analysis. A p-value <0.05 was considered statistically significant.

**Results.** Whole lung Kurtosis (Kurt) is the best FVC correlating CT index (rho = 0.623; p<0.0001). Parenchymal lung skewness (nSkew) is the best CT index correlating with DLCO (rho = 0.582; p<0.0001). ROC analysis showed that Kurt = 6,32 can discriminate very well patients with FVC <70% (sensitivity 80,0%, specificity 74,3%). Similarly nSkew = 2,2 distinguishes subjects with DLco <75% (sensibility 85.7%, specificity 52.2%).

**Conclusions.** Spirometry and CT indexes correlations are consistent with literature. The identification of CT index values corresponding to spirometric cutoff indicative of a considerable limitation of lung function makes TC ILD quantification useful in establishing SSc patients prognosis. Obtaining CT indexes with a free and user-friendly software can contribute to widespread in clinical practice this new SSc ILD assessment.

**PS164**

**SYSTEMIC SCLEROSIS INTERSTITIAL LUNG DISEASE EVALUATION: COMPARISON BETWEEN SEMIQUANTITATIVE AND QUANTITATIVE CT ASSESSMENTS**

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**Background.** The pulmonary fibrosis extent in sistemic sclerosis (SSc) patients is a crucial prognostic value. The gold standard to detect an interstitial lung disease (ILD) is the chest Computed Tomography (CT). ILD can be estimated through semiquantitative radiological scores and quantitative methods. The first ones are time consuming and they have a considerable inter- intra-observer variability. Quantitative scores are based on the detection of the parameters of the distribution of lung attenuation (also called CT indexes) which can be obtained only by using expensive and not so much user-friendly softwares.

The main aim of this work is to investigate whether a DICOM-viewer open-source software (OsiriX) can obtain CT indexes correlating with a semiquantitative score performed by an experienced radiologist. Secondary objectives are: to evaluate the discriminative ability of CT indexes in identifying patients with

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**3rd Systemic Sclerosis World Congress**

**Poster Session**

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**S-81**

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**S-81**
severe pulmonary involvement (according to radiologist’s opinion), and to establish which method (quantitative vs semi-quantitative) takes more time.

Methods. ILD detectable on chest CT of 32 patients with SSc was assessed with a radiologist’s semi-quantitative score. The same CTs were blindly processed by a rheumatologist using OsiriX to obtain the distribution parameters of lung attenuation. The semiquantitative score and the CT indexes were correlated through the Spearman rank test, the discriminative ability of CT indexes was verified using the ROC curve, and the best CT index was determined by the manufacturer, were as follows: CEA <2.5 ng/ml, CA19.9 <33 U/ml, CA125 <66 U/ml, DLCO, 79.5±16.7%; DLCO (predicted), 22.2±8.6; and DLCO (predicted), 16.4-22.8. Interestingly, 52.9% of patients with ILD showed stable lung function without significant mortality (mean survival time, 30.0 years with 95% CI of 26.3-33.9). The clinical characteristics of these patients included normal values of pulmonary function test (functional vital capacity, 79.5±16.7%; DLCO, 66.3±20.5%), no evidence of pulmonary arterial hypertension measured by echocardiography and no evidence of gastrointestinal involvement.

Conclusion. Certain subset of SSc patients with ILD may be treated without immunosuppressive treatment. Our results suggest a way to avoid potentially harmful immunosuppressive treatment in SSc patients with ILD.

PS161

ENHANCED ACTIVATION OF TGFbeta-RELATED SIGNAL-ING MOLECULES IN MONOCYTES FROM HEALTHY AFRI-CAN AMERICANS AND SSc ILD PATIENTS

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Background. We reported recently that healthy AA monocytes share abnormalities with Scleroderma-associated Interstitial Lung Disease (SSc ILD) monocytes including low caveolin-1 levels. Because the level of TGFbeta is higher in the blood of healthy AA than in healthy C and because TGFbeta treatment decreases caveolin-1 levels in healthy C monocytes, we here have determined whether TGFbeta signaling is activated in SSc ILD and healthy AA monocytes, and is regulated by caveolin-1.

Methods. The study was approved by the university’s IRB for Human Subject Research. Monocytes were isolated from the blood of SSc ILD patients and healthy donors by negative selection. The caveolin-1 scaffolding domain (CSD) peptide was used to restore caveolin-1 function to cells deficient in caveolin-1. TGFbeta treatment increased the migration cells treated with CSD or control peptide. Smad2/3, pSmad2/3, ERK, pERK, and in healthy AA monocytes compared to healthy C monocytes, while other ties with Scleroderma-associated Interstitial Lung Disease (SSc ILD) monocytes were expressed only at low levels in both AA and C monocytes. CSD treatment were inhibited ERK activation in AA and SSc and Smad2/3 activation in SSc monocytes. Treatment of healthy C monocytes with TGFbeta upregulated pERK and Smad2/3. This effect of TGFbeta was also reversed by restoring caveolin activity with CSD. We previously demonstrated that monocyte migration is enhanced in healthy AA monocytes and SSc monocytes and that this enhancement is reversed by CSD. Here we show that TGFbeta treatment increases the migration of both healthy C and healthy AA monocytes by a similar ratio (about 2.5-fold (p<0.0001), so the enhanced migration of AA monocytes compared to C monocytes was maintained following TGFbeta treatment. Treatment with CSD inhibited migration by >50%, demonstrating that the enhanced migration of TGFbeta-induced healthy AA monocytes is due to their relative lack of caveolin-1. TGFbeta treatment was also upregulated in AA and SSc monocytes and its expression was also inhibited by CSD.

Conclusion. Our results demonstrate that high serum TGFbeta and low caveolin-1 levels in monocytes may play a role in the predisposition of the AA population to SSc ILD via enhanced TGFbeta signaling and the resultant effects on monocyte migration.

PS166

CLINICAL CHARACTERISTICS OF SYSTEMIC SCLEROSIS PATIENTS WITH INTERSTITIAL LUNG DISEASE WHO DO NOT REQUIRE IMMUNOSUPPRESSIVE TREATMENT

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Background. Systemic sclerosis (SSc) is a connective tissue disease characterized by thickening of the skin and internal organs. Interstitial lung disease (ILD) is one of the major causes of death in this disease. Certain subset of ILD patients can be closely observed without potentially harmful immunosuppressive treatment. However, clinical characteristics of these patients are not clearly defined.

Method. A total of 151 SSc patients who were cared at Seoul National University Hospital between 1978 and 2013 were enrolled in this study. All of the patients were diagnosed as SSc according to the preliminary criteria of SSc by American College of Rheumatology and were diagnosed as having ILD based on chest computed tomography or radiography. Detailed data on clinical characteristics, treatment and its outcome were obtained by reviewing medical records. After calculating survival outcome of the patients, characteristics of the patients who did not require immunosuppressive treatment were defined.

Result. The mean (± S.D) age at diagnosis of SSc was 48.7 ±12.9 years with 88.7% of female predominance. ILD was diagnosed at the time of SSc in most of the patients. Among 151 patients, 72 (47.1%) required an immunosuppressive treatment which includes 45 cyclophosphamide, 8 azathioprine, 16 glucocorticoids and 3 others. During a total of 1,743 person-years of follow-up, 40 patients died (0.02 death/person-year). Mean survival time after diagnosis of SSc was 25.4 years (95% confidence interval (CI), 22.2-28.6) and that of SSc patients who received immunosuppressive treatment was 19.6 years (95% CI, 16.4-22.8). Interestingly, 52.9% of patients with ILD showed stable lung function without significant mortality (mean survival time, 30.0 years with 95% CI of 26.3-33.9). The clinical characteristics of these patients included normal values of pulmonary function test (functional vital capacity, 79.5±16.7%; DLCO, 66.3±20.5%), no evidence of pulmonary arterial hypertension measured by echocardiography and no evidence of gastrointestinal involvement.

Conclusion. Certain subset of SSc patients with ILD may be treated without immunosuppressive treatment. Our results suggest a way to avoid potentially harmful immunosuppressive treatment in SSc patients with ILD.
CAI25 may have a negative prognostic role, being associated with lung fibrosis as documented by HRCT and PFTs. Further studies on higher number of patients are warranted in order to identify a complementary biomarker for lung involvement in SSc among TAs, or alternatively a surrogate biomarker with prognostic significance.

PS168

RESIDUAL VOLUME: A CANDIDATE AS EARLY MARKER OF INTERSTITIAL LUNG DISEASE INSYSTEMIC SCLEROSIS PATIENTS?

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Background. Interstitial lung disease (ILD) affects 40% of systemic sclerosis (SSc) patients. In clinical trials and in clinical practice, pulmonary function test (PFT) and high resolution chest tomography (HRCT) are useful to assess the lung disease. Although a variety of PFT parameters have been used to study ILD in SSc, only the forced vital capacity (FVC) and diffusing capacity of the lung for carbon monoxide (DLCO) have been validated as an outcome measures in clinical trials. The changes of the residual volume (RV), in SSc patients, have never been evaluated.

Objectives. To assess RV predictive value for the presence of ILD-SSc and to investigate possible RV changes over 1 years of follow-up time, in SSc patients.

Method. 70 consecutive SSc patients (age 59.7 y ± 4.5; disease duration: 8.4 y ± 1.2; males: (n=) 7; females: (n=) 63) were enrolled; all patients underwent clinical examinations and PFT (RV, DLCO, TLC, FVC), every 6 months for 1 year, and HRCT at baseline and after 12 months. 31 patients had ILD at baseline. The results are expressed as means ± 1 standard deviation. Differences between baseline and follow-up parameters were evaluated by ANOVA for repeated measures. The hazard ratio were calculated by Cox regression.

Results. RV significantly decreases in 12 months (baseline: 95,84%±5,8; a 6 months: 87,84%±4,07; 12 months: 82,48%±4,5; p=0,013). We want underscore that DLCO, FVC, TLC tend to decrease in 12 month but no significantly. We subdivided patients with ILD and patients without and we found that: RV difference significantly (p=0,04) between SSc patients with ILD (baseline: 89,2% ± 9,7; 6 months: 81,67%±6,47; 12 months: 79,8%±5,1) and SSc patients without ILD (baseline: 109%±8,09; 6 months: 100,7%±6,1; 12 months: 92,2%±9,9). PFT parameters (DLCO, TLC, RV) values lower than 75%, did not represent a risk to develop ILD at 12 months (Fig. 1).

Conclusion. Although we cannot demonstrate that RV has a predictive value for ILD; its faster decrease than DLCO, FVC, TLC can make RV a candidate as early markers of ILD development. A larger cohort of SSc patients and a longer follow-up may unravel this issue.

Fig. 1.
follow-up period (SD) were 57 (15) year-old and 157 (316) months, respectively. Ambrisentan was initiated at the mean age (SD) of 60 (15). The mean value (SD) of % functional vital capacity (FVC), KL-6, and NT-pro BNP were 78 (19) %, 1221 (944) U/ml, and 218 (297) pg/ml, respectively. Phosphodiesterase type 5 inhibitor (in 7 patients, 64%), beraprost (in 5, 45%), tacrolimus (in 2, 18%), cyclosporine (in 1, 9%), and prednisolone (in 8, 73%) were included as concomitant medications. After the treatment with ambrisentan, progressive dysnea developed in 6 patients (55%). Ambrisentan was discontinued in 2 patients (18%) according to the recommendation regarding IPF. Additional 3 patients (27%) shortly withdrew from ambrisentan because each patient developed abdominal distension, dizziness, and edema, respectively. Among 7 patients treated with ambrisentan for more than 6 months, pulmonary function test was consecutively available in all patients except one with severe respiratory failure. Among the 6 patients, a worsening of % FVC with more than 10% and 5% was seen in 3 (50%) and 1 (17%) patient, respectively, and the deterioration of CTD-ILD with ground-glass opacities was seen in 3 patients by chest CT during the treatment with ambrisentan. An improvement of % FVC by nearly 10% was noted in one patient after the cessation of ambrisentan.

Conclusion. The result showed potential association of ambrisentan with the deterioration of CTD-ILD. The possibility could not be denied that it was just a natural course of the disease. Further analysis with a larger population is needed to clarify its association.

PS172

COMPARISON OF BAL AND SERUM CYTOKINES AND PREDICTIVE VALUE OF SERUM CYTOKINES IN SYSTEMIC SCLEROSIS PATIENTS

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Objective. To identify a specific pattern of BAL and serum cytokines in patients with systemic sclerosis (SSc) and pulmonary involvement and to investigate their association with survival.

Methods. BAL cytokines (IL-6, IL-7, IL-8, IL-10, CCL2, CCL4, TGF-β, TNF-α) were measured in 24 SSc patients with interstitial lung diseases (ILD), the same cytokines were measured in serum by bioplex analysis in 153 SSc patients fulfilling the ACR criteria, including the 24 SSc-ILD patients. Pulmonary involvement was documented and patients were followed up for a mean period of 66.2 months.

Results. SSc patients with pulmonary involvement had different BAL and serum cytokine patterns and BAL cytokines were mostly comparable or higher (IL-7, IL-8, TNF-α) than serum cytokines; there was some correlation of BAL and serum cytokines (serum IL-8 with BAL IL-8 and TNF-α, serum TGF-β with BAL IL-7, CCL2 and TNF-α). BAL cytokines IL-8 and CCL2 were increased in patients with ILD and pulmonary hypertension (PH-ILD) compared to patients with ILD only. Of the serum cytokines, IL-6 was significantly increased in patients with ILD and PH-ILD compared to SSc patients without pulmonary involvement. Levels of CCL2 were lower in patients with PAH and PH-ILD than in patients without pulmonary involvement and CCL4 was lower in patients with PH-ILD. The serum cytokine IL-6 could predict survival in patients with SSc, all patients with pulmonary involvement, pulmonary hypertension and SSc-ILD patients. In addition, IL-8 was identified as a novel predictive marker for survival in a SSc-ILD cohort.

Conclusion. In conclusion, the analysis of both BAL and serum cytokines implicates a role as biomarkers for distinct but different cytokines in both compartments. Our findings extend earlier work on the association of serum cytokines with clinical manifestations and survival. IL-6 and IL-8 may be interesting targets for therapeutic trials.

PS173

LYMPHOCYTE DEPLETION IN SYSTEMIC SCLEROSIS-ASSOCIATED INTERSTITIAL LUNG DISEASE AFTER TREATMENT WITH STANDARD AND LOW DOSES OF RITUXIMAB

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Background. There is increasing data suggesting potential beneficial effects of rituximab (RTX) in systemic sclerosis, but the adequate RTX dosage in systemic sclerosis-associated interstitial lung disease (SSC-ILD) have not yet been clearly defined. The extend of B-cell depletion in pts treated with different doses of RTX is not investigated.

Objectives. to evaluate the peripheral blood B lymphocyte depletion in SS-ILD after therapy with different doses of RTX

Material and methods. RTX was added to the ongoing treatment with corticosteroids of 30 pts (28 female), median age 47 years, range 17-71. The median disease duration before RTX treatment was 7 years (range 0.9-18) and the median post-treatment follow-up time was 12 months (range 6-34). Twenty pts was administered an infusion of 1g RTX 2 times, 8 pts – 500 mg 2 times and 2 pts - 500 mg once. B cell depletion was analyzed by flow cytometry.

Results. B-cell depletion was induced effectively in all pts at baseline. At Month 12 B cells in the peripheral blood were still depleted (0-0.00501109g/1) in 18 (60%) pts, reduced to 0.0060-0.05 109/l in 11 (37%) pts and in one pts B lymphocyte recovery was shown. At the end of the study pts receiving 2 g RTX had lower B lymphocytes level (0.006±0.01; median 0.0007) than pts receiving 1 g (0,02±0.06, median 0.004), but differences were not significant. Mean dose of RTX in completely depleted pts did not differ from incompletely depleted ones (1, 4±0, 6 g ± 1, 27±0, 5 g accordingly). Twelve months after therapy 25 (83, 3%) pts improved significantly (“good result” of treatment) and 4 (13, 4%) pts had “moderate effect”. One (3, 3%) pts (showed recovery of B-cells) was stable for
11 month but then developed the flare. Twenty two pts received immunosuppres- 
sants before RTM treatment and 9 - after. 

Conclusion. low dose 1 g RTX is comparable with typical RTX dosing 2 g with 
respect to B-cell depletion and the good effect on clinical outcome in patients 
with SS-IPL. This observation suggests that different therapeutic strategies could 
be taken into consideration.

PS174 SMALL ANIMAL MRI FOR NON-INVASIVE Longitudinal FOLLOW-UP OF PULMONARY FIBROSIS IN MICE

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Background. Pulmonary fibrosis, either idiopathic or secondary to diseases such as systemic sclerosis, is a devastating and life threatening disorder for which effective treatment is still lacking. The bleomycin-induced pulmonary fibrosis model is well-characterized and the most widely used mouse model. The result- ing fibrosis is routinely quantified by end-stage histological assessments, lacking the ability to follow-up on disease progression and potential therapeutic effects in the individual animal. At present, imaging tools for the evaluation of lung disease with good temporal and spatial resolution in vivo are limited.

Objectives. To optimize and evaluate lung MRI protocols to visualize disease onset and progression in the bleomycin-induced model of lung fibrosis. We compared prospectively and retrospectively gated MRI sequences and validated our results with established CT imaging of lung fibrosis and histochemical tech- niques.

Methods. Male C57Bl/6 mice were intratracheally instilled with bleomycin (0.05U in 50 µl of PBS) or sham. The mice were scanned with MRI and CT at baseline and weekly until 3 weeks after installation. After the last imaging time point, mice were sacrificed, ex vivo CT data acquired and the lungs were isolated for histological analysis and collagen quantification. MRI images were acquired on a 3T (Bruker Biospin, 20 cm) in combination with a 7.5cm quadrature coil, using the following sequences: (1) a respiratory triggered RARE sequence, (2) a respiratory triggered ultra short echo (UTE) sequence and (3) a retrospectively gated FLASH sequence IntraGate. For reconstruction, 70% of the respiration and ECG period was used. MRI data were quantified using ImageJ.

Results. The prospectively gated UTE and RARE protocols as well as retro- spectively gated IntraGate-FLASH imaging were able to visualize an increase of hyperintense focal spots over time, corresponding to progression of lung fibrosis as corroborated by lung CT images. Quantification of the mean lung signal inten- sity shows an increase over time, which was confirmed by the decrease in aerated lung volume quantified from the CT data and by histology.

Conclusions. The evaluated MRI protocols were all able to non-invasively visu- alize and quantify lung disease progression. Moreover, the IntraGate-FLASH protocol does not need setup of respiratory triggering for lung imaging, making it easy to use and efficient alternative to more conventional sequences. Where CT provides poor soft tissue contrast, MRI has the potential to provide contrast differences between vasculature, fibrotic areas and inflammation, without concerns for radioactivity when scanning repetitively.

PS175 PULMONARY INVOLVEMENT IN SSC PATIENTS – A SINGLE CENTRE EXPERIENCE

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Background. Intestinal lung disease (ILD) is the most frequent pulmonary complication and it is a major cause of death in systemic sclerosis (SSc). SSc- 
ILD has two patterns: the non-specific interstitial pneumonia (NSIP) and usual interstitial pneumonia (UIP).

Objective. To assess the computer tomographic (CT) patterns of lung disease in patients with systemic sclerosis interstitial lung disease (Ssc-ILD) and the asso- ciation with clinical, immunological parameters and the presence of pulmonary arterial hypertension (PAH).

Methods. This is a retrospective study of 42 Ssc patients who have been evalu- ated by high resolution computer tomography (HRCT) in our clinic. The patients underwent physical examination, evaluation of skin involvement, 6-minute walk test (6MWLT), echocardiographic assessment, immunological assessment and pulmonary assessment by HRCT and/or diffusion capacity for carbon monoxide (DLCO). Clinical data obtained by review of the medical records were classified according to current criteria.

Results. All the patients evaluated by HRCT were symptomatic or/and had a modified DLCO. From 42 patients evaluated by HRCT 33 (78,57%) patients had ILD pattern. Of those with ILD, 27% (24 of 33 subjects) had a nonspecific interstitial pneumonia (NSIP) pattern and 73% (9 of 33 subjects) had the usual interstitial pneumonia (UIP) pattern. There were 4 males: 2 with UIP pattern and 2 with NSIP pattern, and 29 women: 7 with UIP pattern and 12 with NSIP pat- tern. Eighteen of 33 (55%) subjects had limited skin involvement, 14 of 33 (42%) had diffuse skin involvement and one patient had scleroderma sine scleroderma. The onset and progression of dyspnea or the 6MWLT showed a poor correlation with the HRCT pattern (p=0,05). Antinuclear antibodies (ANA) were positive in high titer in both NSIP and UIP pattern with poor association. On echocardiographic evaluation the group with UIP pattern had a higher percent (33%) of patients with probably PAH (PAP>50 mmHg) than the group with NSIP pattern (4% (p=0,05). In the UIP group 44,4% of patients had diastolic dysfunction compared with 16,7% the NSIP group (p=0,05).

Conclusions. In our group the UIP pattern was more frequent then in other re- ports. Women were more likely to have the NSIP pattern. The group with UIP pattern had a higher percent of patients with PAP>50 mmHg and with diastolic dysfunction. These findings may suggest that the presence of UIP pattern can be associated with PAH and diastolic dysfunction.
of pred+rib or pred+dpa received both 1% of the patients. Triple combinations in 112 patients were pred+mtx/aza, pred/ccy/aza and pred/ccy/mtx.

Conclusion. Use of immunosuppressants is frequent in SSC-ILD patients showing a wide variety of single and combined substances. Prospective studies are necessary to define indications and outcomes. The EU-funded international DesScipher research project was initiated to achieve this goal, comprising 5 prospective observational trials addressing the most frequent medical problems in SSC patients.

PS177

ALPHA2 (V) CHAIN AND COLVA2 INDUCES THE FIBRILLOGENESIS PROCESS IN DISTORTED LUNG FRAMEWORK OF SYSTEMIC SCLEROSIS

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Background/Purpose. Fibrosis is a process associated with several diseases such as systemic sclerosis (SSc) and may involve some vital organs such as the lungs. Among the types of collagens involved in SSc, collagen V (COLV) can be highlighted considering its immunological aspects. It is known that mutations in COLV gene are involved in vascular diseases and that its unusual increase is correlated with the pathogenesis of SSc. Considering these characteristics, the aim of this study was to evaluate if the changes in total COLV mRNA expression, previously described in the literature, may be a reflex of the abnormal expression between its chains (COLV1 and COLV2) in the lungs of patients with SSc.

Methods. Patients. Expression of α1(V)(2)α2(V) and α1(V) and α2(V) molecular isoforms of COLV and tridimensional reconstruction (3D) were evaluated in 10 patients with SSc without pulmonary hypertension that underwent surgical lung biopsy and 6 controls of normal individuals who died from trauma. The SSc diagnosis and the work was approved by the Ethics Committee (CAPESp 9906/08).

Results. The α2(V) immunostaining showed distorted and strongly thickened fibers in lung with irregular bundles of α2(V) distributed in parallel and perpen dicular arrangements. These distributions resulted in a dense network around of the vessels in SSc patients compared with thin fibers pattern from the healthy controls. In contrast, α1(V) expression was lower interstitial compartment of the lung when compared with respective controls. Histomorphometric analysis of SSc lung demonstrated increased expression of the α2(V) in thickened alveolar septa, compared to controls (6.0±2.29α, p<0.01) as well as the molecular profile demonstrated increased COLVA2 gene expression in SSc lung (19.75 ± 3.187, p=0.001). Interestingly, α2(V) expression was 70% more frequent than α1(V) molecular isoform in SSc lung.

Conclusion. The overexpression of α2(V) chain and COLVA2 gene may drive the fibrillogenesis process in distorted lung framework from SSc patients, reinforcing the participation of COLV in this disease.

PS178

EFFICACY AND SAFETY OF INTRA VENOUS CYCLOPHOSPHAMIDE IN SCLERODERMA LUNG DISEASE OF ELDERLY

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Background. The efficacy of cyclophosphamide for scleroderma lung disease has been demonstrated in several randomized controlled trials. Infection is most concerning adverse event of the therapy, especially in elderly patients.

Objectives. The aim of this study was to evaluate the efficacy and safety of intravenous cyclophosphamide for interstitial lung disease (ILD) in elderly patients with scleroderma.

Methods. We performed a retrospective study of scleroderma patients with ILD who were at least 70 years old and treated with intravenous cyclophosphamide. Patients’ data, including pulmonary function test, six-minute walk test and adverse events regarding cyclophosphamide therapy, was collected.

Results. Four patients, including three women and one man, were included. Mean age, follow-up period and cumulative CYC dose were 75 years, 15.7 months and 3.31g. At the end of the follow-up period, FVC, DLCO and six-minute walk test improved: 62.3% and 77.6% (P=NS); 52.4% and 60.3% (P=NS); 421.4m and 543.7m (P=NS). There were any adverse events except for mild thrombocytopenia.

Conclusion. Intravenous cyclophosphamide is a highly effective therapy for ILD with few adverse events in elderly patients.

PS179

PULMONARY ARTERIAL HYPERTENSION, CLASSIFICATION CRITERIA

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Objective. To analyze the fulfillment of the old ACR 1980 and the new ACR-EULAR Preliminary Classification Criteria for Systemic Sclerosis (SSc) in patients with severe pulmonary arterial hypertension (PAH) associated to SSc.

Patients and methods. From 1990, all patients with clinical diagnosis of SSc were included in a database containing demographic and clinical information. Severe PAH patients, defined by mean pulmonary arterial pressure (mPAP)>40mmHg in right heart catheterization, in the absence of lung fibrosis and left cardiac dysfunction, were selected. The old ACR1980 and the new ACR-EULAR criteria were applied to the group. Clinical characteristics, hemodynamics and survival were compared between patients with or without ACR1980 criteria, using Chi-Square, t test and Kaplan-Meyer analysis.

Results. From 404 patients, 36 (9%, 2m/34f, age 56±16y) had severe PAH as mPAP 26±17mmHg. Time from Raynaud onset to HAP diagnosis was 16±11y. Two had diffuse and 34 limited cutaneous disease. ANA were positive in 34 (94%), ACA in 26 (72%) and αRNP in 4 (11%). None had aSc170. Mean mPAP was 55±11mmHg, wedge pressure 10±3mmHg, and pulmonary arterial resistance (PAP) 13±7WU. Only 19/52% fulfilled the old ACR1980 criteria, but all patients fulfilled the new ACR-EULAR criteria. From the 17 patients not fulfilling the old ACR criteria, all presented Raynaud, 16(94%) sclerodactily, 8(47%) finger edema, 13(76%) telangiectasia, 4/15(27%) calcinosis and 13/14(93%) low DLCO. One patient had renal crisis. Capillaroscopy was abnormal in 15/16(96%), ANA was positive in 14(82%), ACA in 11/16(69%) and αRNP in 2/16(13%). Only proximal sclero derma, ischaemic lesions and calcinosis (p<0.0001) for all) were more frequent in patients fulfilling the old ACR 1980 criteria than in those fulfilling only the new ACR-EULAR criteria. Hemodynamics were similar in both groups. Median survival was also similar. After 6±9 years of follow-up, 13 patients fulfilling and 12 not fulfilling the old ACR1980 criteria had died.

Conclusions. The new ACR-EULAR criteria for the classification of SSc have an excellent performance in patients with SSc-associated severe PAH. Since nearly half of this group of patients do not fulfill the old ACR1980 criteria, and present only with minor signs of the disease before developing HAP, our study points out: 1) the need to apply the new criteria to all patients with Raynaud and SSc suspicion in clinical practice, and 2) as SSc-HAP has better prognosis if diagnosed and treated early, it seems mandatory to screen all SSc patients, even those with very mild limited disease, to detect HAP as early as possible.

PS180

EPOPROSTENOL RESCUE THERAPY IN SYSTEMIC SCLEROSIS-ASSOCIATED PULMONARY ARTERIAL HYPERTENSION AND IDIOPATHIC PULMONARY ARTERIAL HYPERTENSION

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Background/Purpose. Epoprostenol has been demonstrated to improve hemodynamics, functional class, and six-minute walk distance (6MWD) in systemic sclerosis-associated pulmonary arterial hypertension (SSc-PAH) and idiopathic pulmonary arterial hypertension (IPAH) patients. In contemporary practice, it is currently reserved for patients who have failed treatment with endothelin receptor antagonists and/or phosphodiesterase-5 inhibitors. The effect of epoprostenol rescue therapy on survival has not been evaluated. The objective of this study was to evaluate the role of intravenous epoprostenol as rescue therapy in the SSc-PAH and IPAH patients.
Methods. Patients attending the University Health Network Pulmonary Hypertension Program between 1998 and 2012 were included if they had a diagnosis of SSc-PAH and IPAH based on a mean pulmonary artery pressure (mPAP) of >25 mmHg and a pulmonary capillary wedge pressure of <15 mmHg on cardiac catheterization, and had been treated with intravenous epoprostenol after treatment with endothelin receptor antagonists and/or phosphodiesterase-5 inhibitors for PAH. The primary outcome was survival. Survival was defined as the time from initiation of epoprostenol to death from any cause. Patients were censored as of May 1, 2012. Survival was evaluated using Kaplan-Meier curves.

Results. 1140 patients were reviewed to identify 36 patients with SSc-PAH and 24 patients with IPAH treated with epoprostenol after failure with oral pulmonary hypertension specific therapies. 83% of SScPAH and 75% of IPAH patients were female. The mean (standard deviation) PAH duration prior to initiation of epoprostenol was 3.3 (5.7) years for SScPAH and 2.1 (2.1) years for IPAH patients. Median 1-, 2-, 3-, 4-, 5-year survival for SSc patients was 85.7%, 60.7%, 53.6%, 46.1%, 42.3%; and for IPAH patients was 83.3%, 70.8%, 65.8%, 59.2%, 59.2%. There was no significant difference in survival between the SScPAH and IPAH patients treated with epoprostenol (p=0.13).

Conclusion. Our findings demonstrate desirable long-term survival and support the use of epoprostenol as rescue therapy for SSc-PAH and IPAH patients.

PS181
SEX DISPARITIES IN SURVIVAL OF SYSTEMIC SCLEROSIS-ASSOCIATED PULMONARY ARTERIAL HYPERTENSION AND IDIOPATHIC PULMONARY ARTERIAL HYPERTENSION PATIENTS
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Background/Purpose. Systemic sclerosis (SSc) associated pulmonary arterial hypertension (PAH) and idiopathic PAH (IPAH) are conditions with poor survival. There is evidence to suggest that sex affects survival. The primary objective of this study was to evaluate the effect of sex on survival in SSc-PAH and IPAH. We secondarily evaluated the effect of sex on disease onset, time to diagnosis, disease progression and treatment.

Methods. Patients were included if they attended the Toronto Scleroderma Program or the University Health Network Pulmonary Hypertension Program; had a diagnosis of SSc-PAH or IPAH defined as a mean pulmonary artery pressure >25mmHg and age > 16 years. Sex was defined as self-reported biological and physiological characteristics at birth (male, female). The primary outcome was the time from diagnosis to death from all causes. Secondary outcomes were sex differences in age of diagnosis, disease duration and SSc manifestations. Cox proportional hazards model were used to evaluate survival.

Results. 52 male and 267 female SScPAH; and 47 male and 107 female IPAH patients were identified. Male SSc patients had a shorter mean (standard deviation) time from SSc diagnosis to PAH diagnosis (5.6 (8.7) versus 8.4 (9.6), p=0.047), increased frequency of renal crisis (19% versus 9%, p=0.04), interstitial lung disease (67% versus 49%, p=0.02), and digital ulcers (29% versus 19%, p=0.001). Male IPAH patients had a higher frequency of diabetes (30% versus 12%). Despite adjusting for these differences, male SScPAH patients have decreased 1-, 2-, 3-, and 5-year survival (82.6%, 70.6%, 60.8%, 48.2%) compared to females (84.4%, 73.4%, 64.2%, 52.8%). Similarly, male IPAH patients have decreased 1-, 2-, 3-, and 5-year survival (93.4%, 87.9%, 84.8%, 77.7%) compared to females (94.5%, 91.0%, 88.7%, 83.2%).

Conclusion. Sex disparities appear to exist in survival of SSc-PAH and IPAH patients. Further investigation is needed to evaluate this disparity, mechanisms for disparity, and the role of a targeted screening and treatment approach.
subjects had AC, 39 (24%) NUC, 28 (17%) had other, 11 (7%) Scl70, 9 (6%) RNA polymerase III (RNAPol), 8 (5%) U1RNP autoantibodies. The mean SSc disease duration at PAH diagnosis was longest for AC (19.3±13.4y) and shorter for DCSSc (12.2±9.8, compared to AC =p0.02). Thirty-five (21%) subjects died over a mean follow-up time of 2.4±1.7 median (2, 0.7-2.2 years). 1-, 2-, 3-, and 5-year survival across all antibody groups was 93%, 86%, 76%, and 63%; 1-year survival estimates were 92% for AC; 91% for NUC; 76% for Scl70; 100% for U1RNP, 88% for other. No patients with RNAPol or negative autoantibodies died over the follow-up period. For all autoantibody groups, unadjusted and adjusted HR revealed no statistically significant association between risk of death and autoantibody positivity.

Conclusion. Anticentromere and NUC autoantibodies are prevalent in SSC patients with PAH. PAH may be a late complication in AC patients, but may occur earlier in SSc patients with other autoantibodies. There does not appear to be a significant association between SSC antibody type and survival in patients with PAH.

PS184
THE SIGNIFICANCE OF A ‘NORMAL DlCO’ IN SCLERODERMA (PHAROS) COHORT

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Background. The Pulmonary Hypertension Assessment and Recognition of Outcomes in Scleroderma (PHAROS) is a prospective longitudinal study of patients at risk of developing pulmonary arterial hypertension (PAH) and those who have definite pulmonary hypertension (PH). Pulmonary function tests (PFT), which capture the diffusion capacity (DLCO), are obtained in the routine care on SSc patients in this cohort. The purpose of this study was to describe the significance of a normal DLCO identified on PFT in PHAROS.

Methods. Entry criteria into PHAROS for SSc patients at high risk for PAH included: DLCO <55% predicted, a forced vital capacity (FVC) (%/DLCO) ratio >1.6 or an estimated pulmonary arterial systolic pressure (PASP) on echocardiogram >35mmHg. PAH is defined by a mean pulmonary artery pressure (mPAP) >15mmHg, a pulmonary capillary wedge pressure (PCWP), left atrial pressure, or left ventricular end-diastolic pressure less than or equal to 15 mmHg, and a pulmonary vascular resistance (PVR) greater than 3 Wood units. Patients complete are seen yearly for physical examination, PFT, echocardiogram, 6-minute walk, and clinical outcomes. We used Fisher’s exact to examine associations between two categorical variables and unpaired t-test for continuous variables. Significance was assigned at p<0.05.

Results. In this SSc patient population with PAH (n=166), DLCO of >60% at time of RHC (n=17) versus ≤60% (n=133). The significant PPT data in this group with normal DLCO versus ≤60%, includes A PFT that was lower, (91% vs 79% predicted, p=0.05) and mean DLCO that was higher 76.9% vs. 73.5% predicted (p=0.001). RHC parameters do not differ significantly between those with normal DLCO and those with DLCO ≤60%.

Of the 17 patients with DLCO initially >60%, 5 patients showed a DLCO <50% predicted on repeat PFT; 7 had very mild PAH with a PVR <300, which for 2 on repeat RHC was non progressive; 2 had repeat RHCs that showed significant diastolic dysfunction. Only 3 of these 17 patients had significant PH with non-normal DLCO, but also had increased PVR, and increased basic natriuretic peptide (BNP). None of the 166 patients died. There were no significant differences in demographics (age, sex, race, disease duration, SSc subtype, or antibody status).

Conclusion. Normal DLCO in PAH in SSc is very uncommon and rarely is severe. If it severe other clinical identifiers such as increased BNP, or RHC parameters such as increased PVR were present.

PS185
UTILITY OF B-TYPE NARIETRIPEPTIDES IN THE ASSESSMENT OF PATIENTS WITH SYSTEMIC SCLEROSIS-ASSOCIATED PULMONARY HYPERTENSION IN THE PHAROS REGISTRY

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Purpose. Elevations of B-type natriuretic peptide (BNP) and N-terminal proBNP (NT-proBNP) have been associated with worse outcomes in patients with pulmonary arterial hypertension (PAH). Elevated NT-proBNP has been integrated into novel PAH screening algorithms for patients with systemic sclerosis (SSc). We sought to assess the prognostic utility of natriuretic peptide levels in SSc patients at high risk for PAH (pre-PAH) or with definite PH diagnosed by right heart catheterization (RHC) within 6 months of enrollment. Criteria for pre-PAH include any one of the following: diffuse PAH (diffusing capacity (DLCO) <55% predicted, forced vital capacity/ DLCO ratio >1.6, or pulmonary artery systolic pressure on echocardiogram >40 mmHg. Patients with definite PAH have a resting mean pulmonary artery pressure >25 mmHg, A pulmonary capillary wedge pressure <15 mmHg was used to differentiate Group I PAH from Group II (PH related to left heart disease). Those with moderate or severe interstitial lung disease on chest imaging and FVC <60% predicted were included in Group III (PH related to hypoxemia).

Methods. PHAROS is a multicenter prospective cohort of SSc patients at high risk for PAH (pre-PAH) or with definite PAH diagnosed by right heart catheterization (RHC) within 6 months of enrollment. Criteria for pre-PAH include any one of the following: diffuse PAH (diffusing capacity (DLCO) <55% predicted, forced vital capacity/DLCO ratio >1.6, or pulmonary artery systolic pressure on echocardiogram >40 mmHg. Patients with definite PAH have a resting mean pulmonary artery pressure >25 mmHg, A pulmonary capillary wedge pressure <15 mmHg was used to differentiate Group I PAH from Group II (PH related to left heart disease). Those with moderate or severe interstitial lung disease on chest imaging and FVC <60% predicted were included in Group III (PH related to hypoxemia).

Results. 205 definite PH (135 Group I, 35 Groups II, 35 Group III) and 187 pre-PAH patients had natriuretic peptide levels available. Mean BNP and NT-proBNP levels were significantly higher in the definite PH compared with the pre-PAH patients (471.7±892.3 vs. 103.8±300.4 pg/mL and 1490.8±2506.1 vs. 125.0±189.8 pg/mL, p<0.0001). Group III patients had the lowest BNP and NT-proBNP levels, but there was no significant difference between Groups I and II.

In both the definite PH and Group I patients, NT-proBNP had stronger correlations with hemodynamic parameters than BNP (Table). The sensitivity and specificity of BNP>100 and NT-proBNP>210 for a diagnosis of Group I PH was 55% vs. 68% (p=0.19) and 72% vs. 81% (p=0.07), respectively. 14 pre-PAH
patients developed definite PH (10 Group I PAH) during a mean follow-up time of 3.7±1.4 years. BNP>100 and NT-proBNP>210 were not predictive of the development of PH or PAH, however, patients who developed PAH had a trend toward higher baseline NT-proBNP, but not BNP, levels compared with those who did not meet the criteria (149.4±6.7 vs. 125.7±197.7, p=0.06). In the definite PH group, 33 deaths occurred (17 Group I PAH). Neither BNP nor NT-proBNP was predictive of death.

Conclusions. NT-proBNP may be a better biomarker than BNP for early identification and monitoring of PAH in SSC patients, but confirmation of our results is necessary.

Table. Correlations Between Natriuretic Peptide Levels and Baseline Hemodynamics in Patients with Incident Systemic Sclerosis Associated Pulmonary Hypertension.

<table>
<thead>
<tr>
<th></th>
<th>r=Correlation</th>
<th>r=Correlation</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Mean±SD (N)</td>
<td>p-value</td>
</tr>
<tr>
<td></td>
<td>with BNP</td>
<td>with NT-proBNP</td>
</tr>
<tr>
<td>BNP, pg/mL</td>
<td>471.7±892.3 (141)</td>
<td>NA NA NA</td>
</tr>
<tr>
<td>NT-proBNP, pg/mL</td>
<td>1490.8±2506.1 (64)</td>
<td>NA NA</td>
</tr>
<tr>
<td>Mean pulmonary artery pressure, mmHg</td>
<td>38.1±11.1 (166)</td>
<td>0.43 &lt;0.001 0.53 &lt;0.0001</td>
</tr>
<tr>
<td>Pulmonary vascular resistance</td>
<td>510.2±385.5 (162)</td>
<td>0.36 0.001 0.55 &lt;0.0001</td>
</tr>
<tr>
<td>Cardiac output, L/min</td>
<td>5.0±1.7 (163)</td>
<td>-0.28 0.0027 -0.53 &lt;0.0001</td>
</tr>
</tbody>
</table>

B. Group I Pulmonary Arterial Hypertension

|                                | r=Correlation | r=Correlation |
|                                | Mean±SD (N)   | p-value       |
|                                | with BNP      | with NT-proBNP|
| BNP, pg/mL                     | 460.7±897.6 (95) | NA NA NA |
| NT-proBNP, pg/mL               | 1861.8±2949.4 (40) | NA NA |
| Mean pulmonary artery pressure, mmHg | 39.6±11.1 (106) | 0.32 0.006 0.53 0.001 |
| Pulmonary vascular resistance | 584.8±419.3 (104) | 0.36 0.002 0.56 0.0008 |
| Cardiac output, L/min          | 4.8±1.6 (105) | -0.23 0.06 0.62 0.0001 |

Conclusions. SSc-PAH patients had a higher risk of death than SSc patients without PAH after diagnosis of pulmonary hypertension by cardiac catheterization. The median survival SSc-PAH patients after diagnosis PAH by cardiac catheterization were 30 month. The hazard ratio for total mortality in the SSc-PAH group was 6.8 [95% confidence interval (CI) 2.1–16.7] compared to SSc without PAH (p=0.001).

Conclusion. SSc-PAH patients had a higher risk of death than SSc patients without PAH. The data obtained are comparable with results obtained previously; indicate the nature of a fatal disease in the absence of specific PAH therapy.
ECHOCARDIOGRAPHIC ALTERATIONS IN A SERIES OF PATIENTS WITH SYSTEMIC SCLEROSIS

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Aims. To describe the prevalence and types of echocardiographic abnormalities in a cohort of patients with scleroderma.

Material and method. A descriptive study based on the assessment of echocardiograms performed on a cohort of patients diagnosed with systemic sclerosis and followed up in a specialized unit in systemic autoimmune diseases at an Andalusian (Spain) third level hospital. Most echocardiograms were performed as part of the screening program of pulmonary arterial hypertension that is being carried out in our unit.

Results. 149 patients (pts) were assessed. Echocardiographic alterations were detected in 112 pts (75.1%). 1) Tricuspid insufficiency in 75 (50.3%; mild in 86.6%), and was associated with high systolic pulmonary pressure in 43 pts (57.3%) and with dilated right cardiac chambers in 11 pts (14.7%). 2) Left ventricular (LV) hypertrophy in 40 (26.8%); mild in 36 (90%) and moderate en 4 (10%). 3) Diastolic dysfunction in 36 (24.2%); light in all but 1. 4) Aortic valvulopathy en 22 (14.8%) with insufficiency in 18 (12.1%; mild in 10, moderate in 2 (11.1%) and stenosis in 2 (7.2% mild in all of them). 5) Mitral valvulopathy in 19 pts (12.7%) with insufficiency in 18 (12.1%; mild in 15, moderate in 3 (16.7%); stenosis in 1 (0.6%). 6) Pericardial effusion in 9 (6.0%); mild in 8 (88.9%) and moderate in 1. 7) Other alterations: left atrial dilatation in 15 pts (10.1%), left ventricle diastolic dysfunction in 1 (0.7%).

Discussion. Cardiac involvement is a serious manifestation of scleroderma is associated with decreased survival. The frequency of subclinical involvement depends on the methods used for its detection and echocardiography, along with clinical assessment, remains the tool of choice for early diagnosis.

Conclusions. 1) By systematic echocardiographic study, we found a very high prevalence of alterations among patients with scleroderma. 2) Valvular dysfunction, especially tricuspid, with or without underlying elevation in pulmonary artery pressure, was the most frequent abnormality found. 3) A high prevalence of diastolic dysfunction and other frequently associated data, such as left ventricular hypertrophy and left atrial enlargement were detected.

ELEVATED SERUM LEVELS OF MACROPHAGE MIGRATION INHIBITION FACTOR (MIF) AND STEM CELL GROWTH FACTOR beta (SCGF beta) IN PATIENTS WITH PULMONARY ARTERIAL HYPERTENSION (PAH)

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Background. Pulmonary Arterial Hypertension (PAH) is an important vascular disease that can be either idiopathic or secondary to autoimmune diseases, in particular it represents one of the most threatening complications of Systemic Sclerosis (SSc). Macrophage Migration Inhibitory Factor (MIF) and Stem Cell Growth Factor β (SCGF-β) are pleiotropic cytokine with important proinflammatory and immunoregulatory functions. MIF appears to be important in determining the endothelial damage and seems to contribute to lung bipsis vasoconstruction in murine models and to play a key, but controversial, role in wound repair (1.2). Moreover in SSc patients serum levels of MIF are increased compared to healthy controls and has been associated with the development of ulcers and PAH (3,4). SCGF-β is also involved in the pathogenesis of some demyelinating neuropathies and its levels increase in idiopathic dilated cardiomyopathy (5,6).

Objectives. The aim of our study was to measure serum levels of MIF and SCGF-β in SSc patients with and without PAH as well as in those with primary PAH.

Patients and Methods. We enrolled 15 SSc patients with PAH and 13 with primary PAH. We also selected 14 SSc patients without PAH, matched for sex and age. PAH was confirmed by right heart catheterism (PAPmean 25 mmHg). MIF and SCGF-β were measured by ELISA (Bio-Rad Laboratories).

Results. We found significantly higher circulating levels of MIF and SCGF β compared to those SSc patients without PAH, both in patients with primary PAH (MIF median 270 pg/ml vs 175 pg/ml, p=0.03; SCGF-β median 18845 pg/ml vs 12054 pg/ml, p=0.004) and with PAH secondary to SSc (MIF median 333 pg/ml vs 175 pg/ml, p=0.02; SCGF-β median 17804 pg/ml vs 12054 pg/ml, p=0.02). No statistically significant difference was found between the two groups of patients with PAH, either idiopathic or secondary to SSc.

Conclusions. From these preliminary data we can hypothesize that MIF and SCGF-β are able to play a role in the development of PAH in both primary or secondary forms. These circulating factors may be evaluated in the future as useful biomarkers for this serious vascular disease.

PS191

PULMONARY ARTERIAL HYPERTENSION IN A CONTEMPORARY DRUG REGISTRY: RESULTS OF THE VOLT STUDY, WITH AN EMPHASIS ON PAH ASSOCIATED WITH CONNECTIVE TISSUE DISEASE

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VOLT (VOL-bris Tracking), an EMA regulatory required study, is an open-label, prospective, observational, multicenter registry that has been structured to collect safety information on ambrisentan (AMB) to treat pulmonary arterial hypertension (PAH) when used in clinical practice. Here we present the results with an emphasis on PAH associated with connective tissue disease (CTD).

Methods. Between June 2008 and May 2011, a total of 1003 patients were included in the VOLT programme, of which 238 had a diagnosis of PAH associated with CTD. The study closed in May 2013, 2 years after the final patient was included.

Results & Conclusions. Results will include baseline demographics (aetiology, form of SSc), significant difference in prevalence and symptoms between limited and diffuse with SSc is essential for early detection of PAH. The authors didn’t observed a constant relationship between clinical manifestations of HAP and the values of PASP.

Conclusion. There was a relative high incidence of PAH in our series and slight predominance of PAH in diffuse form, probably due to concomitant pulmonary interstitial fibrosis. There was not a constant relationship between clinical manifestations of HAP and the values of PASP. PAH may be considered here since increased right ventricular systolic pressure is related to the increase of CT ratio (CT ratio>0.55) in chest radiography (p<0.05) and increased brain natriuretic peptide in blood (p<0.05).

PS192

PREVALENCE OF PULMONARY HYPERTENSION IN PATIENTS WITH SYSTEMIC SCLEROSIS

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Introduction. This study analyzed the prevalence of Pulmonary Arterial Hypertension (PAH) in a cohort of patients with Systemic sclerosis (SSc) and correlated with the clinical form of the disease.

Objective. To describe the epidemiological profile of patients included in the study and compare the results between limited and diffuse forms of SSc.

Methods. 28 consecutive patients with confirmed SSc (22 females, 6 males, mean age 51.1±2.1 years), with mean time of 91±6.7 months from SSc diagnosis, were prospectively included in the study. Two chest radiographies were obtained for each during the course of this study. First chest radiography was checked at diagnosis and second chest radiography was checked at research time. The enrolled subjects were agreement on echocardiography and measurement of brain natriuretic peptide. The statistical method was SPSS software version 11.0 (SPSS Inc., Chicago, IL, USA).

Results. Four patients were estimated to pulmonary hypertension by echocardiography. The one patient who taken cardiac catheterization and confirmed to pulmonary hypertension, had severe resting dyspnea and the other had no clinical symptoms. The increased right ventricular systolic pressure is related to the increase of CT ratio (CT ratio>0.55) in chest radiography (p<0.05) and increased brain natriuretic peptide in blood (p<0.05).

Conclusion. The increased of CT ratio (>0.55) in chest radiography is relation to increased right ventricular systolic pressure in systemic sclerosis patients. So the periodic checked chest radiography is important for early detection of the asymptomatic pulmonary hypertension in systemic sclerosis patients.

Table 1. Characteristics of the 28 patients enrolled in this study.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>High pulmonary pressure</th>
<th>Normal pulmonary pressure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex, female (n)</td>
<td>4</td>
<td>18</td>
</tr>
<tr>
<td>Median age (years)</td>
<td>60.50±11.67</td>
<td>50±1.22</td>
</tr>
<tr>
<td>Median disease duration (months)</td>
<td>102.0±30.20</td>
<td>91±13.21</td>
</tr>
<tr>
<td>Median BNP (pg/mL)</td>
<td>183.0±378.77</td>
<td>52±7.07</td>
</tr>
<tr>
<td>Median C/T ratio</td>
<td>0.56±0.01</td>
<td>0.74±0.14</td>
</tr>
<tr>
<td>With ILD (n)</td>
<td>11</td>
<td>9</td>
</tr>
<tr>
<td>With anti-scl-antibody (n)</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>Left atrial pressure</td>
<td>57.2±2.76</td>
<td>25±4.94</td>
</tr>
</tbody>
</table>
| BNP: Brain natriuretic peptide; C/T: ratio cardiothoracic ratio, Pulmonary a pr: pulmonary arterial pressure; ILD: interstitial lung disease; UPI: Usual interstitial pneumonia; NSIP: Non-specific interstitial pneumonitis.

Fig. 1. The correlation of right ventricular systolic pressure and cardiothoracic ratio. (Pearson correlation coefficient: -0.06, p-value: 0.003, Relative risk: 4.00 (95% confidence interval: 2.60 - 7.99)).
**PS194**

**EARLY PULMONARY HYPERTENSION AND EARLY PULMONARY FIBROSIS: HOW CAN I TREAT? AND WHO IS THE FIRST?**

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Universidade Federal da Paraiba, Joao Pessoa, BRAZIL.

Pulmonary Arterial hypertension and Pulmonary Fibrosis are two of the most important mortality causes in patients with systemic sclerosis. The treatment must be intense and immediate. We what we still do not know is what to do with patients that have both complications in early stages. Pulmonary hypertension has a specific treatment that should be avoided when we have evident pulmonary fibrosis, but we show a case of early fibrosis that do not demanded specific treatment and had early confirmed pulmonary arterial hypertension. Another discussion is pulmonary hypertension with small increase of pulmonary capillary pressure suggesting a concomitant pulmonary arterial hypertension. Another discussion is pulmonary hypertension early fibrosis that do not demanded specific treatment and had early confirmed pulmonary arterial hypertension.

**Objective.** The correlation of brain natriuretic peptide and cardiothoracic ratio (p<0.05).

**Results.** The median RDW value of patients with SSc was higher 14.2% (13.5-14.8, 25-75% percentiles) compared both to the group of primary Raynaud’s cases 13.9% (13.4-14.4; p<0.05) and to healthy volunteers 13.6% (13.2-13.8; p=0.01). DcSSc and anti-topoisomerase antibody positive cases showed elevated RDW values compared to lcSSc and anti-topoisomerase antibody negative cases (p<0.05), respectively. RDW showed positive correlation with the inflammatory markers including ESR (p<0.05), CRP (p>0.05) and negative correlation with forced vital capacity (p<0.05) and diffusing capacity of the lung (DLCO) (p<0.05) during the follow-up. A rise of RDW more than 5% during follow-up was associated with an average 8.9% decrease of ejection fraction (LVEF) and 7% of DLCO and these associations were independent from each other.

**Conclusion.** RDW in SSc may represent an integrative measure of multiple pathologic processes including extensive vasculopathy, fibrosis, or ongoing inflammation. An increase in RDW value may indicate an impairment of cardio-respiratory functions.

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**PS195**

**CLINICAL USEFULNESS OF MEASURING RED BLOOD CELL DISTRIBUTION WIDTH (RDW) IN PATIENTS WITH SYSTEMIC SCLEROSIS**

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3University of Pécs, Institute of Family Medicine, Pécs, HUNGARY;
4Semmelweis University, 3rd Department of Internal Medicine, Budapest, HUNGARY.

**Objectives.** Red blood cell distribution width (RDW) is a biomarker quantifying variability of red blood cell size in peripheral blood. Elevated RDW has been found an independent prognostic factor for cardiovascular events. Systemic sclerosis (SSc) is characterised by generalised micro- and macroangiopathy. Our aim was to investigate RDW as a potential biomarker for the assessment of the severity of vascular involvement.

**Patients and Methods.** One-hundred and sixty-eight consecutive SSc patients, 62 with diffuse cutaneous (dcSSc), 106 with limited cutaneous SSc (lcSSc) were investigated at baseline and after 1-year follow-up. Measurements in 93 patients with primary Raynaud’s phenomenon and 40 healthy subjects served as control groups.

**Results.** The median RDW value of patients with SSc was higher 14.2% (13.5-14.8, 25-75% percentiles) compared both to the group of primary Raynaud’s cases 13.9% (13.4-14.4; p<0.05) and to healthy volunteers 13.6% (13.2-13.8; p=0.01). DcSSc and anti-topoisomerase antibody positive cases showed elevated RDW values compared to lcSSc and anti-topoisomerase antibody negative cases (p<0.05), respectively. RDW showed positive correlation with the inflammatory markers including ESR (p<0.05), CRP (p>0.05) and negative correlation with forced vital capacity (p<0.05) and diffusing capacity of the lung (DLCO) (p<0.05) during the follow-up. A rise of RDW more than 5% during follow-up was associated with an average 8.9% decrease of ejection fraction (LVEF) and 7% of DLCO and these associations were independent from each other.

**Conclusion.** RDW in SSc may represent an integrative measure of multiple pathologic processes including extensive vasculopathy, fibrosis, or ongoing inflammation. An increase in RDW value may indicate an impairment of cardio-respiratory functions.

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**PS196**

**ARRHYTHMIAS AND HEART CONDUCTION DISTURBANCES IN PATIENTS WITH SYSTEMIC SCLEROSIS**

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Conduction disturbances in SSc are mostly due to the fibrosis of the sinoatrial node, but direct involvement of the cardiac conduction tissue and its arterial blood supply has also been reported.

**Objectives.** To assess conduction disturbances and cardiac arrhythmias in a consecutive and non selected series of patients with Sclerosis Systemic.

**Patients and Methods.** A total of 142 (122Women-20Men) unselected consecutive pts with SSc were included in our study. They had mean age 51.2 years (range 13-84), disease duration 12.2 years ± 7.5 (range 1-24). All met the preliminary American College of Rheumatology classification criteria for SSc. And according skin cutaneous subsets: 16 pts (11.3%) with Early Sclerosis, 12 pts (8.4%) with intermediate cutaneous SSc, 72 pts (50.7%) with Limited cutaneous SSc, 42 pts (29.6%) with Diffuse cutaneous SSc. As expected all pts suffer from Raynaud’s Phenomenon and nailfold videocapilarscopy (NV) was performed on all patients, and skin sclerosis was measured with Rodnan Skin Score (mRSS). All the patients were assessed for cardiac complaints according to the World Health Organization (WHO) functional class, electrocardiogram (ECG) abnormalities, transthoracic echocardiography (EchoCG) and N-terminal pro-brain natriuretic peptide (NT-proBNP) levels. A subset of 49 pts underwent 24-h Holter-ECG recording.

**Results.** Only 14 pts (9.8%) presented functional class 3-4 according to the WHO classification. Elevated NT-proBNP levels were present in 45 pts (31.6%). EchoCG abnormalities were present in 70 pts (49.2%): left atrial enlargement in 42 pts (35.2%), left heart dysfunction in 16 pts (11.2%), valve abnormalities, mostly tricuspid regurgitation, in 18 pts (12.6%). Possibly or definitely abnormal ECGs were found in 44 pts (30.9%), 20 pts (14%) had AV conduction abnormalities, 5 pts with pacemaker due to AV II block. Left bundle branch block was found in 10 pts (7.0%), 7 pts (4.9%) had septal q wave pattern with narrow QRS complex. Three patients (2.1%) had left ventricular hypertrophy and four patients (2.8%) unspecific ST-T wave abnormalities. A subset of 49 pts underwent 24
h-Holter-ECG recording: thirty-three patients had normal recording, 16/49 pts (11.2%) abnormal recording. The most common finding was an increased number of extrasystoles, eight had >1000/ves/24h, 7 pts had non-sustained ventricular tachycardia ≥3 pts atrial arrhythmias, 2 pts AV I block.

Conclusion. Despite the mild clinical complaints, cardiac abnormalities in EchoCG were found in 49.2% of pts.

PS197

ECHOCARDIOGRAPHY OF THE RIGHT VENTRICLE IN PATIENTS WITH SYSTEMIC SCLEROSIS AND RELATED CTD

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Systemic sclerosis has serious prognosis in the case of the development of organ complications. The presence of cardiac involvement can lead to pulmonary hypertension and the development of severe pulmonary hypertension. Echocardiography at our department is performed routinely in all patients with connective tissue diseases. Suspicion or diagnosis of pulmonary hypertension is found by echocardiographic screening in a low percentage of patients only. A number of authors therefore search for non-invasive predictors of pulmonary hypertension, such as exercise induced pulmonary hypertension. The aim of our study is to evaluate the importance of deformation analysis (global longitudinal strain by speckle tracking) of right ventricle free wall, and other parameters of systolic and diastolic function of the right ventricle from the point of their predictive potential in patients with systemic sclerosis and other related diseases. We present our first results and their possible benefits for the detection of pulmonary hypertension in the group of 25 patients at our centre.

PS198

ASYMPTOMATIC CARDIAC INVOLVEMENT IN THAI SYSTEMIC SCLEROSIS: PREVALENCE AND CLINICAL CORRELATION

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Background. Cardiac involvement is one of the most serious manifestations of systemic lupus erythematosus (SLE). In its absence, the lupus may progress to the lupus nephritis and the development of severe pulmonary hypertension. The presence of cardiac involvement can lead to pulmonary hypertension and the development of severe pulmonary hypertension. Echocardiography at our department is performed routinely in all patients with connective tissue diseases. Suspicion or diagnosis of pulmonary hypertension is found by echocardiographic screening in a low percentage of patients only. A number of authors therefore search for non-invasive predictors of pulmonary hypertension, such as exercise induced pulmonary hypertension. The aim of our study is to evaluate the importance of deformation analysis (global longitudinal strain by speckle tracking) of right ventricle free wall, and other parameters of systolic and diastolic function of the right ventricle from the point of their predictive potential in patients with systemic sclerosis and other related diseases. We present our first results and their possible benefits for the detection of pulmonary hypertension in the group of 25 patients at our centre.

Conclusion. Despite the mild clinical complaints, cardiac abnormalities in EchoCG were found in 49.2% of pts.

PS199

CORRELATION BETWEEN CARDIAC MAGNETIC RESONANCE IMAGING AND ECHOCARDIOGRAPHY IN SYSTEMIC SCLEROSIS

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Objectives. To describe cardiac magnetic resonance imaging (CMRI) findings indicated in actual clinical situations, in a cohort of patients with SSC cardiac involvement (CI), and correlate them with contemporary echocardiography results held in our database.

Material and methods. Twenty one patients from a 413 subject cohort were enrolled from February 2002 to April 2013. They presented definite CI or high suspicion of it. They underwent CMRI with gadolinium contrast using a 1.5T system (Symphony, Siemens, Germany), with a 4-element phased array antenna obtaining functional sequences of multislice cine-MRI.

Results. Seventeen patients (81%) were women. SSC subset distribution was: 10 (47.6%) limited SSC, 9 (49.2%) diffuse SSC, 1 (4.8%) sine SSC and 1 (4.8%) pre scleroderma. Immunologically, antinuclear antibodies were present 20 (95.2%) patients, anticientromere antibodies in 5 (25%) patients, and antitopoisomerase-I antibodies in 6 (30%) patients. Baseline characteristics were: digital ulcers 14 (66.7%), osteomuscular impairment 12 (57.1%), esophageal involvement 17 (81%), interstitial lung disease 15 (71.4%), pulmonary arterial hypertension 9 (42.9%) and none with scleroderma renal crisis. The frequencies of cardiovascular risk factors were: High blood pressure in 5 (23.8%) patients, dyslipidemia 7 (33.3%), diabetes mellitus 2 (9.5%) and smoking 5 (23.8%).

CI was known in 20 patients: pericardial involvement 3 (15.0%), ischemic cardiomyopathy 5 (23.8%), conduction alterations 6 (28.6%). Echocardiographic findings were: left ventricle hypertrophy (LVH) in 9 (42.9%) patients, diastolic dysfunction in 19 (90.5%) and pericardial effusion in 3 (14.3%). Median tricuspid annular plain systolic excursion (TAPSE) was 20mm and median left ventricle ejection fraction (LVEF) was 63%. CMRI findings were: LVH in 4 (19%) subjects, none with diastolic dysfunction, pericardial effusion in 11 (52.4%). Median right and LVEF were both 59%. Left VEF detected by echocardiography and CMRI showed a moderate reliability (Intraclass correlation coefficient=0.55, p=0.004) and a moderate correlation was found between TAPSE and Right VEF (R=0.49, p=0.033). Unweighted kappa for LHV, DD and pericardial effusion assessed by echocardiography and CMRI didn’t show significant reliability.

Conclusion. CMRI seems to have good correlation and reliability compared with echocardiography regarding functional parameters of both right and left VEF. Important differences were noted in heart structural findings (LVH and pericardial effusion), where it may be more sensible. The role of CMRI in clinical practice is still unclear, but it may be more rentable in patients strongly suspicious to have CI in order to prevent further complications.

PS200

CHARACTERISATION OF SUB-CLINICAL PRIMARY MYOCARDIAL DISEASE IN SYSTEMIC SCLEROSIS - PRELIMINARY FINDINGS FROM A CARDIAC MAGNETIC RESONANCE AND ELECTROPHYSIOLOGICAL STUDY

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Background. Clinically overt primary myocardial disease in SSc carries a poor prognosis. The natural history is poorly understood, with no clear approach to identifying the ‘at-risk’ patient. Cardiac CR (MR) is a sensitive tool for detecting functional changes, tissue characterisation and perfusion changes. CMR studies in SSc have rarely correlated with disease phenotype.

Objectives. To identify the patient with SSc most at risk of primary myocardial disease and better understand the pathophysiological mechanisms, through the use of soluble cardiovascular (CV) biomarkers, electrophysiological testing and CMR. This study is a collaborative initiative between rheumatologists and CMR cardiologists.

Method. Fifty patients fulfilling SSc ACR/Le Roy criteria with no known CV disease or diabetes mellitus are being invited for clinical assessment, nail-fold...
SUBTLE IMPAIRMENT OF RIGHT VENTRICULAR FUNCTION IN SYSTEMIC SCLEROSIS WITH LUNG FIBROSIS DETECTED BY TISSUE DOPPLER

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Background. Systemic sclerosis (SSc) is an autoimmune connective tissue disease that courses with fibrosis and microvascular occlusion, involving skin and visceral organs, including lungs and the heart. It is not clear whether involvement of the right ventricle (RV) results from direct organ lesion or indirectly by pulmonary hypertension.

Objective. To assess the relationship between RV performance and lung involvement in SSc.

Methods. Fifty-one consecutive patients from the Sclerodema Outpatient Clinic were submitted to tissue Doppler echocardiography and chest high resolution computed tomography (HR-CT). RV function was evaluated by means of RV fractional area change (FAC), tissue Doppler (systolic) velocity, myocardial performance index (MPI), and tricuspid annular plane systolic excursion (TAPSE). Pulmonary artery systolic pressure (PAP) was estimated by tricuspid regurgitation. Additionally, left ventricular systolic (ejection fraction) and diastolic (transmitral Doppler and mitral annulus tissue Doppler) function was also evaluated. Chest HR-CT was used to assess interstitial lung disease (ILD). According to the CT results, patients were divided in two subgroups: Group 1, including patients with ILD, and Group II with no ILD.

Results. Out of the 51 SSc patients, 37 were female, aged 52±12 years; all patients had normal ventricular function, as assessed by LVEF >55% and FAC >40%. 43 patients had chest HR-CT. There was no significant difference age or disease duration in groups I (n=26) and II (n=17). Except for decreased tissue Doppler velocities, all indexes of RV performance were similar for both groups.

Conclusion. In patients with SSc and ILD, tissue Doppler systolic velocities seem to identify early myocardial involvement, despite a preserved RV systolic performance.

CARDIAC TROPONIN T AND ANTI-CARDIAC TROPONIN I ANTIBODIES IN PATIENTS WITH SYSTEMIC SCLEROSIS: A MONOCENTRIC, RETROSPECTIVE PILOT STUDY

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Background. Cardiac troponins (cTn) are widely used as biomarkers for the diagnosis and quantitation of cardiac injury (1). Autoantibodies against cTnI, especially against cTnI (anti-cTnI), have been recently described in association with cardiac dysfunction (2). However, their clinical significance is still unclear. Systemic sclerosis (SSc) is a chronic autoimmune connective tissue disease that is associated with heart involvement, although often clinically occult (3,4). Hence, the value of elevated cTn levels and a possible autoimmune response against cTnI as biomarkers in patients with SSc were the aims of this study.

Methods. Out of our monocentric SSc cohort we retrospectively identified 113 of 190 patients in whom routine laboratory assessment including high-sensitivity cTnI was performed. Stored biosamples, available for 60/113 patients (53.1%), were used to assess auto-cTnI titres as previously described (5). A 2x2 table, using chi-square test, compared the results of cTnT and anti-cTnI. If available, cardiac magnetic-resonance-imaging (cMRI) data were retrospectively evaluated to assess early myocardial gadolinium enhancement (T1 ratio, as a marker for hyperemia and capillary leakage) as well as edema (T2 ratio).

Results. Out of 113 patients with available results for cTnT, 41 patients (36.3%) had a positive and 72 (63.7%) a negative result. Biosamples were available for 21 cTnT positive and 39 cTnT negative patients. Anti-cTnI were detected in 17 samples (28.3%); in 8 (38.1%) cTnT positive compared to 9 (23.1%) cTnT negative patients (p=0.218). Anti-cTnI titres were 1:40 in 7, 1:80 in 6 and 1:160 in 4 samples. cMRI data were available for three anti-cTnI positive patients (all diffuse cutaneous subtype). All of them had a distinct change in the T1 ratio (6.4-8.9), not in the T2 ratio. Late enhancement (gold standard for the detection of myocarditis) was present in one patient (6).

Conclusion. The preliminary results of this pilot study suggest that cTnT levels are elevated in about one third of SSc patients, and anti-cTnI are present in about a quarter of cTnT negative patients. Whether cTnT and/or anti-cTnI autoantibodies might serve as new biomarkers in SSc heart disease need to be evaluated in further prospective trials.

Literature

CARDIAC VALVE MORPHOLOGY AND LEFT VENTRICULAR FUNCTION IN PATIENTS WITH SYSTEMIC SCLEROSIS (SSC) AND MATCHED POPULATION CONTROLS

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Objective. To investigate cardiac valve morphology and left ventricular ejection fraction (LVEF) in patients with systemic sclerosis (SSc) and matched population controls. We also studied the occurrence and relationship between manifest cardiovascular disease (CVD) and abnormal echocardiography findings.

Methods. 110 patients (62±12 years) with SSc were compared with 105 age and gender matched population-based controls (61±12 years). CVD was defined as a history of objectively verified angina pectoris, myocardial infarction, cerebral infarction or intermittent claudication. Echocardiography was performed to assess valvular abnormalities and left ventricular function.
Results. 44 SSC patients had an abnormal echocardiogram compared to 23 subjects in the control population (p<0.001). On group level SSC patients had lower (but normal) LVEF (p=0.02). Three of the SSC patients had undergone valve replacement, and one had a significant valve insufficiency. Two subjects in the control group had undergone valve replacement. Valve thickening or valve prosthesis was found in 28 patients and 19 controls (NS). 20 SSC patients and 7 control patients had previous myocardial infarction (MI), 8 had angina (among them two with MI), 7 patients had peripheral vascular disease, among them 5 had undergone surgery (2 of them also had an MI). Among patients with CVD 8 had valve thickening or prosthesis, 5 had LV hypokinesia, 3 had LVEF < 35, six had PAH (defined as T1 velocity>2.9/ms). Among controls with CVD 3 had MI, 4 had CTVL. Three controls with CVD had valve thickening, all had normal LVEF and none had PAH.

Conclusion. SSC patients have a higher prevalence of abnormal echocardiograms than population based controls and previous CVD was also more common among SSC patients. On group basis SSC patients had lower (but normal) LVEF though more SSC patients than controls had regional hypokinesia (p=0.02). Valve thickening or valve prosthesis was not more common among the SSC patients than among population controls.

PS204
PERICARDECTOMY ON CONSTRUCTIVE PERICARDITIS AND DIFFUSE SYSTEMIC SCLEROSIS: FORTUITOUS ASSOCIATION?
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Aims. Asymptomatic pericardial effusions commonly occur in SSC. Moreover it’s observed also large effusions causing tamponade and can even occur prior to skin thickening and the diagnosis of SSC. We report 2 singular cases of constructive pericarditis which are associated in the following by the appearance of diffuse SSC.

Case report:
• The initial case report is referring to 47 old woman witch antecedent – 15 years ago – is characterized by pericardectomy in constructive pericarditis presumed tuberculosis, and treated in both by surgical and medical treatment (6 months of anti-tuberculosis regimen). She developed progressively fibrosis pulmonary, progressive skin thickening, sclerodactyly, characteristic scleroderma facies, apertistatic esophagus and right heart failure (arrhythmia). The investigation established the diagnosis of diffuse SSC and the right heart failure. The symptoms and specifically treatment improve the symptoms.
• The second case is similar and is referring to 36 years old woman witch developed 2 years after pericardectomy on presumed tuberculous constructive pericarditis a diffuse SSC. The SSC is characterized by severe malabsorption syndrome (decreased peristalsis throughout the gastrointestinal tract, leading to bloating, satiety, and pseudo-obstruction crisis). The facies is characteristic and the others syrings are suggestive of the SSC diagnosis (hyperpigmentation, sclerodactyly, contracture, Raynaud phenomenon…). The treatment is optimized referring to the actualized recommendations and improve the digestive manifestations.

Discussion. Pericardial abnormalities in scleroderma are common and usually asymptomatic. However, clinically symptomatic pericardial disease (5%-16%) is far more frequent than autopsy-demonstrated pericardial involvement (33%-72%) as reported by many authors. Large pericardial effusions are exceptional and can lead to pericardial tamponade and are a marker for poor outcome. These situations are associated to right failure in heart disease, pulmonary hypertension and renal crisis. The constructive pericarditis is not reported as common in SSs and constitutes a singular presentation (fortuitous association?).

Conclusion. Presumed as tuberculous – referring to the epidemiological context – or attributed to viral infections some constructive pericarditis could be the first expression in asymptomatic SSC (misdianagosed SSC) particularly in the forms of the SSC without scleroderma and justify early immunological tests and nailfold capillaroscopy in indeterminate etiology of constructive pericarditis.
SCLERODERMA AND MYOCARDIAL INFARCTION: IS NOT FORTUITOUS ASSOCIATION!

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Aim. To bring back an observation characterized by myocardial infarction (MI) revealing a scleroderma in its cutaneous form.

Observation. Its about 58 years old woman, BMI at 25, hypertensive 4 years ago and stabilized by monotherapy which in April 2012 present a myocardial infarction. The echocardiography identifies the presence of disorders of the segmentary kinetics of the LV, with deterioration of the contractile function (SEF at 50%) without obviousness of pericardial effusion, neither of intracardiac thrombus, nor of pulmonary hypertension (PH). The angiographic data highlight a thrombotic very tight stenosis of the proximal AIV at 80% extending to ostium, CD rudimentary with spasm in end of probe, vascular exploration does not show any aneurysmic plaques.

Conclusions. 1.Nearly 40% of patients had BMI>25. 2. A high percentage of patients had hyperhomocysteinemia. 3. The percentage of subjects who had increased IMT and/or carotides plaques is high, around 40%. 4. Endothelial dysfunctional function was found in more than half of the cases, and it was severe in almost 40%.

SCF207

DATABASE ANALYSIS OF CARDIOVASCULAR RISK FACTORS IN 123 DANISH PATIENTS WITH SYSTEMIC SCLERODERMA

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Background. Systemic scleroderma (SSc) is a connective tissue disease with abnormalities in vascular, immunological and fibrotic pathways. The vasculopathy is characterized by fibrinoliminal proliferation of small vessels and vasospastic episodes triggered by cold or stress. This may lead to tissue ischemia. Primary cardiovascular involvement is well-known in SSc and is considered a leading cause of mortality in SSc patients after lung fibrosis.

Increasing evidence suggests that primary myocardial affection is associated to repeat focal ischemic injury leading to subsequent irreversible myocardial fibrosis. However, the exact mechanism of the pathogenesis is unknown. Most available data is based upon clinical evaluation, electrocardiogram, ecocardiography and thoracic X-ray and CT-scans.

Methods. In order to describe cardiovascular involvement and evident cardiovascular risk factors we investigated an array of clinically important cardiac parameters in a Danish SSc cohort consisting of 123 patients. We obtained data such as blood pressure, ventricular function, eco-estimated palumal arterial hypertension, NYHA class, cardiac and other biomarkers along with lung function, smoking history, mdRedan skin scores, Raynaud’s phenomenon during a period of one year. Statistical analyses was performed to describe any clinical relevant association of cardiovascular parameters in this population using descriptive statistics and logistic regression.

Results. Our preliminary data analysis demonstrates substantial correlations between SSc and cardiovascular risk factors and cardiac involvement per se. All data will be presented in the poster.

Conclusion. Cardiac involvement occurs in SSc patients and the information presented may constitute clinical prognostic values. Furthermore, our preliminary data may give rise for the implementation of novel cardiac monitoring techniques such as cardiac MRI suitable for the routine clinical practice.
Conclusions. Minor DIF was found for FACT-F items for the French and Dutch versions compared to the original English, which had only a small effect on the overall score. Therefore, scores generated with the FACT-F in English, French, and Dutch SSc patients can be reasonably pooled without adjustment for linguistic differences. If our results are replicated, however, the translations of several items, particularly the Dutch translation of items 7 and 8, should be reconsidered, especially given the influence of the FACIT system in other approaches to measure fatigue in chronic diseases. The importance of assessing cross-language measurement equivalence prior to pooling outcomes obtained in different languages should be emphasized.

PS210

ASSESSMENT OF SENSITIVITY TO CHANGE OF THE DISEASE ACTIVITY SCORE IN SYSTEMIC SCLEROSIS

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Background. Systemic sclerosis (SSc) is a rare multi-systemic disease which may have a bad prognosis. Moreover treatment options are limited. Continuous research concerning this topic is ongoing. To improve the research in SSc and to facilitate the interpretation of clinical trials, there is a need of a standardized disease activity index as outcome measure. The Disease Activity Score (DAS), proposed by the European Scleroderma study group, meets nearly all the OMERACT-standards of truth, discrimination and feasibility. Only the sensitivity to change remains to be attested.

Aim. This study assesses sensitivity to change of the DAS in patients with early and severe Diffuse cutaneous Systemic Sclerosis (DcSSc) treated with rituximab.

Methods. 12-months follow-up (open-label study) of 14 consecutive patients with early DcSSc. Patients received an infusion of two times 1000mg rituximab at month 0 and 6, together with 100mg methylprednisolone. Low-dose prednisolone (no more than 10 mg/day) was allowed, provided patients were taking a stable dose at least 12 weeks before inclusion. All disease-modifying antirheumatic drugs (except methotrexate) were stopped 12 weeks before screening. Patients were on a stable dose methotrexate (10-25 mg/week) as background therapy since at least 12 weeks. Clinical read outs (modified Rodnan skin score, mRSS; lung function and echocardiography) and DAS were performed at month 0, 3, 6 and 12. Mixed models analyses (MMA) were used to evaluate changes in parameters over time.

Results. There was a clinical significant change in skin score with a mean (SD) mRSS of 24.8 (4.44) at baseline and 10.4 (3.12) at month 12 (MMA p<0.001), a mean/median percentage improvement over 12 months of 58%/59%. Indices of internal organ involvement remained stable throughout the study (MMA: DLCO p=0.044, FVC p=0.478, TLC p=0.206, FEV p=0.283, LVEF p=0.291, sPAP p=0.790) (see Table I). In parallel, interestingly, the DAS decreased statistically and clinically significant with a mean (SD) of 4.3 (1.79) at baseline and 0.7 (0.83) at month 12 (MMA p<0.001) (see Table II). The mean/median percentage improvement over 12 months was 84%/86% respectively. Five serious adverse events occurred, considered to be probably unrelated to the study medication.

Conclusion. A significant improvement of the DAS was observed, in line with the significant improvement of the mRSS and the stabilization of internal organ involvement. To our knowledge this is the first study to attest sensitivity to change of the DAS in a clinical trial setting in the subset of patients with early DcSSc.

Table I. Changes in clinical parameters in patients with early and severe Diffuse cutaneous Systemic Sclerosis (DcSSc) treated with rituximab (N=14).

<table>
<thead>
<tr>
<th>Variable</th>
<th>Statistic</th>
<th>0M</th>
<th>3M</th>
<th>p value*</th>
<th>6M*</th>
<th>p value*</th>
<th>12M</th>
<th>p value*</th>
<th>p value MMA</th>
</tr>
</thead>
<tbody>
<tr>
<td>mRSS</td>
<td>Mean (SD)</td>
<td>24.8 (4.44)</td>
<td>18.9 (6.29)</td>
<td>&lt;0.001</td>
<td>14.1 (4.17)</td>
<td>&lt;0.001</td>
<td>10.4 (3.12)</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Min, max</td>
<td>Median (Q3)</td>
<td>24.5 (21.0, 28.3)</td>
<td>18.0 (13.8, 25.0)</td>
<td></td>
<td>16.0 (9.5, 17.5)</td>
<td></td>
<td>10.0 (9.0, 11.5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DAS Mean (SD)</td>
<td>4.3 (1.79)</td>
<td>2.0 (1.35)</td>
<td>&lt;0.001</td>
<td>1.1 (0.67)</td>
<td>&lt;0.001</td>
<td>0.7 (0.83)</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Min, max</td>
<td>Median (Q3)</td>
<td>3.5 (3.4, 5.6)</td>
<td>1.8 (1.4, 3.0)</td>
<td></td>
<td>1.0 (0.5, 1.8)</td>
<td></td>
<td>0.5 (0.5, 1.0)</td>
<td></td>
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</tbody>
</table>
**PS211**

**EXPLORING THE IMPACT OF FOOT DISABILITY IN SYSTEMIC SCLEROSIS**

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**Background.** While it is established that foot pathology in patients with systemic sclerosis (SSc) is associated with disability, the impact of such problems has yet to be determined. The aim of this study was to explore the physical and psychological consequences of foot pathology in SSc.

**Methods.** General and disease specific information was collected from 121 SSc patients attending the outpatient clinic at Leeds and 51 healthy controls who were invited to participate in the study. All participants completed three patient-reported outcome measures: the Manchester Foot Pain and Disability Index (MFPI); MOS SF-36, and Hospital Anxiety and Depression Scale (HADS). Data analysis was undertaken using the Mann-Whitney test for between-group comparisons and Spearman’s ρ to determine correlations between measures.

**Results.** Of the 121 patients recruited (106 female; median age, 59 years, ranges 25 to 86 years), 96 had lcSSc; 24 had dcSSc, and one had SSc sine scleroderma, with a median disease duration of nine years (IQR: 4,13) and a median modified Rodnan Skin Score (mRSS) of 27 (IQR: 4). The control group comprised 51 healthy volunteers (43 female; median age, 49, ranges 21 to 81 years). In terms of foot problems, patients with SSc had significantly greater foot-related disability than controls (median MFPI function score 11 vs. 0), greater foot pain (median MFPI pain score 5 vs. 0) and poorer perception of foot appearance (median MFPI appearance score 1 vs. 0) all p values=0.001. Of note, patients with SSc had significantly worse general functional status (SF-36 median physical score 30 vs. 56), mental health perception (SF-36 median mental health score 46 vs. 56) anxiety (HADS median anxiety score 8 vs. 5) and depression (HADS median depression score 6 vs. 1) than controls (all p<0.001).

In order to explore the specific impact of foot pathology, the MFPI subscales scores were correlated with general physical and psychological outcomes. Not surprisingly, foot function was significantly correlated with physical subscale of the SF-36 (r=0.63, 95%CI [0.766 to -0.478]), but notably also with the mental summary subscale of the SF-36 (r=0.45, 95%CI [0.605 to -0.309]) and both anxiety (r=0.41, 95%CI [0.254 to 0.608]) and depression subscales of the HADS (r=0.60, 95%CI [0.432 to 0.735]) all p values ≤0.001.

**Conclusions.** This study demonstrates people with SSc have significant foot disability and that this is associated with significant detrimental physical and psychological consequences. This study highlights the need for further studies aimed at improving foot outcomes in people with SSc.

**PS212**

**TRANSITION OF CARE AND LONG-TERM OUTCOMES OF JUVENILE SYSTEMIC SCLEROSIS DURING ADOLESCENCE: RESULTS FROM A FRENCH SINGLE-CENTER CASE-CONTROL STUDY**

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**Introduction.** Juvenile Systemic Sclerosis (SSc) is a rare systemic connective tissue disorder that is responsible for a high rate of morbidity and mortality. Long-term outcomes of patients with juvenile SSc remain poorly characterized. The aim of this study was to describe the transition of care from Pediatric to an adult Internal Medicine department and long-term outcomes of patients with juvenile-onset SSc, by conducting a retrospective single-center case-control study.

**Patients and Methods.** Thirty patients with SSc diagnosed before the age of 17 and previously followed in Pediatric departments were included. The control group comprised 39 patients randomly selected from all patients with a SSc diagnosis after 18 years old, matched by sex and disease duration. All patients were followed in the department of Internal Medicine of Cochin Hospital. We retrospectively collected from both pediatric and adult medical records demographic, epidemiological, clinical, immunological data and treatments.

**Results.** In the juvenile-onset group, 11/13 (85%) patients were female and 7/13 presented a diffuse SSc. Mean age at diagnosis was 12.5 years (7.0-17.4). No patient had anti-centromere, 3/13 (23%) anti-Scl70 and 2/13 (15%) anti-U1RNP autoantibodies.

At the first visit to the adult department, mean disease duration was 6.6 years (0.9-19). While juvenile-onset patients had a significantly higher incidence of calcinosis (8/13 (62%) vs 5/39 (13%); p=0.001), they had a lower incidence of pulmonary hypertension (0/13 (0%) vs 10/39 (26%); p=0.05) and lung fibrosis (1/13 (8%) vs 16/39 (41%); p=0.039) compared to the adult-onset group. At the time of last follow-up, mean disease duration was 10.3 years (4.5-18.6). Survival rate was lower among the juvenile-onset group but this difference was not significant (10/13 (77%) vs 37/39 (95%); p=0.092) and bowel involvement had a significantly higher incidence (7/13 (54%) vs 8/39 (21%); p=0.034). Juvenile-onset patients had received significantly more steroids 3/13 (23%) vs 8/39 (26%) (p=0.049) and methotrexate 7/13 (54%) vs 6/39 (15%); p=0.01), without a higher incidence of major side effects. Factors associated with a poor prognosis in juvenile-onset SSc were lung fibrosis and pericarditis.

**Conclusion.** At the time of transition to adult care structures, patients with juvenile-onset SSc have more severe musculoskeletal damages and lower incidence of lung involvement than patients with adult-onset SSc. The long-term prognosis of juvenile SSc is poor. We suggest that close collaboration between adult and pediatric structures could improve both life expectancy and quality of life by standardizing the management of damage and detection of cardiac and pulmonary complications.

**PS213**

**IN SYSTEMIC SCLEROSIS, ANXIETY AND DEPRESSION, ASSESSED BY HOSPITAL ANXIETY DEPRESSION SCALE ARE INDEPENDENTLY ASSOCIATED WITH DISABILITY AND PSYCHOLOGICAL FACTORS**

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**Background.** Anxious and depressive symptoms are frequent in Systemic Sclerosis (SSc). Our aim is to assess their prevalence, their association with district and global disability and psychological variables and potential differences between subsets.

**Methods.** 119 SSc patients (14 men and 105 women; 74 with ISc and 45 with dcSSc; age: 59.46 ± 13.87 years; disease duration, 10.74 ± 7.42 years) and 50 age- and sex-matched controls were assessed by Hospital Anxiety Depression Scale (HADS) for anxious (HADS-A) and depressive (HADS-D) symptoms and for comorbidity of anxiety and depression. Clinical depression and anxiety were defined for HADS score cut-off ≥8 or higher. Patients were also assessed for psychological symptoms (Rosenberg Self-Esteem Scale ‑RSE-, Coping Orientation to Problems Experienced ‑New Italian Version ‑COPE-NIV-), hand (Hand Mobility In Scleroderma Test ‑HMAS-, Cochin Hand Functional Disability Scale ‑CHFDs-, fist closure, hand opening) and face disability (Mouth Handicap in Systemic Sclerosis Scale‑MHISS-, mouth opening), global disability and fatigue (Health Assessment Questionnaire ‑HAQ‑, Functional Assessment of Chronic Illness Therapy‑Fatigue Scale ‑FACIT‑).

**Results.** In SSc patients, HADS-D (6.14±3.97) and HADS-A (6.66±4.09) were higher than in healthy controls (4.72±2.88 and 5.16±3.05) (p<0.05), but not different in JSSC versus dSSC (p=NS). Both depression and anxiety in SSc were 36%: 1519 patients (13%) had only depression, 15/119 (13%) presented only anxiety and 28/119 (23%) had both depression and anxiety.

Depressive patients with comborbid anxiety had significantly higher HADS-D score than patients with depression only (11.39±1.73 vs. 9.4±1.64; p=0.001). In controls, depression and anxiety were 10% (5/50) and 20% (10/50), lower than in SSc (p<0.05); the co-presence of depression and anxiety, (2/50 subjects 4%) was lower than in SSc (p<0.001) and depressive subjects with comborbid anxiety had significantly higher HADS-D score than those with depression only (9.52±1.4 vs. 9.4±2.86; p=0.001). In SSc, by bivariate analysis, HADS-A and D were positively correlated with HAQ, HAMIS and CHFDs, HMISS, FACIT, RSES and COPE-NIV Avoidance Strategy, and, only HADS-A, also with COPE-NIV Social Support (p<0.05 in all cases).

By multiple regression, HADS-D was independently associated with FACIT-F (p<0.001), RSES (p<0.001), HMISS (p<0.016), together explaining 50% of variance. HADS-A was independently associated with RSES (p=0.006), COPE-NIV Avoidance Strategy (p=0.003), COPE-NIV Social Support (p=0.008), FACIT-F (p=0.022) and HMISS (p=0.029), explaining 41% of variance.

**Conclusions.** In SSc, depression and anxiety are frequent and correlate to local and global disability and psychological characteristics. Depressive patients with comborbid anxiety have higher level of depressive symptoms.
PS214

SYSTEMIC SCLEROSIS DIAGNOSED IN ELDERLY: A FRENCH RETROSPECTIVE STUDY OF 27 PATIENTS

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Introduction. Mean age at the time of diagnosis for systemic sclerosis (SSc) is around 50 years (y). One study showed a peak of incidence in Caucasian women aged 65-74 y, but data are lacking about specificities of SSc diagnosed in elderly. The aim of this work was to describe SSc phenotype when diagnosis is made after 70 y of age.

Patients and methods. Retrospective study from a single center French cohort over the period 1995-2013. Only patients aged 70 y and more at the time of diagnosis of SSc and fulfilling the ACR criteria for the diagnosis of SSc were included. Demographical, clinical, and paraclinical data at the time of diagnosis were retrospectively collected and analyzed.

Results. Among 246 patients, 27 (11%) were included (89% of women). At the time of SSc diagnosis, age was 78.6±y. Patients were Caucasian in 26 cases, and no silica exposure was noted. Patients had the following comorbidities: left cardiac failure (22%), cancers (22%), including lung (n=2), breast (n=2), and colon (n=1) cancer, diagnosed on average 4.9 y before SSc. In 58% of cases, SSc had started recently suggesting a real elderly disease, whereas for 42% of patients, minor signs of SSc were present before the age of 70 without any diagnosis of SSc. SSc was mainly cutaneous limited (96%), and Rodnan score was 7.8±6. Anti-centromere Ab were detected in 76% of cases. Signs at the time of diagnosis of SSc included: Raynaud phenomenon (96%), ischaemic digital ulcers (26%), digital pitting scars (18%), telangiectasia (66%), sicca syndrome (26%), gastro- sphageal reflux (59%), watermelon stomach (14%), anal incontinence (11%), extensive interstitial lung disease (30%) which was significantly more frequent among patients over 80 (p=0.046). Pulmonary arterial hypertension (PAH) was suspected in 13 patients using cardiac ultrasonography, distance at the 6-min walk test was 118.7±4m, and mean TCO2 was 38% of expected value in these patients. Only 5 patients underwent routine heart catherization, and 4 had PAH (mPAP=54±17, pulmonary wedge pressure=11±6 mmHg, cardiac index=2.1±1 L/min/m2). Conclusion. In more than 10% of patients, SSc is diagnosed after 70 y of age, which mainly correspond to real forms of disease starting in the elderly. At this age, diffuse scleroderma are uncommon and 20% of the patients have past history of cancer. Watermelon stomach seems to be frequent (14%), PAH is frequently suspected and is the first sign leading to SSc diagnosis in at least 15% of cases.

Results. In the SSc patient group a TAS-20 score indicating alexithymia (> 61) was present in 15 subjects (30%), while in 11 (22%) patients the TAS-score indicated a borderline status (50-60). The prevalence of alexithymia was significantly higher than in the healthy subject group, where it was found in 4 cases (11%) (p=0.038). The proportion of subjects with moderate to severe depression (BDI>23) was greater in the SSc patient group (12 pts, 24%) than in healthy subjects (1 pt, 3%) (p=0.01). The SSc group of patients showing alexithymia and borderline status (26 patients, 52%) was found to have a significant correlation with disease duration longer than 5 years (p=0.038). Moreover the SSc group with alexithymia had a strong correlation with moderate to severe depression (p=0.0002). There was no statistically significant difference between the diffuse and the limited forms.

Conclusions. We found that SSc patients are more likely than healthy subjects to have difficulty in identifying and describing feelings, presenting higher alexithymia scores. Our data underline also that the severity of the emotional impairment of alexithymia is related with longstanding disease. Besides a moderate to severe depression is more prevalent in the patient group. These results underline the importance of considering emotions in SSc patients.

References

PS215

ALEXITHYMIA: UNSPEAKABLE SUFFERING, A PREVALENCE STUDY IN SYSTEMIC SCLEROSIS

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Introduction. Systemic Sclerosis (SSc) is associated with chronically painful symptoms. Patients with SSc may be at particular risk for depression due to the high levels of overall disability that may influence the emotional suffering. The psychological construct of alexithymia, literally meaning “no words for mood”, was firstly coined in 1972 to describe people who lack the ability to communicate their feelings and who seem unable to fantasize (1).

Objective. To evaluate the prevalence of alexithymia in ScS patients, comparing its prevalence with that of a group of healthy subjects.

Methods. We used the Italian validated translation of Toronto Alexithymia Scale (TAS-20) (2) to assess the alexithymic trait. It was administered to 50 ScS patients (F/M = 48/2; mean age = 59 years; diffuse form/limited form = 24/26; presence or history of digital ulcers in 20 patients and a mean disease duration 10 years) and to 37 healthy subjects (F/M = 35/2; mean age = 56 years). We also measured depressive symptoms by administering the Italian validated version of Beck Depression Inventory (BDI) to both groups.

Results. In the SSc patient group a TAS-20 score indicating alexithymia (> 61) was present in 15 subjects (30%), while in 11 (22%) patients the TAS-score indicated a borderline status (50-60). The prevalence of alexithymia was significantly higher than in the healthy subject group, where it was found in 4 cases (11%) (p=0.038). The proportion of subjects with moderate to severe depression (BDI>23) was greater in the SSc patient group (12 pts, 24%) than in healthy subjects (1 pt, 3%) (p=0.01). The SSc group of patients showing alexithymia and borderline status (26 patients, 52%) was found to have a significant correlation with disease duration longer than 5 years (p=0.038). Moreover the SSc group with alexithymia had a strong correlation with moderate to severe depression (p=0.0002). There was no statistically significant difference between the diffuse and the limited forms.

Conclusions. We found that SSc patients are more likely than healthy subjects to have difficulty in identifying and describing feelings, presenting higher alexithymia scores. Our data underline also that the severity of the emotional impairment of alexithymia is related with longstanding disease. Besides a moderate to severe depression is more prevalent in the patient group. These results underline the importance of considering emotions in SSc patients.

References
PS217
SURVIVAL PROGNOSTIC FACTORS AND CAUSE OF DEATH IN 213 IRANIAN PATIENTS WITH SYSTEMIC SCLEROSIS
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Background. The natural history of systemic sclerosis varies and depends on severity of organ involvement. The role of gender, race, extension of skin involvement, scleroderma in visceral organs and serologic factors has been shown in mortality of systemic sclerosis.

Aim of the Study. To determine survival and causes of death in a cohort of Iranian SSc patients and to analyze influence of demographic, clinical and immunologic variables on survival.

Material and methods. The study population included 213 consecutive SSc patients first seen between February 1998 and June 2013 in Firoozgar hospital. The patient’s onset was defined as the Raynaud’s phenomenon or non-Raynaud’s scleroderma related sign or symptoms. The frequency of clinical features, organ system outcomes, and survival within patients with specific antibody were cumulative over the course of the disease. The predictive value of hypothetical prognostic variables associated with death was initially examined by univariate statistical methods for continuous or categorical data, for all patients who died versus all who survived. The variables with P<0.2 in univariate analysis were included in a Cox-proportional model; a forward strategy was used for modeling.

Results. The study includes 186(87.3%) women and 27(12.3%) men. Eighty three of 213 patients had diffuse SSc and 130 limited SSc. Thirty one (14.5%) patients died. Deaths were due to cardiac involvement in eleven, progressive pulmonary fibrosis in four, isolated pulmonary arterial hypertension in three, cardiopulmonary and gastrointestinal bleeding in one, scleroderma renal crisis and malignancy each in two patients. Cause of death in six patients was not available. Cumulative 5 years and 10 survivals based on Kaplan-Meier analysis were 89%, 87% after the patients develop first symptoms of disease. Survival rate after 15 and 20 years were 77% and 35%.

Univariate analysis: The patients with age >40 years, time interval from symptoms to entry >5 years, esophageal reflux at presentation, friction rub at first visit and pulmonary arterial hypertension, scleroderma renal crisis arthritis, FVC percentage <70%, interstitial fibrosis in HRCT, hypertension >139/89, pericardial effusion and presence of anti-TOPO antibodies that in log-Rank test had P values<0.02, included in the Cox proportional hazard model.

Multivariate analysis: The forward conditional selection procedure in Cox proportional hazard model showed that DLCO<60% and time interval from symp- toms to entry>5 years, were independent prognostic factors.

Conclusion. The cardiac and pulmonary represented the main causes of death in this first Iranian series with systemic sclerosis.

Key words. Systemic Sclerosis. Survival.

PS219
A SYSTEMATIC REVIEW ON THE DEVELOPMENT OF DISEASE ACTIVITY INDICES IN SYSTEMIC SCLEROSIS
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Background and aim. To improve the research in Systemic Sclerosis (SSc) and to facilitate the interpretation of clinical trials, there is a need of a standardized disease activity index as outcome measure. This study gives an overview of the present disease activity indices in SSc and reports their validation status.

Methodology. We systematically reviewed the literature on disease activity indices in SSc (development, use and validation status). The Pubmed database was searched without time limit on the following search terms: systemic sclerosis, disease activity (index) and validity (OMERACT, truth, discrimination, feasibil- ity). The assessment of the qualitative validation status of the present indices was based on the ‘Outcome Measures in Rheumatologic Clinical Trials’-filter (OMERACT filter). The filter comprises truth (face validity, credibility; content validity, covers all aspects of the construct to be measured; construct validity, represents ‘biological sense’, which requires comparison to a golden standard), discrimination (sensitivity to change, discrimination between situations that are of interest; reliability, high reproducibility and low inter- and intrarater variabil- ity) and feasibility (can be applied easily). The quantitative validation status of the present indices was assessed according to the definitions of the American College of Rheumatology (ACR) committee on quality measures. An index was considered ‘preliminary’ if no quantitative validation existed and ‘provisional’ if the index was quantitatively validated in previously collected cohorts. To be fully approved by the ACR, the index needs to be validated prospectively in a clinical trial setting.

Results. Three disease activity indices have been found in literature namely, the Disease Activity Score (DAS) by the European Scleroderma Study group, the 12-point index by Minier et al. and the Combined Response Index for SSc (CRISS) by the Scleroderma Clinical Trials Consortium. Of those, the DAS is the most thoroughly investigated index. There is evidence that the DAS is a valid, reliable and feasible index but its sensitivity to change still needs to be assessed. As the DAS is not yet validated prospectively in a clinical setting, it is considered as a provisional index by the ACR. The 12-point activity index and the CRISS are preliminary indices.

Conclusions. Three indices to measure disease activity in patients with SSc are described in literature. The DAS is the most thoroughly assessed. Only its sensi- tivity to change remains to be attested and it needs prospective validation to be considered as fully validated. The indices developed by Minier et al. and the CRISS are still preliminary indices.
THE VALIDITY OF THE SATISFACTION WITH APPEARANCE SCALE AND THE BRIEF SATISFACTION WITH APPEARANCE SCALE FOR PATIENTS WITH LIMITED AND DIFFUSE SYSTEMIC SCLEROSIS

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Background. The Satisfaction with Appearance Scale (SWAP) was developed to measure body image distress (BID) among burn victims, and later adapted for patients with systemic sclerosis (SSc). A short form of the measure (Brief-SWAP) was derived from the full version. Both measures yield factor-analytically derived subscales. Although both versions have been validated in SSc, their factor structures have never been compared for use with patients with limited versus diffuse SSc.

Objective. To determine the comparability of the factor structures of the SWAP and the Brief-SWAP for patients with limited versus diffuse SSc.

Methods. Participants were adults participating in the UCLA Scleroderma Quality of Life Study with a rheumatologist-diagnosed limited (n = 101) or diffuse (n = 83) SSc. The SWAP evaluates six factors: Social Impact; the Brief-SWAP has two subscales evaluating Social Discomfort and Dissatisfaction with Appearance. Multiple-group confirmatory factor analysis (CFA) was used to determine if the factor structures of the SWAP and the Brief-SWAP were the same for individuals with limited and diffuse SSc. Both statistical (Satorra-Bentler Chi Squared), and practical (RMSEA, CFI, SRMR) indicators of model fit were considered. For RMSEA and SRMR, values <.08 and <.05 were considered to indicate acceptable and good model fit, respectively. For CFI, values ≥.90, and ≥.95 were considered to indicate acceptable and good model fit, respectively.

Results. For the 14-item SWAP, fit indicators supported the proposed four-factor structure for both limited and diffuse SSc. A model in which the number of factors, item loadings for each factor, factor covariances, and factor covariances were constrained to equivalence across disease subtypes satisfactorily fit the data (Chi-squared [172] = 228.59, p<.01; RMSEA = .06; CFI = .95; SRMR = .07). The Brief-SWAP fit indicators supported the two hypothesized factors for both limited and diffuse SSc. A model with these same constraints (Chi-squared [217] = 37.76, p<.01; RMSEA = .07; CFI = .97; SRMR = .08). 12 significant predictors for death and disease worsening were the diffuse cutaneous subset, and the presence of DUs at presentation, with hazard ratios [95% confidence interval] (HR[CI95%]) of 14.2 [1.3-151] and 38 [2.9-501] respectively.

Conclusions. Conduction blocks on the baseline ECG predicted PAH with a HR [95%CI] of 12.8 [5.1-508]. Significant predictors for DUs were active DUs and calcinosis at presentation: HR [95%CI] = 5.2 [1.1-26] and 6 [1.1-33] respectively. None of the parameters tested as potential predictors of the respiratory function decline achieved statistical significance.

TARGETING FEAR OF DISEASE PROGRESSION IN RHEUMATIC DISEASES: A CASE STUDY IN SYSTEMIC SCLEROSIS


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Background. Living with a recurrent chronic illness, such as a rheumatic disease, causes uncertainty and fear of the future for many patients. Patients have to deal with complications and relapses of the disease, increasing restrictions in daily functioning, progression of the disease, and for some rheumatic diseases, such as systemic sclerosis (SSc), a reduced life expectancy. Indeed, patients with SSc have reported uncertainty about the future, fear of disease progression, dependency on others, and fear of becoming physically disabled as important sources of stress, and this was found to be associated with more depressive symptoms. However, although the need for psychosocial support is high in patients with SSc and increasingly recognized by professionals, so far the evidence regarding the development and testing of psychological interventions is limited. To address the need for support, we developed a cognitive-behavioural intervention targeting concerns about the future and depressive symptoms in patients with SSc.

Objective. To illustrate an individually, tailored cognitive-behavioural protocol for the treatment of depressive symptoms and fear of progression in a patient with SSc, and to preliminary study its effectiveness.

Methods. An intervention protocol consisting of an intake interview and 10 face-to-face sessions with a psychologist was developed based on cognitive-behavioural principles. Because of the complexity of symptoms and complaints due to SSc, the psychological intervention was embedded in an interdisciplinary care program also consisting of physical therapy, occupational therapy, and specialized nurse care. A case study was conducted including a 55 years old female with a diagnosis of systemic sclerosis for 9 years. Diary measures utilizing visual analogue scales for depression, fear of progression, fatigue and pain were completed twice a week and validated questionnaires were completed pre- and post- and at follow-up.

Results. The diary measures showed large variability over time, and no clear effect of the intervention could be identified. The post- and follow-up measures showed substantial changes decreases in depressive symptoms and fear of progression. The secondary outcomes fatigue and helplessness showed the most remarkable changes.

Conclusion. The presented intervention is an example and starting point for the treatment of depressive symptoms and fear of disease progression in systemic sclerosis and other progressive chronic somatic diseases. Elements of the presented intervention can be integrated in psychological care in medical health settings. The effectiveness of the intervention should be established in future studies.
PS223
CORRELATIONS BETWEEN LUNG INVOLVEMENT, QUALITY OF LIFE AND FUNCTIONAL DISABILITY IN PATIENTS WITH LIMITED SYSTEMIC SCLEROSIS

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Introduction. Systemic Sclerosis (SSc) is a connective tissue disease that usually impairs the respiratory function. Moreover many Authors have shown that SSc worsens patients' Health Assessment Questionnaire (HAQ), Short Form 36 Physical Component Summary (SF36-PCS) and Mental Component Summary (SF36-MCS).

The aim of this work is to verify whether there is correlation between the quality of life and pulmonary involvement in the patients’ subset with limited-SSc (lSSc).

Materials and Methods. We enrolled 27 lSSc (according to ACR criteria). SF36 and HAQ were given to each one. Pulmonary involvement was evaluated with Baseline Mahler’s dyspnea Index (BDI) - a patient self-administered scale, spirometry and semiquantitative radiological assessment of pulmonary fibrosis detectable on chest Computed Tomography (according to the method suggested by Goh et al. 2008). The correlations between SF36, HAQ and lung involvement severity were investigated with Spearman’s rank test. A p-value <0.05 was considered statistically significant.

Results. SF36-PCS and SF36-MCS correlate with Mahler’s BDI (respectively rho = 0.49 , p=0.009 and rho = 0.40 , p=0.037). The best SF36 subsets which correlate with dyspnea are Vitality (rho = 0.58 , p=0.002) and General Health (rho = 0.45 , p=0.019). Mahler’s BDI correlates also with the HAQ (rho = 0.43 , p=0.028). No statistically significant correlation was found between SF36, HAQ and the spirometrical values or semiquantitative radiological assessment of pulmonary fibrosis.

Conclusions. The lSSc patients enrolled in this study have an impaired quality of life as widely demonstrated in the literature. However, quality of life reduction and functional ability decrease are only related to the respiratory “subjective” impairment (assessed by the Mahler’s BDI). In fact no correlation with objective lung damage (assessed by spirometry and semiquantitative radiological assessment of pulmonary fibrosis) was detected.

PS224
DEATH IN SYSTEMIC SCLEROSIS

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Aims. To study survival and causes of death in a cohort of patients with Systemic Sclerosis ‘SSc’.

Methods. Patients with SSc fulfilling the ACR criteria followed up between January 1997 and December 2012 in a single center of internal Medicine were included. Clinical and investigations (laboratory, radiology, anthropomathoply...) data were reviewed from medical charts.

Results. We report 19 patients from cohort of 135 (14%) patients who died in the last ten years. The sex-ratio is 0.21. Among the total of 19 dead patients, 79.9% had limited SSc and 26.3% had lc SSc. Of the deaths, 89.4% were attributed directly to SSc. Four cases of non-SSc causes are attributed to stroke in arteriosclerosis (1), infectious diseases (2) and malignancy (lymphoma). The others identified cases of death were four cases attributed to pulmonary arterial hypertension, two cases to pulmonary fibrosis, one case to severe malabsorption with Wernicke encephalopathy, four cases to cardiac-related scleroderma causes, one case to acute congestive failure in renal crisis, one case of cirrhosis in Reynolds syndrome and a case of veno-occlusive disease. We propose to discuss the other correlations observed referring to the genre, the mean age at death, the mean duration of follow-up, the proteinuria, the skin score of Rodnan, the immunological profile and the presence of other co-morbidities.

Conclusions. Death among the patients with SSc is still high. Our data indicates an increased per cent of deaths among men affected by SSc (26.6%) compared to the women (12.5%). The majority of the cases being attributed to pulmonary arterial hypertension (despite the screening) and the primitive heart SSc diseases. The causes of mortality justify to develop the specialized centers to care the SSc recognized having the poor prognosis among the rheumatic diseases.
MORTALITY IN SSC AND ITS ASSOCIATION WITH CLIMATE CONDITIONS – AN ANALYSIS BASED ON THE EUSTAR DATABASE

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Objective. Given the impending thread of global warming and climate change, there are no data linking climate data and especially mortality in SSc patients. With the help of the large EUSTAR database, we analysed the association of climate data and mortality in SSc patients.

Methods. The mortality of SSc patients within the EUSTAR database from 2003-2011 was analysed. For 214 deaths, a geographical location and climate data information was used, the association of mortality with the month of death, the geographical location and temperature at the day of death was investigated. In addition, the risk of death at a certain temperature.

Results. Although there was some variation, deaths peaked during winter months (November-February) and there was a slower rise in the summer. There was no significant association between temperature and mortality. However, the analysis showed that smoking appears to only impact upon disease severity rather than increasing risk of development. The objective of this study was to investigate the effect of cigarette smoking on multiple visceral organs and the extent of skin disease in SSc.

Methods. Eighty-four patients who fulfilled the preliminary American College of Rheumatology criteria of SSc were enrolled in this study. Patients were categorized into three groups based on smoking status, namely: never-smoker, ex-smoker and smoker. All of them underwent evaluations of pulmonary function test with measurement of forced vital capacity, carbon monoxide diffusing capacity. Among them, a comorbid situation towards the final outcome.

Conclusion. In this small series, causes of death were considered directly related to SSc in 41% of patients, lower than described elsewhere. A combination of lung and heart involvement was the main cause of death in this group. In most deaths considered to not be directly related, SSc was felt to contribute greatly as a comorbid situation towards the final outcome.

Table. Causes of death in SSc related patients.

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CAUSES OF DEATH IN A COHORT OF ARGENTINE PATIENTS WITH SYSTEMIC SCLEROSIS

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Background. Several papers addressing causes of death in systemic sclerosis (SSc) patients usually agree that between 55% (Eustar) and 65% (Brazil) are directly disease related, lung and heart involvement being the main causes. We decided to look at our experience with relation to causes of death in our cohort.

Methods. Patients with SSc seen by the Rheumatology section between 2000-2011 were retrospectively analyzed. Data on clinical manifestations, disease subtypes and antibodies were obtained. Patients were classified into diffuse cutaneous (dc) and limited cutaneous (lc) subsets (Le Roy et al’s criteria).

Results. As from the year 2000, 230 patients (194 females) were seen at our institution as out/ in patients. Sixty-three (27%) had diffuse SSc and 167 (73%) limited. One hundred and nine (47%) were followed for over three years; total follow up was 688 patients-years. Seventeen of these have died under our care and 120 are being currently followed (incidence mortality rate: 25/1000 patients-years). Ten year survival rate was 82% for limited and 55% for diffuse variants respectively (HR: 1.56; 95% CI: 0.55-4.4).

Anti-Scl-70 was present in 16% of all patients and 41% of those with diffuse SSc. Anti-centromere antibodies were detected in 51% of patients overall and 70% of limited SSc. Of the 17 patients who died, in 7 (41%) the cause was directly disease related (Table 1). Only one patient died from pulmonary fibrosis or pulmonary hypertension “alone”, versus 5 who had a combination of interstitial lung disease, pulmonary hypertension or myocardial involvement.

Two patients suffered from alveolar hemorrhage at time of death, in combination with other manifestations.

Of the 10 unrelated causes of death, 3 died from sepsis, 2 pneumonia, 2 GI hemorrhage, 1 hepatic insufficiency following primary biliary cirrhosis and 2 after heart valve replacement.

In all of these cases, underlying disease contributed to death as a fundamental concurrency.

Conclusion. In this small series, causes of death were considered directly related to SSc in 41% of patients, lower than described elsewhere. A combination of lung and heart involvement was the main cause of death in this group. In most deaths considered to not be directly related, SSc was felt to contribute greatly as a comorbid situation towards the final outcome.

PS229

MOOD AND ANXIETY DISORDERS IN SYSTEMIC SCLEROSIS PATIENTS

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Aim. To assess the prevalence of mood and anxiety disorders in systemic sclerosis (SSc) patients.

Methods. Between January 2011 and January 2012, 70 SSc patients fulfilling the American Rheumatism Association and/or Leroy and Medger criteria were recruited. Mood and anxiety disorders were assessed by use of the Beck Depression Inventory (BDI) and the Hospital Anxiety and Depression Scale (HADS).
Results. 67 women and 3 men with a median age of 46 years and a disease duration (first non-Raynaud symptom) of 10.28 years. 18 patients had a diffuse scleroderma, 52 patients had a limited scleroderma. 46 patients (66%) had pulmonary fibrosis, 62 (89%) had oesophageal dismotility. The mean functional Health Assessment Questionnaire score was 0.74. 66 (94%) patients met criteria for depression, and 53 (76%) had scores above the cutoff usually taken to define moderate to severe depression. 29 (41%) patients met criteria for anxiety. Only 2 patients had a history of antidepressive drug therapy. Depression was not associated with organ involvement.

Conclusion. Systemic sclerosis is associated with a high prevalence of depression and anxiety. Lack of social support probably promotes their appearance. Adequate screening and treatment of mood and anxiety disorders in SSc are needed.

PS230

SCLERODERMIC PATIENTS: AN INTERDISCIPLINARY APPROACH


Objectives. We experience our life through the skin: from the first loving contact to the last painful separation. Therefore the skin “reminds” all the conflicts between the individual and the external environment. Nowadays there is a great agreement in identifying these conflicts as responsible for the majority of the psychopathologies.

The present work aimed at investigating the psychosomatic features of scleroderma (i.e. the thickening and tightening of the skin) using the Analytic Psychodrama method. This method, through scenes, allows to make conscious different unconscious conflicts, as well as to interpret them.

Method. We studied a group of five women (age: 35-70 years old) for one year. We collected the individual experiences reported by the patients, focusing on the ones that are crucial in the formation of psychosomatic symptoms: the specific relationship with the mother and with the father, the possible arrival of one or more younger siblings, the specific affection/dynamics of the primary and following milieu.

We measured the relational structures between the participants - closeness vs. distance - before and after the group work.

Results and conclusions. Collected data suggest that during the formation of their early personality patients experienced a mother affectionally cold, needy or lacking of contact signals. As a result their skin was not trained to soften up, delighting in maternal warmth and protection. Conversely the skin adapted to defense itself autonomously.

The used method, the Analytic Psychodrama, allowed us to investigate different aspects of the psychic life of each participant. We identified important changes in participants’ body perception as well as in physical contact with the others. We observed the same also in the family context.

Resting on these results, we predict further long-term effects of our approach. According to the principles of psychosomatic medicine, it should affect also the specific clinical aspects of scleroderma.

References
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PS231

SYMPTOMS OF DEPRESSION AND ANXIETY IN CROATIAN PATIENTS WITH SYSTEMIC SCLEROSIS

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Introduction. Patients with systemic sclerosis report high levels of pain, fatigue, disability, and considerably impaired overall physical function.

Methods. We conducted a cross section study which included 16 patients with systemic sclerosis from East Croatia regions. Symptoms of depression and anxiety were evaluated using Zung, s anxiety self-assessment scale and Zung, s depression self-assessment scale.

Results. We enrolled 16 female patients (M = 62 years; range 24-78) who were treated in our Clinic during year 2013.

Four patients were diagnosed with limited systemic sclerosis, and 12 with progressive systemic scleroses. Majority of the patients have an elementary school and only one patient has university degree.

According to Zung, s anxiety scale twelve patients were in the normal range and only four patients were in the minimal to moderate anxiety group. Positive correlations were found between individual clinical signs and symptoms that impair physical appearance or cause pain with total anxiety. Digital ulcers, muscle pain and shortness of breath often cause discomfort, worry and anxiety in patients. Considering the small number of patients resulting data are not statistically significant. According to Zung, s depression scale, thirteen patients were in the normal range and three patients were in the mild depression group. We found a positive correlation between the bone pain, joints and muscular pain and higher overall depression score. Positive correlation was found, although not statistically significant, between gastrointestinal symptoms and depression.

We have found a negative correlation between body mass index and anxiety. The analysis of individual scale items have found that 62% patients feel that their life is changing for the worse; 86% patients reported waking up with a feeling of anxiety and 94% patients reported having had insomnia.

Conclusion. According to Zung, s anxiety and depression scale majority of patients have no mood disorder, more detailed analysis shows that the majority of patients feel daily concerns, grief and discomfort related to their present state of health and fear for the future. Disturbances are more intense when clinical manifestations of the disease like chronic pain, fatigue and gastrointestinal symptoms are present.

PS232

PROSPECTIVE ANALYSIS OF THE CLINICAL BURDEN OF LIMITED CUTANEOUS SYSTEMIC SCLEROSIS OVER 12 MONTHS

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Introduction. Although limited cutaneous systemic sclerosis (lcSSc) is more common, the diffuse subtype has generally received more attention from investigators due to its perceived greater clinical burden. The objective of this study was to evaluate the burden of disease in patients with lcSSc over a period of 12 months.

Methods. Consecutive consenting lcSSc patients attending the outpatient clinic or inpatients ward were recruited and underwent 3 study visits over a 12 month period.

Results. Over recruitment period of 3 months 44 lcSSc patients were enrolled. Of those, 88.6% were female, mean age was 55 years and mean disease duration was over 10 years (range 1-28 years). Overlap syndromes were present in 29.5% of the patients with polymyositis/dermatomyositis (20.5%) and rheumatoid arthritis (11.4%) being most frequent. Half of the patients carried anti-centromere antibodies and 16% were anti-topoisomerase I positive.

Raynaud’s phenomenon was present in 89% of the patients. Over the entire follow-up period 8/44 of the patients had at some point had an active digital ulcer (year prevalence of 18%) and in 5 of the patients there were newly developed ulcers (incidence of 11% over 12 months). Those subjects developed between 1 and 3 new ulcers over the follow up period.

Some degree of pulmonary fibrosis (PF) was found in 50% of the subjects and 30% had clinically significant PF. Pulmonary hypertension had been diagnosed in 16%, cardiac SSC and renal crisis in 4.5% each. Modified Rodman skin score varied between 0 and 14. All had some degree of gastro-intestinal tract involvement and up to 91% of the patients suffered with reflux and abdominal distension. Diarrhoea affected 84% of the patients while constipation was reported 77%.

Half of the patients were receiving disease modifying drugs and 27.3% were treated with oral corticosteroids. Most (91%) were receiving treatment with proton pump inhibitors, 30% were taking pro-motility drugs, 16% were on laxatives and 7% were on anti-motility drugs. 66% of the patients received oral treatment for Raynaud’s and 23% were admitted for treatment with Illoprost on at least one occasion during the year of follow-up.

Conclusions. Despite the relatively small number of participants in this study, the prospective design and protocolised patient assessment allowed for a more detailed record not only of clinically-significant organ-based disease, but also of non-life threatening complications of SSCs, confirming the significant disease-related morbidity associated with lcSSc.
PS233
RECOMMENDATIONS FOR FUTURE PATIENT FOCUSED TRIALS ADDRESSING FOOT PAIN IN SYSTEMIC SCLEROSIS
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Introduction. A patient initiated Randomised Control Trial was undertaken to evaluate the effectiveness of a simple cushioning and thermal insole in reducing foot pain in patients with systemic sclerosis (SSc).

A total of 560 patients were screened across four specialist sites and 141 patients were recruited to the trial. Three trial contacts were required over 12 weeks, with a total of 11 patient reported assessments completed per participant.

Independent patient representatives (with SSc) participated in the trial meetings to inform trial management and design.

Findings. Compliance and completion of patient reported data was excellent; only 11 participants did not complete follow-up. Both the intervention and a sham device yielded a reduction in pain score over 12 weeks but did not meet the pre-specified clinically significant difference. Adjusting for seasonal effect showed only a minimal and insignificant difference in pain between warm and cold months, a factor suggested by the patient representatives.

Patient diary comments highlighted severe effects of foot pain on the participant’s psychological status. Much gratitude and support was shown for the trial throughout.

Recommendations. Patient and public involvement (PPI) is integral for trial success especially in severe systemic diseases and should inform the design from the outset.

To yield good recruitment rates, data collection and compliance, numbers of study visits should be minimised with flexibility and support.

The nature and source of foot pain in SSc and the interaction with footwear choice requires further evaluation. Future intervention studies should be improved by reporting the nature and source of pain and should reflect the patient need throughout all seasons.

An additional non-treatment arm should be incorporated in future trials to explore any potential positive properties of the sham device and any gratitude effect.

Consideration of psychological support for participants is recommended when exploring new areas of chronic disease.

PS234
ROLE OF NURSING IN THE PREVENTION OF SKIN ULCERS IN SSc: A PRELIMINARY STUDY
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Skin ulcers are a frequent and disabling condition in SSc. Most of recent studies have focused on secondary prevention, but the role of primary prevention in SSc skin ulcers has been not yet fully evaluated.

The present study was an exploratory survey, in order to understand if SSc patients are aware of the measures useful to prevent skin ulcers and eventually to adopt them.

All the patients were taking medications for their disease, mainly vasodilators and platelet antiaggregants. 40% of the patients were taking vitamin suplementation. Regarding the questions about personal hygiene, the majority of patients (98%) believed to practice a correct hygiene. However, only 20% of the patients used neutral soaps and more than 60% used alcohol containing perfumes for deodorizing. Moisturizing creams were used only by 22% of the interviewed. Only a minority of patients avoided temperature leaps (38%), but the majority (98%) protected the extremities against cold weather. 36% of the interviewed stated to have an adequate food intake, while 42% did not know and 22% stated to have an inadequate intake. 60% of the subjects stated to take at least one coffee or tea a day. A not negligible percentage of subjects (25%) acknowledged to smoke. A slight but not negligible percentage of subjects (11%) acknowledged an inadequate intake. 60% of the subjects stated to take at least one coffee or tea a day. A not negligible percentage of subjects (25%) acknowledged to smoke.

Consideration of psychological support for participants is recommended when exploring new areas of chronic disease.
PS236

NAILFOLD VIDEOCAPILLAROSCOPY FINDINGS IN SYSTEMIC SCLEROSIS AND PRIMARY RAYNAUD’S PHENOMENON – 12 MONTHS FOLLOW UP STUDY

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The aim of the study. We aim to compare nailfold videocapillaroscopy (NVC) findings between systemic sclerosis (SSc) patients and patients with primary Raynaud’s phenomenon in a Finnish prospective study cohort. NVC status will also be evaluated at 0, 6, and 12 months. In addition, clinical findings, laboratory data, functional test results, and radiological findings will be analyzed. Here, we describe the baseline characteristics and NVC findings of the study patients with SSc diagnosis.

Methods. We enrolled consecutive 152 patients with Raynaud’s phenomenon and SSc patients that were not examined with NVC before. Nailfold capillaries of II-V fingers were examined from both hands by using an optical probe videocapillaroscope mounted with x200 magnification contact lens. Images were analyzed with Videocap software (DS MediGroup, Milan, Italy). The number of capillary loops (NCL), giant capillaries, and hemorrhages in the range of 1 mm field were calculated. The average of two consecutive 1 mm fields was calculated. The average of the eight fingers was calculated. In the future, all of these patients will have their Hamis, health assessment questionnaire, and Rodnan skin score evaluated.

Results. 51 patients out of 152 patients with Raynaud’s phenomenon were diagnosed with SSc. The year of the diagnosis varied between 1970’s to present. Some of the patients were diagnosed during this study. The mean age of the SSc patients was 56.4 years (±13.8 SD, range 24-76 y), and the most of the patients were female (90%). The average number NCL in one finger was ranging between 1.3 and 9.6 and the average NCL of the eight fingers was 5.3 (SD 2.1), median 4.9, IQR25% 4.0, IQR75% 6.8. The number of hemorrhages was ranging from 0 to 1.5 with average of 0.2 (SD 0.34), median 0, IQR25% 0, IQR75% 0.25. The number of giant capillaries average was 0.32 (SD 0.50), median 0.13, IQR25% 0, IQR75% 0.44. Range of the number of the giant capillaries varied between 0 and 2.9.

Conclusions. The following charts from our material (one dot representing one patient) demonstrate that the SSc patients are in different disease stages. As expected, a small number of hemorrhages and giant capillaries were associated with very early stage of the disease when the number of capillaries was high or alternatively, in the very late stage of the disease with small number of capillaries. We are now waiting for the rest of the results for further analyze.

PS237

UTILITY OF NAILFOLD CAPILLAROSCOPY FOR THE VERY EARLY DIAGNOSIS OF SYSTEMIC SCLEROSIS

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Background. A scleroderma-pattern on nailfold capillaroscopy (NFC) evaluation of the microvasculature is predictive of the development of systemic sclerosis (SSc). The proposed European League Against Rheumatism criteria for the very early diagnosis of SSc (VEDOSS) include NFC findings, SSc-specific autoantibodies and clinical manifestations.

Aims. To determine the utility of NFC for the very early diagnosis of SSc in an Asian cohort.

Methods. Patients not fulfilling the American College of Rheumatology criteria for SSc were referred for NFC and consecutively recruited based on the presence of (A) Raynaud’s phenomenon (RP) with or without positive ANA>1/800 (B) Undifferentiated clinical features to suggest SSc; polymyositis or dermatomyositis (C) Asymptomatic isolated positive ANA>1/400. Scleroderma-pattern NFC is defined by the presence of ≥1 giant capillary, avascular areas or >2 dilated capillaries with areas of haemorrhage.

Results. Ninety patients were consecutively recruited from March 2010 to May 2013 (mean age 55 years, 87% female; 76% Chinese, 7% Malay, 10% Indian, 7% other ethnicity). Taking into consideration NFC patterns, the clinical outcomes were normal in 32 patients (35.6%), connective tissue disease (CTD) suspected in 33 patients (36.7%), and definite CTD in 25 patients (27.8%). Forty-one patients had a scleroderma-pattern on NFC, of whom 22 fulfilled VEDOSS criteria, and 19 were suspected to have a CTD, giving an overall diagnostic yield of 24.4% (22/90) for VEDOSS. ANA was positive in 74 (82.2%) patients (n=25 antit-centromere, n=3 anti-Scl70). When stratified according to reasons for referral (Groups A-C above), VEDOSS was most frequently diagnosed in Group A (8 of 20, 40.0%) followed by Group B (11 of 37, 29.7%) and Group C (3 of 33, 9.1%).

Conclusions. NFC is useful for the very early diagnosis of SSc with a diagnostic yield of 24.4%, especially in the subgroup of patients with Raynaud’s phenomenon with or without positive ANA>1/800.

PS238

FINGER SKIN VASCULARIZATION IN PATIENTS WITH SYSTEMIC SCLEROSIS – COMPARISON OF ULTRASONOGRAPHY AND CAPILLAROSCOPY

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Objectives. To assess the level of skin vascularization in hand fingers of patients with SSc using ultrasonography and capillaroscopy, and to estimate the clinical value of these findings.

Methods. The cross-sectional clinical study enrolled 35 pts who fulfilled ACR criteria for classification of SSc. Ultrasound examination was performed using VOLUSON 730 machine equipped with 10 – 16 MHz linear probe. The appearance of Power Doppler (PD) skin signal and dorsal digital artery (DDA) flow of the second (II) and fourth (IV) finger at the level of intermediary (IMF) and distal phalanges (DP) of both hands, were analyzed separately. The dorsal digital artery flow was rated as: 0’ intact, when blood flow can be continuously visible in
whole examined area, 1º reduced, as blood flow was not visible in 1/3 of examination area; 2º reduced, when blood flow was not visible in 2/3 of examination area; 3º reduced, when blood flow was invisible in whole examined area. Capillaroscopy findings were described by both methods: Marniqu and Cangolino.

Result. Thirty-two pts (32/35) were females, mean age of pts was 55.3±10.7 yrs. The mean duration of Raynaud’s phenomenon was 104.3±10.1 months. PD soft tissue signal of right hand finger was present in 14 (40.0%) pts and in 17 (48.5%) pts of left hand finger summary. Reduced DDA flow had 24 (68.6%) pts.

Conclusions. The technique showed an excellent intraobserver reliability in our small sample (intraclass correlation coefficient >0.8). The lack of correlation at other sites may be due to the anatomical sites using VTIQ™ to quantify the shear wave velocity (in m/s). The present study evaluated VTIQ™ as a potentially method for determining absolute skin stiffness in SSc. Invasive, absolute quantification of tissue stiffness. Further studies of VTIQ™ are needed to understand the clinical and scientific potential this new measure of skin involvement in SSc.

Table 1. Clinical features and shear wave velocity values (m/s) in SSc patients and controls.

<table>
<thead>
<tr>
<th>Rodman sites</th>
<th>mRSS at the site of analysis</th>
<th>Nr of SSc cases with, mRSS-D at the site</th>
<th>Shear wave velocity values</th>
<th>patients vs. controls (p value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SSc patients (n=26), mean (SD)</td>
<td>Controls (n=17), mean (SD)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anterior chest</td>
<td>0.5 (0.7)/0-2</td>
<td>17</td>
<td>0.04</td>
<td>0.0001</td>
</tr>
<tr>
<td>Abdomen</td>
<td>0.2 (0.5)/0-2</td>
<td>21</td>
<td>0.04</td>
<td>0.0001</td>
</tr>
<tr>
<td>Upperarm right</td>
<td>0.4 (0.6)/0-2</td>
<td>19</td>
<td>0.04</td>
<td>0.0001</td>
</tr>
<tr>
<td>Upperarm left</td>
<td>0.3 (0.5)/0-2</td>
<td>18</td>
<td>0.04</td>
<td>0.0001</td>
</tr>
<tr>
<td>Forearm right</td>
<td>0.7 (0.2)/0-2</td>
<td>13</td>
<td>0.04</td>
<td>0.0001</td>
</tr>
<tr>
<td>Forearm left</td>
<td>1.1 (0.9)/0-3</td>
<td>14</td>
<td>0.04</td>
<td>0.0001</td>
</tr>
<tr>
<td>Hand right</td>
<td>1.1 (0.9)/0-3</td>
<td>7</td>
<td>0.04</td>
<td>0.0001</td>
</tr>
<tr>
<td>Hand left</td>
<td>1.1 (0.9)/0-3</td>
<td>7</td>
<td>0.04</td>
<td>0.0001</td>
</tr>
<tr>
<td>Phalanx right</td>
<td>1.8 (0.9)/0-3</td>
<td>3</td>
<td>0.04</td>
<td>0.0001</td>
</tr>
<tr>
<td>Phalanx left</td>
<td>1.7 (1.0)/0-3</td>
<td>1</td>
<td>0.04</td>
<td>0.0001</td>
</tr>
<tr>
<td>Thigh right</td>
<td>0.1 (0.3)/0-1</td>
<td>23</td>
<td>0.04</td>
<td>0.0001</td>
</tr>
<tr>
<td>Thigh left</td>
<td>0.1 (0.3)/0-1</td>
<td>23</td>
<td>0.04</td>
<td>0.0001</td>
</tr>
<tr>
<td>Leg right</td>
<td>0.4 (0.6)/0-2</td>
<td>18</td>
<td>0.04</td>
<td>0.0001</td>
</tr>
<tr>
<td>Leg left</td>
<td>0.4 (0.6)/0-2</td>
<td>19</td>
<td>0.04</td>
<td>0.0001</td>
</tr>
<tr>
<td>Foot right</td>
<td>0.6 (0.8)/0-3</td>
<td>15</td>
<td>0.04</td>
<td>0.0001</td>
</tr>
<tr>
<td>Foot left</td>
<td>0.6 (0.8)/0-3</td>
<td>14</td>
<td>0.04</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

Fig. 1. VTIQ™ of the dorsal aspect of the hand in a control (A) and in a patient with SSc (B). Absolute shear-wave velocities (in m/s) within the sample gate (yellow box) are shown quantitatively on the right side. The colour scale depicts graphically the absolute stiffness of all tissues within the region of interest. (red=hard tissue; and blue=soft tissue).

PS239

VIRTUAL TOUCH IMAGING AND QUANTIFICATION: A NEW NON-INVASIVE IMAGING METHOD TO MEASURE SKIN STIFFNESS FOR SCLERODERMA

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Background. Skin involvement is of major clinical and prognostic relevance in systemic sclerosis (SSc) and often the primary outcome in clinical trials. Nevertheless, an objective and sensitive measure of skin involvement is lacking. Virtual Touch Imaging and Quantification (VTIQ™) is a new elastography imaging method that provides qualitative and quantitative information about absolute skin stiffness. Invasive, absolute quantification of tissue stiffness. Further studies of VTIQ™ are needed to understand the clinical and scientific potential this new measure of skin involvement in SSc.

Methods. Skin thickness was clinically assessed by the modified Rodnan Skin Score (mRSS) in SSc patients. Absolute skin stiffness was measured at all mRSS anatomical sites using VTIQ™ to quantify the shear wave velocity (in m/s). The same quantification was also performed in age and gender-matched healthy controls. Intraobserver reliability was calculated in four SSc patients and two healthy controls (HC), in two different scanning sessions, one week apart. Correlations between absolute skin stiffness and mRSS, and comparison between patients and controls were statistically assessed using SPSS software. p values <0.05 were considered significant.

Results. Twenty-six SSc patients were included (mean age 55.3±12.1 years, mean disease duration 12.5 years (range 0.5–36), and mean mRSS 11.8 (range 0–33). Seventeen age and gender matched controls were recruited. Absolute skin stiffness measurements were statistically significantly higher in SSc than in HC, in 11 out of 16 mRSS sites of analysis (see Table I). The absolute skin stiffness was strongly correlated with the local mRSS in the following anatomical sites: forearm, r=0.688, p=0.0001; hand, r=0.577, p=0.0001; and, phalanx, r=0.748, p=0.0001. The technique showed an excellent intraobserver reliability in our small sample (intraclass correlation coefficient >0.8).

Conclusions. Shear wave velocities showed a significant positive correlation with mRSS in four sites. The lack of correlation at other sites may be due to the high proportion of cases with mRSS≥0 and suggests that the clinical assessment has low sensitivity at the lower levels of skin involvement. VTIQ™ represents an innovative and promising technique that provides, for the first time, a non-invasive, absolute quantification of tissue stiffness. Further studies of VTIQ™ are required, but this early study supports the clinical and scientific potential this new measure of skin involvement in SSc.

Table 1. Dorsal digital artery flow in the 2nd and 4th hand fingers of patients with SSc.

<table>
<thead>
<tr>
<th>DDA flow</th>
<th>2º right hand finger (N of pts)</th>
<th>2º left hand finger (N of pts)</th>
<th>4º right hand finger (N of pts)</th>
<th>4º left hand finger (N of pts)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intact (0º)</td>
<td>3 (9.3%)</td>
<td>2 (5.7%)</td>
<td>6 (17.1%)</td>
<td>2 (5.7%)</td>
</tr>
<tr>
<td>1º reduced</td>
<td>16 (45.7%)</td>
<td>12 (34.2%)</td>
<td>15 (42.8%)</td>
<td>13 (37.1%)</td>
</tr>
<tr>
<td>2º reduced</td>
<td>13 (37.1%)</td>
<td>14 (40.0%)</td>
<td>10 (28.5%)</td>
<td>10 (28.5%)</td>
</tr>
<tr>
<td>3º reduced</td>
<td>3 (8.5%)</td>
<td>7 (20.0%)</td>
<td>4 (11.4%)</td>
<td>5 (14.2%)</td>
</tr>
</tbody>
</table>

Only two pts. had normal or type 1 (Marniqu) capillaroscopy findings. Early changes (type 2) were found in 17 (48.6%) pts whereas type 3 (active changes) were present in 9 (25.7%) pts. Five (14.3%) pts had changes of type IV. We found strong significant positive correlation of ultrasonographic and capillaroscopy findings (p=0.001, r=0.547). Rank correlation between level of DDA flow and Raynaud’s phenomenon (r=0.276) and age of pts. (r=0.137) either with presence PD skin signal were not statistically significant (r=0.250).

Conclusion. Dorsal digital artery flow estimated by ultrasonography was reduced in a large number of our patients with systemic sclerosis, and it was mostly of severe intensity. Power Doppler skin signal was often present in finger soft tissue and could probably point to enlarged capillary loops in the examined part of skin. Ultrasonography could be useful tool in estimation of the level of finger vascularisation in patients with systemic sclerosis.
A STUDY COMPARING VIDEOCAPILLAROSCOPY AND DERMOSCOPY IN THE ASSESSMENT OF NAILFOLD CAPILLARIES IN PATIENTS WITH SYSTEMIC SCLEROSIS-SPECTRUM DISORDERs

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Background. Nailfold videocapillaroscopy (NVC), is the current ‘gold standard’ for detecting capillary abnormalities suggestive of a systemic sclerosis (SSc)-spectrum disorder, however it is not widely available: a key question is whether lower magnification, easy-to-use dermoscopy compares favourably. Our objectives were to examine the classifiability of capillaries and the evaluation of abnormality (severity), by both NVC and dermoscopy (and to determine whether these differ between (i) general and specialist rheumatologists (ii) the thumbs and fingers and (iii) the left and right hands) and to compare intra- and inter-rater reliability of both techniques.

Methods. NVC and dermoscopy images were acquired from all 10 nailbeds of 32 subjects with a range of capillary abnormalities. Images were graded (on a web-based interface) on a 0-3 scale of severity: normal, mildly, definitely and grossly abnormal. A key result is that NVC was more classifiable and grading was more severe. Intra- and inter-rater reliability was comparable for the two techniques in the classifiability of images and the grading of severity. The thumb was twice less likely to be graded, images from the left hand were slightly more likely to be classified and there was a small increase in the scoring of severity of images obtained from the right hand.

Table 1. Cross-tabulation of frequency of ratings (with percentages) by NVC and dermoscopy (severity scores are indicated by square brackets).

<table>
<thead>
<tr>
<th>Videocapillaroscopy scores</th>
<th>Dermoscopy</th>
<th>scores</th>
</tr>
</thead>
<tbody>
<tr>
<td>normal</td>
<td>mildly definitely grossly unable to classify abnormal abnormal abnormal class</td>
<td>Sub-total Total</td>
</tr>
<tr>
<td>[0]</td>
<td>[1]</td>
<td>[2]</td>
</tr>
<tr>
<td>normal</td>
<td>92</td>
<td>130</td>
</tr>
<tr>
<td>mildly abnormal</td>
<td>65</td>
<td>140</td>
</tr>
<tr>
<td>definitively abnormal</td>
<td>18</td>
<td>50</td>
</tr>
<tr>
<td>grossly abnormal</td>
<td>1</td>
<td>12</td>
</tr>
<tr>
<td>unable to classify</td>
<td>106</td>
<td>112</td>
</tr>
<tr>
<td>Sub-total</td>
<td>236</td>
<td>438</td>
</tr>
<tr>
<td>Total</td>
<td>1920</td>
<td>(100.0)</td>
</tr>
</tbody>
</table>

Conclusion. Our results suggest that dermoscopy is comparable to NVC. NVC images were more likely to be classifiable, and were graded more severely. Intra- and inter-rater reliability were similar for both techniques. Small, yet significant differences were noted in the classifiability and the grading of severity between the left and right hands and the thumbs and fingers. Further research is warranted to validate dermoscopy in the assessment of patients with SSc-spectrum disorders.

LONGITUDINAL ASSESSMENT OF SCLERODERMA SKIN BY OPTICAL COHERENCE TOMOGRAPHY: PRELIMINARY VALIDATION OF SENSITIVITY TO CHANGE OVER-TIME

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Background. Optical coherence tomography (OCT) is a quantitative reliable tool to assess skin involvement in Systemic Sclerosis (SSc) (1). However the sensitivity to change over-time has not been evaluated. The present study aimed to compare skin assessment by OCT over-time in patients with SSc.

Methods. We performed 52 OCT scans of dorsal forearms on 26 sites of analysis from 17 SSc patients (9 dcSSc, 8 lcSSc; 64.5years disease duration) at 0 and 24 months.Clinical skin involvement was assessed using the modified Rodnan skin score (mRSS). Minimum and Maximum Optical Density (Min and Max OD) of the mean-A scans were calculated employing Matlab software (1).Comparison of the local mRSS with Min and Max OD at the 2 time-points was performed by paired t-test.

Results. Fourteen sites with local mRSS0 did not change over 24 months. Accordingly, both Min and Max OD showed an average +2.98% and -0.05% change, respectively (p<0.05). Six sites of analysis improved by 2 mRSS points (three from “2” to “1”, three from “3” to “1”). In these sites Min OD showed an average increase of 23.92% (p=0.00084) and Max OD of 25.13% (p=0.00081). In 4 sites of analysis mRSS improved by 1 point (two from “3” to “2”, one site from “2” to “1”, one site from “1” to “0”). In these sites Min OD and Max OD showed no significant improvement (Min OD 1.93% vs Max OD of 8.15%; p>0.05 for both). Furthermore, both Min and Max OD showed a trend forward a decrease (−3.54%, −5.41% respectively) at the 2 sites of analysis with worsening mRSS (one point increase) but the low sample size did not allow to perform a statistical evaluation.

Conclusions. Although preliminary for the low number of observations, this study provides the first evidence suggesting that OCT of the skin is sensitive to change over-time and it changes consistently with mRSS. The lack of improvement of OCT in sites with a mRSS of 1 deserves further studies to determine whether this is correlated with poor accuracy of mRSS or room for improvement in OCT analysis. Studies including a larger number of patients and sites of analysis with different grades of skin involvement and improvement/deterioration of clinical score are needed to reach a definitive validation.

References
Results. 18 patients (11M, 7F) with LSF entered the study. Eleven patients had PRS, 4 ECDS, 3 progressive emphalitis atrophy. CBCT Scan was sensitive in detecting the degree of facial asymmetry in different spatial planes, coincident with those affected by the disease (upper planes for patients with ECDS and lower planes for those with PRS). In addition, CBCT better evidenced the presence of disease evaluating the soft tissue thickness as compared to bone involvement.

Conclusions. This preliminary data show that CBCT is a reliable and safe technique quantifying the asymmetry of the face in disease affected areas, particularly for the soft tissue. CBCT may have a potential role as gold standard for the assessment of the disease course. A sensitive to change study is in progress.

PS243
NON-INVASIVE ASSESSMENT OF SILENT LIVER FIBROSIS IN PATIENTS WITH SYSTEMIC SCLEROSIS

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Background. Although up to 90% of patients systemic sclerosis (SSc) have been estimated to have gastrointestinal involvement, liver disease (without any cause other than SSc itself) has been reported only rarely in this disease. Liver biopsy is considered the gold standard for an accurate assessment of liver fibrosis. However, it is an invasive and expensive tool, so there has been increasing interest in non-invasive assessment of evaluation of liver stiffness (LS) by transient elastography (TE) which have been recently demonstrated to be useful for the diagnosis of various grades of fibrosis in the course of chronic liver diseases.

Objectives. To evaluate the presence of liver fibrosis in a series of SSc patients, without any functional sign of liver disease and any cause other than SSc itself, and to identify any possible associations with demographic data, disease duration and disease phenotype.

Methods. Thirty-nine SSc patients (33 females and 6 males) without liver disease, mean age 63±13.2 years, disease duration 10.5±8.6 years, and a sex- and age-matched control group, were consecutively studied. LS was evaluated using TE (Fibroscan; Echosens, Paris, France) and measured in kPa. We adopted 5.3 kPa as the cutoff for abnormal LS values.

Results. Seventeen (43.5%) SSc patients had abnormal LS values when patients were classified into two groups according to the cutoff (group A <5.3 kPa, group B >5.3 kPa); the median LS value was 4 kPa in group A and 7.1 kPa in group B. There were no significant differences between the two groups in disease duration, demographics, laboratory variables or disease characteristics. Among medi- cations, a significant difference for patients on endothelin receptor antagonist therapy was seen in group B (p=0.02).

Conclusions. TE suggested, in a non-invasive fashion, liver fibrosis in 43.5% of our SSc patients, a result of a primary hepatic involvement. LS measurements could be suggested for assessing chronic liver fibrosis in SSc, even in absence of abnormal liver function serological tests. However, further studies are required to investigate whether treatment regimens can influence the progression of liver fibrosis, or if they should be modified when abnormal LS values are identified.

PS244
CHANGES IN THE THICKNESS AND STIFFNESS OF PALMO-PLANTAR SOFT TISSUES IN PEOPLE WITH SYSTEMIC SCLEROSIS

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Objective. To compare thickness and relative stiffness of palmo-plantar soft tissues between people with systemic sclerosis (SSc) and healthy controls (HC).

Methods. Soft tissue thickness and stiffness, at one palmar site [third metacarpophalangeal joint (3rdMCPJ)] and two plantar sites [third metatarsophalangeal joint (3rdMTPJ) and heel], were measured by high-frequency ultrasound and compression- elastography, respectively, in 25 SSc patients and in 18 HC.

Results. Twenty-five SSc patients (23 females, 2 males) with a mean age of 56.6 (9.9) years and mean disease duration of 11.1 (7.0) years and 18 controls with a mean age of 51.9 (10.6) years were included. Nineteen patients had limited SSc and six had diffuse SSc.

Conclusions. Palmar skin was thicker in SSc cases than controls: 0.15 mm (0.13 to 0.16) vs. 0.11 mm (0.10 to 0.12), p<0.001 and fibro-fat pad in the plantar surface of 3rdMTPJ was thinner: 0.41 (0.35 to 0.47) vs. 0.52 (0.44 to 0.59), p<0.05, in the SSc group than in the control group.

Fibro-fat pad at the palmar site was stiffer in the SSc group than in the control group: 0.7 (0.6 to 0.9) vs. 0.5 (0.4 to 0.6) and plantar heel: 0.9 (0.7 to 1.1) vs. 0.5 (0.4 to 0.6) (all p<0.05).

Conclusion. Measurements of soft tissue relative stiffness by compression-elastography add a new dimension to the clinical assessment of soft tissue in SSc. Changes in thickness and stiffness of palmo-plantar soft tissues may lead to functional limitations as well as a decrease in skin attenuation properties and ability to distribute foot-ground contact load affecting the foot during walking. Further studies are needed to define the role of compression-elastography in SSc patients with hand and foot problems.
One hundred patients were investigated: 26 cases with Ssc showed incomplete involution of their thymus by means of CT scan. The median follow up period of 11 (2-48) months.

57.1% (n=16) of these patients showed incomplete involution of the thymus at post-transplantation setting. CT examinations were carried out at suspended end-

Objective. To determine whether the presence of calcinotic lesions is accompanied by local features of micro-vasculopathy by investigating the video-capillaro-

Methods. We adopted an Optilia Digital video-capillaroscopy system equipped with 200x magnification lens. 144 images were collected in 4 surrounding quadrants within 3mm of calcinotic lesions and at their contra-lateral unaffected skin in the same Region of interest (ROIs). Two rheumatologists blinded to the clinical details independently analysed the images for presence of: non-specifically enlarged capillaries, Giant capillaries, Haemorrhages, loss of capillaries, disorganisation and ramifications. Images were scored and data were analysed by non-parametric tests.

Results. Eighteen calcinotic lesions and contra-lateral ROIs were analysed from 11 patients. Loss of capillary areas were observed in all calcinotic lesions vs 7 contra-lateral ROIs (p=0.0001). Non-specifically Enlarged capillaries were observed at 17 lesions vs 11 ROIs (p=0.031), giant capillaries, disorganisation and capillary ramifications were observed at 7, 9 and 5 lesions, respectively, while none were observed in any ROIs (p=0.016, p=0.004, p=0.063). Haemorrhages were observed at 5 lesions and 2 ROIs (p=0.25).

Conclusion. Features of severe micro-vasculopathy are observable in plain skin by video-capillaroscopy and may be specifically associated with calcinotic lesions in Ssc.

Poster Session 3rd Systemic Sclerosis World Congress

PS246 VIDEO-CAPILLAROSCOPY OF PERI-CALCINOTIC SKIN INDICATES SPECIFIC FEATURES OF SEVERE MICRO-VASCULOPATHY ASSOCIATED WITH CALCIUM DEPOSITS IN SYSTEMIC SCLE
dersma

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Introduction. The underlying pathogenesis of systemic sclerosis (SSc) is still a matter of discussion but alterations of the immune system definitely play an important role. Recent studies on incomplete thymic involution in patients with SSc raised the suspicion that thymic abnormalities might be associated with increased risk for autoimmune diseases. Resettling the 'immunologic clock' by autologous stem cell transplantation (aSCT) is a promising therapeutic option. Aim of this study was to evaluate thymic alteration in SSc patients before and after aSCT.

Methods. All patients underwent non-enhanced chest-CT both in the pre- and post-transplantation setting. CT examinations were carried out at suspended end-inspiratory volume from apex to base on multidetector CT-scanner (SOMATOM Sensation 16/64 or 128 Siemens, Germany). All images were assessed by an experienced chest radiologist reviewed at a mediastinal window. We used following criteria for definition of an abnormal thymus: a length and/or thickness >13mm for diffuse enlargement or a length >7mm for multinodular thymic enlargement.

Results. We evaluated 28 (16 female, 12 male, mean age at transplantation 38.75 years) who all have had a chest-CT scan within 3 months before transplantation. 57.1% (n=16) of these patients showed incomplete involution of the thymus at baseline, with 10 patients showing hyperplastic and 6 nodular thymus. If we exclude the cases who were ≤5 years at the time of transplantation 14 (25%) or 56% showed an incomplete involution. In 16 of these patients follow up CT scans were available, showing a non significant reduction of the thymic surface over the median follow up period of 11 (2-48) months.

Conclusion. More than half of the patients considered for transplantation for severe SSc showed incomplete involution of their thymus by means of CT scan. This very high percentage is most probably explained by the negative selection of very ill patients considered for transplantation. This goes in line with previous reports of abnormal enlarged thymus especially in patients with progressive disease. Transplantation leads to a downsizing of the thymus, an observation which will be further evaluated

PS247 THYMIC FINDINGS BEFORE AND AFTER AUTOLOGOUS STEM CELL TRANSPLANTATION FOR SEVERE SYSTEMIC SCLERODERMA – A RETROSPECTIVE STUDY USING COMPUTED TOMOGRAPHY IN THE PRE- AND POST-TRANSPLANTATION SETTING

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Background. Vascular damage and fibrotic process represent the pathophysiological hallmarks of systemic sclerosis (SSc). Peripheral microangiopathy can be early detected by nailfold videocapillaroscopy, whereas modified Rodnan skin score (mRSS) is the most extensively validated technique to estimate the severity of skin involvement. Recent studies have considered the role of ultrasound elastosonography, suggesting that this technique can identify the reduction of dermal elasticity. Our study was aimed to explore possible correlation between nailfold capillaroscopic patterns and finger dermal stiffness evaluated with elastosonography in SSc patients.

Methods. For the present study 20 subjects, who met the ACR criteria for scleroderma were recruited. They underwent complete clinical examination, NVC and ultrasound evaluation. NVC was performed in each patient as reported elsewhere. Patients were divided according to 3 described patterns of microvascular damage on the basis of NVC: 'Early', 'Active' and 'Late'. Ultrasound elastography was performed at palmar surface of each finger tips. Images were obtained by applying repetitive skin compression as previously described. The elastogram, which reflects the relative elasticity of the tissues, was created as a color coded map (i.e. blue=areas of great stiffness, red=areas of low stiffness). Images were analyzed by a proprietary software (Esaote elastosonography module, Esaote, Inc., Italy) that allows to obtain a numeric evaluation of stiffness expressing the global percentage of hardness. 'Skin stiffness' was computed by considering the average of eight fingers for each patient.

Results. Mean age of patients was 61±12.3 years. Mean disease duration was 7.3±5.7 years. A significant positive correlation (r=0.43, p=0.02) was found between Skin stiffness and NVC. For the case control analysis, we compared subjects showing 'Late pattern' (n=12) with subjects showing 'Active and Early pattern' (n=8). Table shows that subjects were comparable for age and both disease and Raynaud's phenomenon duration (p=NS). Finally, the highest skin stiffness were found in patients showing the late pattern when compared to the subjects showing 'Active and Early pattern' (p=0.03).

PS248 RELATIONSHIP BETWEEN ELASTONOSONOGRAPHY AND CAPILLAROSCOPIC PATTERNS IN SYSTEMIC SCLERODERMA

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Background. Vascular damage and fibrotic process represent the pathophysiological hallmarks of systemic sclerosis (SSc). Peripheral microangiopathy can be early detected by nailfold videocapillaroscopy, whereas modified Rodnan skin score (mRSS) is the most extensively validated technique to estimate the severity of skin involvement. Recent studies have considered the role of ultrasound elastosonography, suggesting that this technique can identify the reduction of dermal elasticity. Our study was aimed to explore possible correlation between nailfold capillaroscopic patterns and finger dermal stiffness evaluated with elastosonography in SSc patients.

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Poster Session 3rd Systemic Sclerosis World Congress

S-110

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Summary. Nailfold capillaroscopy allows to visualize and study the capillaries by simple transillumination. The presence of megacapillaries and a decreased capillary density are the hallmarks of the sclerodermia capillary pattern, which can be detected by nailfold capillaroscopy.

Objectives.

- research the sclerodermia capillaroscopic patterns in the various autoimmune diseases with Raynaud’s phenomenon.
- prevalence of the other non specific capillaroscopic anomalies.

Patients and methods. One hundred patients were investigated: 26 cases with undifferentiated connective tissue disease (UCTD), 20 patients with systemic lupus erythematosus (SLE), 4 patients with dermato/polyiositis, 10 with rheumato
toid arthritis, 16 cases with primary Sjögren’s syndrome and 24 patients with systemic sclerosis (SSc). 99 of these patients are female, the average age is 40.3 years. These patients were all explored by capillaroscopy.

Results. All patients (100%) with dermatomyositis showed the sclerodermia capillaroscopic pattern, 70.8% of systemic sclerosis, 42.3% of undifferentiated con
nective, 30% of lupus disease, 31.2% of Sjögren’s syndrome and one case (10%) of patients with rheumatoid arthritis also exhibited the same pattern.

Conclusion. Sclerodermia capillaroscopic pattern is often present in systemic sclerosis and dermatomyositis. Furthermore, it has also been described in other autoimmune disease such as Sharp syndrome, patients with Raynaud’s phenomena and UCTD may also exhibit this pattern. Therefore, capillaroscopy seems to be a useful tool for the early selection of those patients who are potential candidates for developing sclerodermia spectrum disorders.
Objective. To determine and characterize the sonographic abnormalities in joints and tendons of patients with scleroderma (SSc).

Methods. Ten patients with the diagnosis of scleroderma (2 dcSSc, 8 lcSSc) regardless of whether or not have arthralgia and/or arthritis were recruited to the patients from the wrist, metacarpal and proximal phalangeal joints of both hands in dorsal and volar sides and ankle with the examination of periartricular structures. Erosive changes were evaluated from the lateral longitudinal and transvers views of the 2nd MCP, 5th MCP, 2ndPIP and ulnar styloid of both hands. The presence of synovitis (synovial hypertrophy and/or joint effusion), tenosynovitis, erosions and Doppler signal were investigated.

Changes according to definitions of OMERACT group study were recorded (Wakefield 2005). My Lab 70 (Esaote Biomedica, Italy) sonography machine was used with a 6-18 mHz probe for the sonographic evaluation.

Results. Median disease duration and age were 9.8(2-21), 52(31-60) years respectively. All the patients fulfilled American college of rheumatology classification criteria for SSc.

Synovitis of the carpal recesses were found in 10 of the 20 evaluated wrists. In 6 of the 10 wrists with synovitis had PDS. None of the MCP joints have synovitis. On the other hand, synovitis has been observed in 13 of 100 PIP joints and 7 of them had PDS.

Extensor tenosynovitis was detected in 8 wrists and 5 of them with the hypertrophy of tendon sheath. Erosion was detected in 4 of 2nd and 5th MCP (4/40), 6 of 2nd PIP (6/20) and 7 of ulnar bone (7/20). Physical examination was determined only 4 tender, 2 swollen wrist joints .

Synovitis has been detected in 6 of 20 examined ankle and 2 of them with PDS signal. Tenosynovitis was detected in 4 of them and all with the tendon sheath thickness. More then one tendon was involved in all 4 ankle. On the other hand 2 swollen, 4 tender ankle joints were determined with the clinical examination.

Conclusion. Sonography may be a useful method to detect and categorize musculoskeletal pathologies in SSc since joint and tendon involvement can be silent and challenging for the clinician to assess by physical examination only. Tendon pathology was a frequent finding at wrist extensor and ankle tendons in SSc. Ankle joint and tendon pathology as common as wrist joints and tendon pathology in SSc.

### Table

Case control-analysis: Comparison between subjects with ‘Late Pattern’ and subjects with ‘Active and Early pattern’.

<table>
<thead>
<tr>
<th></th>
<th>Early n= (Active=6)</th>
<th>Late n= (Late=12)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>56.3±9.0</td>
<td>64.3±13.8</td>
<td>NS</td>
</tr>
<tr>
<td>RP duration (years)</td>
<td>11.5±9.8</td>
<td>16.2±12.8</td>
<td>NS</td>
</tr>
<tr>
<td>Disease duration (years)</td>
<td>6.1±4.8</td>
<td>8.1±6.5</td>
<td>NS</td>
</tr>
<tr>
<td>Skin thickness 46.7±6.2</td>
<td>55.7±9.3</td>
<td>0.03</td>
<td></td>
</tr>
</tbody>
</table>

All data are reported as mean + SD. RP: Raynaud’s phenomenon; NS: not significant.

### Conclusion

According to our data, although partially influenced by the relatively small number of subjects, elastosonographic findings in SSc patients are strictly correlated with NVC patterns of microvascular damage. Our observation if validated in subsequent studies involving a greater number of patients could lead to better define a novel role of elastasonography in skin evaluation during the course of SSc.

### References


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**PS250**

**MUSCULOSKELETAL ULTRASONOGRAPHY FINDINGS IN SCLERODERMA PATIENTS**

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**INTERSITIAL LUNG DISEASE ASSOCIATED WITH SINE SCLERODERMA SYSTEMIC SCLEROSIS: A CASE PRESENTATION**

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### Introduction

Intersitial lung disease (ILD) may be the first manifestation of systemic sclerosis (SS) in a previously healthy patient, since the association between ILD and SS has a prognosis and therapeutic implications, this association must be evaluated at the initial approach of ILD.

### Case Presentation

A 51 year old male patient with a diagnosis of idiopathic non-specific interstitial pneumonitis (NSIP) (Figure 1) since 2 years ago was referred to our institution for a lung transplant evaluation. He was under treatment with aza-thioprine 75 mg / day, meprednione 10 mg/day, N-acetylcysteine 1200 mg / day. During the evaluation symptoms consistent with gastroesophageal reflux, post prandial dyspepsia and discloration of the fingers with pallor, cyanosis and erythema triggered by exposure to cold were detected. Physical examination revealed crackles Velcro, digital pallor and acrocyanosis compatible with Raynaud’s phenomenon, digital pitting scars of finger tips (Figg. 2 and 3) and no evidence of skin sclerosis, sclerodactyly or puffy fingers.

A naiifold videocapillaroscopy was performed showing an active scleroderma pattern with frequent giant capillaries, capillary microhemorrages, mild disorganization of capillary architecture and mildly ramified capillaries (Fig. 4). A high-resolution esophageal manometry revealed absence of peristalsis (aperistalsis) of the smooth muscle esophageal segment and hypotensive lower esophageal sphincter (Fig. 5). A chest CT was performed showing a pattern of NSIP and significant esophageal dilation in the distal third with an air-fluid level (Fig. 6). An antinuclear antibody (ANA) showed a speckled pattern 1/640, anti-centromere and anti-topossomerase 1 antibodies were negative.

The diagnosis of systemic sclerosis sine scleroderma was made with pulmonary, esophageal and vascular involvement. The patient started with nifedipine, proton pump inhibitors and cyclophosphamide with good clinical response.
TOLERABILITY OF INTRAVENOUS PROSTANOIDS ILOPROST THROUGH ELASTOMERIC PUMP DEVICE IN SCLERODERMA PATIENTS

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Background and purposes. Intravenous prostanoids are commonly used in the treatment of complicated Raynaud’s phenomenon (RaP). Those drugs are over all moderately tolerated and their use through long-term infusion require daily admission in dedicated facilities. Furthermore, traditional peristaltic pumps (12 hours infusion protocol) do not allow complete emptying of iloprost vials.

Our aim is to describe a case series of scleroderma patients treated with iloprost through elastomeric pump, avoiding hospitalization.

Methods. Prostanoid therapy (iloprost 50 mcg) was loaded into the elastomeric pump at hospital, setting infusion rate at 24-48 mL/hour. Patients were instructed to avoid even mild physical activity, then returned to their homes for the period of administration (24 hours). A telephone alert system was enabled in order to quickly provide assistance in case of side effects.

Clinical notes of scleroderma subjects admitted to Clinical Immunology Branch were reviewed. Complete data about their condition are reported. Tolerance to treatment was classified into none, poor, moderate and good. Improvement rate of digital ulcers are given as well.

Results. Data were available for 14 patients (71.4% female), median age 53.5 years (IQR 48-60). Six cases were systemic sclerosis (one complicated by heart involvement). Six cases had RaP, 35.7% had digital ulcers.

Median duration of therapy was 33 months (IQR 15-84). Ten subjects (71.4%) showed good tolerance, while one patient suspended because of poor tolerance. Side effects were common, including headache (21.3%), dizziness (both 14.2%) or arterial hypo/hypertension (14.2%). Only one patient was not able to receive the whole vial of iloprost as scheduled. RaP was at least relieved in 55% of cases. Out of 5 cases with digital ulcers, 2 showed improvement or full recovery.

Conclusions. Elastomeric pump administration of prostanoids in scleroderma subjects seems a safe procedure with impressive tolerance. Our experience revealed minimized toxicity and hospital stays, allowing improved quality of life and better resources use (including the whole emptying of iloprost vials). Full patient compliance and adequate surveillance systems are deemed mandatory in order to avoid adverse events.

Our data support the need for larger study of a promising technique aimed to improve the managing of prostanoid therapy.
evolution of the cutaneous sclerosis (one with infliximab and the other with adalimumab), with no response. The three other patients with erosive arthritis who did not respond to previous treatment (methotrexate and leflunomide) did respond well to etanercept (two patients) and adalimumab (one patient). In one of these three patients the therapy was able to be discontinued after two years but not in the other two who remain in treatment until today (years).

2) Patients treated with RTX: Case 1: RTX was indicated because of an advanced interstitial lung disease (ILD) with respiratory failure and secondary pulmonary hypertension that didn’t respond despite previous treatment with cyclophosphamide (CYM) and mycophenolate (MFP). The RTX treatment was able to slow down the progression. Case 2: A patient with dSS and interstitial lung disease with anti-Scl70 y pANCA (anti-MPO) antibodies suffered a severe pulmonary hemorrhage with a complete response to RTX (2011; July); in 2013 July she suffered a glomerulonephritis together with high titers of anti-MPO antibodies and again with a good response to RTX.

Conclusion. In our experience anti-TNF treatment is a suitable option for erosive arthritis treatment SS patients. On the other hand, aggressive cutaneous sclerosis did not respond to anti-TNF treatment. Our impression, in the case of aggressive interstitial lung disease, was that RTX slows down the clinical worsening. In the case ANCA vasculitis associated with dSS clinical response to RTX was favorable for both renal and lung manifestations.

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*Age at diagnosis; years from diagnosis; SE: systemic sclerosis; nucl: nucleolar; fs: fine speckled; BT: biological therapy.

PS255

**ILPROST AS CYCLIC SIX-DAY PER MONTH. LONG TERM EFFICACY IN SCLERODERMA PATIENTS**

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Introduction. Scleroderma is a treatable but not curable disease, characterized by a poor prognosis. Previous studies have defined prognostic factors useful for assessing the severity of the clinical picture and to predict patient survival. So, stabilizing the disease as long as possible may represent an important therapeutic goal. The aim of the study is to evaluate the evolution of the disease and to identify possible prognostic factors in a group of consecutive patients accessed to the Unit of Rheumatology Catania’s hospital, Italy, from 2006 to 2013.

Methods. Retrospective analysis of a database of 44 patients (44F, 50.8±12.5 years), treated with iloprost for a mean duration of 28.0±16.5 months. Iloprost was administered with a regimen of daily infusion for six consecutive days per month, from 18 to 11 months, but we weren’t able to stop prednisone therapy (mean dosage 5 mg/daily).

The most interesting observation was a decrease in Raynaud phenomenon intensity (p<1 year) and in the number of digital ulcers (DU) (p<1 year) and in the number of digital ulcers (DU) (p<1 year).

After 12 month of therapy patient number 1 has stopped steroid therapy and maintain a good response both on skin than in vascular involvement.

**Conclusions.** Tocilizumab proved good efficacy in obtaining improvement in skin involvement in Systemic Sclerosis also in patients who underwent many different therapies in personal history; besides Tocilizumab showed an encouraging efficacy reducing vascular manifestation of the disease, including Raynaud phenomenon and digital ulcers, but this data have to be confirmed with serial nailfold capillaroscopy.

PS257

**ALTERNATIVE BIOLOGICAL MODEL FOR PRECLINICAL TESTING**

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Development of each novel formulation needs to pass the essential step of preclinical testing. To make this phase more comprehensive and animal friendly, here we propose an alternative biological model based on the chorioallantoic membrane of the fertilized chicken egg (CAM) (1). It is suitable for a wide range of applications such as treatment efficacy, personalized medicine, phototherapy, xenografts and angiogenesis development. The CAM model brings advantages of a low cost experimental setup, fast accumulation of experimental data, applicability of a wide range of investigated substances, high repeatability of data. The immune system of the chicken embryo is not active till the certain egg development day (EDD), assisting an effective tissue adaption on the CAM. Diverse cell samples taken directly from patients or hybrid cell culture lines can be easily particular, iloprost seems to confirm the hypothesis that monthly iloprost infusions for six hours a day during six consecutive days could have a beneficial effect against PAH development or worsening, according to the results of the study and in agreement with many previous evidences.

**TOCILIZUMAB IN SYSTEMIC SCLEROSIS, A SINGLE CENTRE EXPERIENCE**

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Background, there few report in literature about the efficacy of the monoclonal antibody against IL-6 Tocilizumab (TCZ) for cutaneous involvement in Systemic Sclerosis (SSc), these data seem encouraging.

Methods. We enrolled SSc patients with an active skin disease according EULAR/EUSTAR criteria (nMSSS >14) who failed previous recommended therapies for cutaneous involvement. These patients released informed consent and underwent preliminary investigations including Quantiferon test, skin biopsy and nailfold capillaroscopy.

They were treated with a standard TCZ amount of 480 mg/month i.v. despite weight.

mRSS was re-evaluated after 3, 6 and 12 month, capillaroscopy was controlled after 12 month.

Concomitant steroid therapy was administered but no steroid-bolus were performed before TCZ treatment.

Materials. Three patients were enrolled. Two patients presented DeScs, one LeScs.

Patient 1 had LeSc with mRSS = 25 in July 2010 treated with three methylprednisolone bolus and methotrexate; despite therapy, after 1 year, mRSS = 20 Patient 2 had DeScs with mRSS = 22 in July 2011 treated with three methylprednisolone bolus and methotrexate; after 6 months mRSS = 20 despite therapy. Patient 3 had a DeScs with mRSS > 20 from 2009 treated with Cyclophosphamide followed by azathioprine and mycophenolate mofetil for 1 year in 2012. She started methotrexate and 6 month her mRSS = 18.

All patients underwent skin biopsy (both clinically involved and healthy skin) studied in morphological way and by immunohistochemistry with anti-IL-6 antibodies. After 6 months of therapy we observed an improvement in skin involvement in all three patients (pt 1 mRSS from 20 to 13; pt 2 mRSS from 20 to 12; pt 3 mRSS from 18 to 11), but we weren’t able to stop prednisone therapy (mean dosage 5 mg/daily).

The most interesting observation was a decrease in Raynaud phenomenon intensity (p<1 year) and in the number of digital ulcers (DU) (p<1 year) and in the number of digital ulcers (DU) (p<1 year) and in the number of digital ulcers (DU) (p<1 year).
transferred to the next stage of preclinical trials (2). The CAM is a biological model that can match the mouse model in *in vivo* investigations, having additional advantages in the experimental time frame. The natural cellular barriers and circulation are present in a way easily accessible for treatment and observation.

**References**


**PS259**

**OPTIMIZED FORMULATION OF ENDOGENOUS NEUROPROTECTIVE AGENT**

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**Drug Discovery Department, Actelion Pharmaceuticals, Basel, SWITZERLAND.**

Systemic Sclerosis (or Scleroderma) is an autoimmune disease characterized by skin and internal organ fibrosis, caused by microvascular dysfunctions. The microvascular damage seems to be a consequence of endothelium autoimmun response, followed by inflammatory cascade and massive deposition of collagen. Endothelin-1 (ET-1) is involved in the inflammatory and fibrotic processes by increasing the concentration of pro-inflammatory and pro-fibrotic cytokines and it is considered one of the most relevant mediators of vascular damage in scleroderma. It is indeed found in very high concentration in serum of sclerodermic patients. Moreover, in these pathological conditions there is an increased expression of ET-1 principal receptors (ETA and ETB), which mediate the detrimental action of ET-1, often resulting in a change of ETA/ETB ratio. The aim of the present study is to evaluate the in vitro effect of macitentan, an orally active tissue-targeting dual endothelin receptor antagonist, and its major metabolite (ACT-132577) on alpha smooth muscle actin (αSMA) expression, evaluated on dermal fibroblasts from healthy subjects and on dermal fibroblasts from lesional skin.

**SIS: IN VITRO EVIDENCES**


**PS259**

**MACITENTAN IN THE TREATMENT OF DERMAL FIBROSIS IN PATIENTS AFFECTED BY LIMITED SYSTEMIC SCLEROsis: IN VITRO EVIDENCES**

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**Drug Discovery Department, Actelion Pharmaceuticals, Basel, SWITZERLAND.**

Systemic Sclerosis (or Scleroderma) is an autoimmune disease characterized by skin and internal organ fibrosis, caused by microvascular dysfunctions. The microvascular damage seems to be a consequence of endothelium autoimmun response, followed by inflammatory cascade and massive deposition of collagen. Endothelin-1 (ET-1) is involved in the inflammatory and fibrotic processes by increasing the concentration of pro-inflammatory and pro-fibrotic cytokines and it is considered one of the most relevant mediators of vascular damage in scleroderma. It is indeed found in very high concentration in serum of sclerodermic patients. Moreover, in these pathological conditions there is an increased expression of ET-1 principal receptors (ETA and ETB), which mediate the detrimental action of ET-1, often resulting in a change of ETA/ETB ratio. The aim of the present study is to evaluate the in vitro effect of macitentan, an orally active tissue-targeting dual endothelin receptor antagonist, and its major metabolite (ACT-132577) on alpha smooth muscle actin (αSMA) expression, evaluated on dermal fibroblasts from healthy subjects and on dermal fibroblasts from lesional and non-lesional skin from sclerodermic patients. The combination of macitentan and its major metabolite reduced the levels of αSMA after 48 hours in sclerodermic fibroblasts from lesional skin. No relevant changes in αSMA levels were found in fibroblasts from non-lesional skin, whose behavior is similar to that of dermal fibroblasts from healthy patients.

**PS260**

**RAPID RESPONSE OF DIGITAL ULCERS TO BOSENtan IN SYSTEMIC SCLEROsis**

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Systemic sclerosis is a multisystem disorder of unknown aetiology. Pulmonary and cutaneous manifestations of the disease cause significant morbidity, affect quality of life and are resistant to therapeutic interventions. The aim was to describe two cases of systemic sclerosis patients with digital ulcers who were successfully managed by the administration of the dual endothelin receptor antagonist bosentan. A patient, male, aged 67 years, presented with systemic sclerosis. He was diagnosed three years ago, having presented with Raynaud’s phenomenon, cutaneous thickening and hardening over the digits, weight loss, muscle involvement and positive ANA. He had been treated with cyclophosphamide and nifedipine. Subsequently he was lost to follow up for two years presenting thereafter with cutaneous manifestations of systemic sclerosis, small mouth opening, Raynaud’s phenomenon, cutaneous thickening and hardening over the digits and digital ulcers. A chest CT scan performed revealed mild pulmonary manifestations while a cardiac echogram was normal. Clinical examination revealed multiple digital ulcers affecting both hands. Iloprost i.v. infusion was administered, followed by bosentan 62.5 mg twice daily and nifedipine 30 mg. A month later the digital ulcers were healed. Bosentan was continued and the patient remains free of ulcers. A patient, female, aged 50 years, with a history of limited cutaneous systemic sclerosis and digital ulcers appearing intermittently presented with a digital ulcer in the right hand. Laboratory evaluations revealed a negative Scl 70 and positive SSA-Ro. She was treated with i洛prost i.v. and antibiotics, the ulcer persisting. Bosentan 62.5 mg twice daily was administered for a month, being increased thereafter to 125 mg twice daily. A month later the digital ulcer healed, bosentan is continued and the patient remains free of ulcers.

Digital sclerosis is a multisystem disorder which was treated systemically.**
SAFETY AND EFFECTIVENESS OF MYCOPHENOLATE IN SYSTEMIC SCLEROSIS: A SYSTEMATIC REVIEW

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Methods. A literature search of Medline, Embase, Cochrane Central Register of Controlled Trials, and CINAHL (inception - September 2012) was performed. Titles and abstracts were screened to identify studies that described the use of mycophenolate in SSc patients. Inclusion criteria included exposure to mycophenolate, and reporting of modified Rodnan skin score (MRSS), ventilatory function (FVC), diffusing capacity of carbon monoxide (DLCO); or adverse events. The primary outcome was gastrointestin al events occurring after the initiation of mycophenolate. Secondary safety outcomes included myelosuppression, infection, malignancy, and death occurring after the initiation of mycophenolate. Results. 616 citations were identified and 20 were included in the analysis. 477 patients have been exposed to mycophenolate. The mean disease duration ranged between 0.8-14.1 years. There were 89 non-lethal adverse events, of which 43 (48%) were gastrointestinal and 46 (52%) were non-gastrointestinal adverse events.

Conclusions. Observational studies report mycophenolate is effective improvement or stabilization in FVC, and 5 observational studies report stabilization or improvement in MRSS.

IDENTIFICATION OF ICD-9 CODES ASSOCIATED WITH SCLERODERMA RENAL CRISIS

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1Stanford University School of Medicine, Division of Immunology and Rheumatology, Palo Alto, USA; 2Stanford University School of Medicine, Department of Dermatology, Palo Alto, USA.

Methods. We identified patients with SRC from our database of 429 patients with SSc evaluated at Stanford University Medical Center from 2005 to 2012. All patients with SRC had a rapidly progressive oliguric renal insufficiency with no other explanation and/or rapidly progressive hypertension occurring during the course of SSc. We collected demographic information, clinical features, symptoms and complications of SRC, autoantibodies, treatments, outcomes, and ICD-9 codes associated with each SRC case. Results. Ten patients with SRC were identified (9 female, 8 diffuse cutaneous SSc, mean age at SRC onset 54±10.8 years). Nine patients were ANA positive, 7 with nucleolar pattern, 2 patients were Scl-70 positive, and 1 was Anti-RNA polymerase III positive. Mean time from first non-Raynaud’s symptom to SRC was 3.5±4.7 years. Six patients (60%) used prednisone before SRC (with a mean dose of 43 mg/day). Mean systolic and diastolic blood pressure at SRC onset was 200±33 mmHg and 115±27 mmHg; one patient was normotensive. Nine patients required hospitalization, with a mean length of stay of 16.5±13.5 days. Mean creatinine, hemoglobin, and platelet count at SRC presentation was 3.0±1.6 mg/dl, 9.8±5.6 g/dl, and 244±104 x 10^9/L, respectively. Five patients had active urine sediment with proteinuria, hematuria or casts. Nine patients were treated with angiotensin converting enzyme inhibitors, although 7 needed combination anti-hypertensives to control blood pressure. Five patients required dialysis during hospitalization and only 1 was able to discontinue dialysis 13.8 months later. Ten patients developed end-stage renal disease after SRC. We identified ICD-CM-9 codes associated with the SRC episode in 7 patients. All had ICD-CM-9 code 710.1 corresponding to scleroderma, 6 (96%) had ICD-CM-9 code 401.9 (hypertension), 3 (43%) had ICD-CM-9 code 584.9 (acute renal failure). The given similar clinical features seen in SRC and thrombotic thrombocytopenic purpura (TTP), it is not surprising that 3 (43%) SRC cases had ICD-CM-9 code 446.6 for TTP. Conclusions. The combination of ICD-CM-9 codes 710.1, 401.9, 584.9 and/or 446.6 may be helpful to identify cases of SRC using large administrative databases, but our results require validation in another cohort.
JUVENILE SCLERODERMA: TREATMENT EXPERIENCE OF A SINGLE ONE CENTER

M.K. Osmiining, N.A. Geppe, J.O. Kostina, E.Y. Afonina, O.V. Shpitsitokvenka
J.M. Schenon First Moscow State Medical University, Pediatric Department, Moscow, RUSSIA.

Treatment consensus in Juvenile scleroderma (JS) is hard to be achieved due to low incidence, heterogeneity of JS, lack of controlled studies. Efficacy of 5 treatment regimens (TR) was analysed retrospectively in 426 JS patients (pts), among them 375 pts with localized JS (ILS),- systemic sclerosis (JSS), 21- Mixed connective tissue disease (MCTD).Follow up period was 1-10 years (M=5). TR efficacy was estimated by skin score, skin thickness (Duromert), square of skin lesion, joint immobility, laboratory,instrumental data.

1 TR - Penicillamine (PA) 8-10 mg/kg/d along 3-4 years was used in 70 JLS pts (32- circumscribed deep morphea (CDM), 10- generalized morphea (GM), 10 - "en coup de cabre" (ECDS).8- linear morphea on limbs(LM). PA was effective in 98% of CDM.

2 TR - PA 8-10 mg/kg/d for 3-5 years + Prednison(P) 1mg/kg/day for 6-10 weeks, then tapered and stopped in 12 mo. - in 165 JLS pts (46-LM,45-unilateral GM (UGM), 44-GM,30- ECDS; and 30 JSS pts. 2 TR was effective in 90% OF UGM & LM pts,48% ECDS pts, 87% JSS pts.

3TR - Methotrexate (MTX) 10-15 mg/m2/ wk for 2-5 years we used in 68 JLS pts (28-LM, 23- GM, 17- ECDS). TR was benefit in 92% LM & GM pts,50 % ECDS.

4TR-MTX 10-15 mg/m2/ wk for 2-5 years + Pr 1mg/kg/day for 8-10 weeks, then tapered and stopped in 12 mo. - in 70 JLS (33- UGM, 14- LM, 12- GM, 11- ECDS) & 21 MCTD pts.

5TR was effective in 97% of UGM, LM, GM pts, in 60% ECDS, in 90% MCTD pts. We prefer parental use of MTX (Metocet/Metex),itr was effective & safely used in 80 JS pts, with no relapses despite permanent pricks of skin with injections, side effects occurred in 0% in contrary to 4% in oral MTX pts.

5 TR - Cyclophosphamide (CYC) IV 20mg/kg + Pr 1mg/kg for 6 mo. in 6 pts with interstitial lung disease (ILD).We achieved reverse of ILG in all pts. SNPs of NOS3(G894T), MMP 1(G-1607GG), MTHFR, SLC(L91A), GGH were genotyped in 216 of our JS pts, as potential predictors of treatment response. Polymorphism GG in NOS3(G894T) showed strong correlation with clinical efficacy of Pa in our cohort.

Our data suggests that PA & Pa+Pr are still effective TR for several forms of ILS (CDM,UGM, ISS) especially useful in pts with recurrent infections, tuberculosis,those who live in cold climate, endocrine disorders, intolerance to MTX. TR with MTX are more effective than TR with PA.ILD is rare in JS, especially usefull in pts with recurrent infections.

Our data suggests that PA & PA+Pr are still effective TR for several forms of JS, especially in patients with systemic sclerosis (SSc). However, some of these studies were based on small cohorts and wide ranges of prevalence were reported. Therefore to overcome these limitations of individual studies, we sought to perform a meta-analysis to determine the accurate prevalence of polyautoimmunity in JS.

Methods. We performed a systematic review and a meta-analysis of literature in MEDLINE and Embase databases from January 1960 to March 2013. All cohort studies reporting on prevalence of other AIDs known to be associated with SSc were analyzed. Prevalence of polyautoimmunity and of each AID were then calculated by dividing the number of patients with polyautoimmunity (or the specific AID investigated) by the number of patients studied. We then calculated the pooled estimate for all studies (with 95% confidence interval (CI95%)), which was backtransformed afterward using the DerSimonian and Laird method.

With the prevalences calculated, aggregation for different AIDs was calculated by dividing the prevalence of a given AID in SSc-patients by the prevalence in the general population.

Results. Ten studies reporting polyautoimmunity were identified, corresponding to a total of 6102 SSc patients (women 87.1%, 35% of diffuse cutaneous subtype). Mean age at assessment was 57.6 (± 3.1) years and mean disease duration 10.6 (±2.3) years. Overall 1432 patients with at least one AID were identified, corresponding to a weighted prevalence of polyautoimmunity equal to 25.7 % [CI 95%: 20.1%-31.6%]. 208/5139 SSc-patients had at least two additional AIDs resulting in a weighted prevalence of 3.9% [3.3% -4.4%]. Patients with polyautoimmunity were more frequently women (607/654 (92.8%) vs. 1524/1755 (86.8%); p<0.01) and of limited cutaneous subtype (314/385 (81.6%) vs. 925/1439 (64.3%); p<0.01). The most prevalent associated AIDs were autoimmune thyroid disease (10.4%) followed by Sjögren’s syndrome (7.7%) and dermatomyositis/polymyositis (5.6%). Primary biliary cirrhosis and rheumatoid arthritis were detected in 3.0% and 4.2% of SSc-patients, respectively, whereas prevalence of systemic lupus erythematosus was equal to 2.6%. Recurrence risk values were calculated to approximately 1120 for dermatomyositis/polymyositis, 750 for primary biliary cirrhosis, 108 for systemic lupus erythematosus, 26 for Sjögren’s syndrome, 5 for autoimmune thyroid disease and 4 for rheumatoid arthritis.

Conclusion. Our results confirm that polyautoimmunity is a frequent condition in SSc, affecting a quarter of SSc-patients. The impact on the phenotype and also on the management and therapy will need to be addressed now in further works.

CLINICAL AND SEROLOGICAL COMPARATIVE ANALYSIS OF SYSTEMIC SCLERODERMA WITH OR WITHOUT OVERLAP SYNDROMES IN A LARGE BRAZILIAN COHORT

Division of Rheumatology, Universidade de São Paulo, São Paulo, BRAZIL.

Background. There are scarce data comparing clinical and serological features in patients with systemic sclerosis (SSc) and SSc overlap syndromes (SSc-OS) due to the rarity of these associations.

Objective. To analyze clinical and SSc-associated serological profiles including a panel of novel described antinuclear antibodies (AHoA) in a large cohort of Brazilian patients with SSc and SSc overlap syndromes.

Methods. Three hundred twenty-eight SSc patients attending the Scleroderma Outpatient Clinic of a tertiary referral university hospital from 2000 to 2011 were enrolled. Clinical and demographic data were obtained from an electronic register database. Serum samples were analyzed for the presence of antinuclear antibodies (indirect immunofluorescence on HEP-2 cells), antibodies to Scl-70, PM-Scl, RNA-Pol III, CENP-A/CENP-B, and Ro/SS-A (52 and 60 kDa) (ELISA), and antinuclear antibodies (ANoA) fibrillarin, Ku, Th/To and NRO80 (immunoblotting using commercial available standardized kits).

Results. Two hundred ninety seven patients were classified as SSc and thirty-one patients as SSc-OS (13 with systemic lupus erythematosus, 10 with polymyositis,
Chronic widespread pain (CWP) is a healthcare problem with great impact on mental health, professional life and quality of life. It can be a consequence of many disorders; however, there are few reports concerning its prevalence during the course of other diseases. Systemic sclerosis (SSc) is a multisystem autoimmune disease characterized by vascular injury and progressive skin and organ fibrosis. Moreover, the patients’ quality of life can be worsened by the presence of CWP. The aim of this study was to compare the prevalence of CWP in patients with limited (l-SSc) or diffuse SSc (d-SSc). Methods: The study evaluated 111 consecutive patients with SSc (females 91%, mean age 60.8, range [23-84], overall mean disease duration 92±61 m.). All of the patients were evaluated in terms of the disease activity, markers of inflammation, the presence of antibodies, serum vitamin D levels, and disease duration. The higher prevalence of CWP among patients with SSc does not correlate with advanced age. The presence of ACAs is a risk factor for CWP, which correlates with the clinical manifestations of the disease. However, it does not correlate with the presence of SSc.

**PS270**

**SERUM ADROPIN LEVEL AND ENHO EXPRESSION IN SYSTEMIC SCLEROSIS**

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**Introduction.** Systemic sclerosis (SSc) is an autoimmune multisystemic disease characterized by vasculopathy, inflammation and progressive fibrosis of the skin and internal organs. However, the pathogenesis of SSc is still not fully understood. Adropin, a secreted protein, is encoded by the Energy Homeostasis Associated (ENHO) gene. It is expressed by a variety of tissues and cells. It has been implicated in several pathological and physiological processes such as angiogenesis, apoptosis. Adropin-treated endothelial cells exhibited greater proliferation, migration and capillary-like tube formation and less permeability and tumor necrosis factor alpha-induced apoptosis via altering PI3K-Akt and ERK1/2 pathways and activating VEGFR2. If so, adropin may have the potential role in the pathogenesis of SSc. Therefore, in the present study, we investigated the serum adropin levels and ENHO expressions in patients with SSc.

**Methods.** The study included 27 patients with SSc, 39 patients with Behcet’s disease (BD) as control patients, and 20 healthy controls (HC). The patients were fulfilling the established classification criteria. For each SSc patient, modified Rodnan skin score, Valentini disease activity index and Medsger disease severity scale were assessed. Serum adropin levels were analyzed by ELISA method. ENHO and GAPDH gene expressions by peripheral blood mononuclear cells were analyzed by real-time PCR. One-way ANOVA, post-hoc Tukey test and chi-square test were applied to statistical analysis.

**Results.** The serum adropin levels were higher in the SSc and BD groups than in the HC group (p=0.023 and p=0.001, respectively, Table 1). However, there were no significant differences among the groups in terms of ENHO expressions (PANOVA=0.149). 15 of the SSc patients had limited cutaneous subtype. There was no significant difference between the limited and diffuse cutaneous subtypes in terms of serum adropin level and ENHO expression. Moreover, serum adropin level and ENHO expression were not associated with the disease activity and severity indices. ENHO expression was correlated with the triglyceride levels in the BD group (r=-0.580, p=0.007) and LDL-cholesterol (r=-0.542, p=0.001) levels in the HC group.

**Conclusion.** The augmented serum adropin levels may be expected in the chronic inflammatory disease, and seem not to be characteristic of only SSc. Moreover, although it increases in SSc, it is not associated with any activity and severity index of the disease. Therefore, it may be concluded that adropin is not involved in the pathogenesis of SSc. However, further studies are needed to explain the precise role of adropin in SSc.

**Table 1.** The demographics, serum adropin level and ENHO expression in the study group.

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<td>Mean age (years)</td>
<td>44.0±13.1</td>
<td>37.1±10.9</td>
<td>48.9±13.7</td>
<td>0.001</td>
</tr>
<tr>
<td>Mean disease duration (years)</td>
<td>6.7±6.1</td>
<td>7.5±6.7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>27.3±4.0</td>
<td>25.7±4.3</td>
<td>24.9±5.0</td>
<td>0.102</td>
</tr>
<tr>
<td>Adropin (ng/ml)</td>
<td>1.12±0.52</td>
<td>1.92±0.81</td>
<td>1.67±0.65</td>
<td>0.001</td>
</tr>
<tr>
<td>ENHO expression</td>
<td>1.19±0.11</td>
<td>1.25±0.12</td>
<td>1.26±0.08</td>
<td>0.149</td>
</tr>
</tbody>
</table>

HC: healthy control; BD: Behcet’s disease; SSc: systemic sclerosis; BMI: body mass index. When compared to the HC group: p=0.023 and p=0.001. When compared to the BD group: p=0.001.
PS271
PREVALENCE AND PREDICTIVE VALUE OF SCLERODERMA–SPECIFIC SERUM AUTOANTIBODIES IN THE GENERAL POPULATION OF A NORTHERN ITALIAN AREA


University of Milan, Milan, ITALY; "Humanitas Clinical and Research Center, Rozzano (MI), ITALY; Bergamo local health authority (ASL), Bergamo, ITALY; "Aeska diagnostics, GERMANY; "Pollicinico San Pietro, Ponte San Pietro (BG), ITALY.

Background. The prevalence of sclerodermia (SSc)-specific serum autoantibodies (autoAbs) is generally obtained from large datasets including blood donors or employees, thus resulting poorly representative of the general population. Similarly, it is challenging to determine the risk of developing a connective tissue disease (CTD) in subjects positive for serum autoantibodies in the absence of an adequate observation. Our aim is to determine the prevalence and predictive value of anti-centromere (ACA), anti-Scl70, and anti-CENP-B autoAbs in a large cohort of Italian subjects participating in a 13-year longitudinal study.

Methods. The general population of a Northern Italian area was randomly selected 1:4 and enrolled in 1999 in a clinical epidemiology study and 71% of resident subjects (age 18-75) participated to the study (mean age 42, female/male 1:1.5). Subjects were blindly tested for ANA and anti-ENA including anti-Scl70 and anti-CENP-B using commercially available indirect immunofluorescence and ELISA. Administrative data were then analyzed to determine if study subjects had developed SSc following the 13 years. Results. Serum ANAs were detected by IF in 18.1% (titre ≥1:80) and 5.7% (titre≥1:160) of tested samples and the pattern was speckled in 52.2% of cases and centromeric in 0.3%. The prevalence of anti-Scl70 was 1.45% and anti-CENP-B 0.5% by ELISA. In all cases, prevalence rates were higher in women but predominance was lower than classically reported for CTD. The predictive value of autoantibodies was obtained from the analysis of copyamptex exemptions, even if this approach does not account for 11% of the population with total expense waiver for low income or advanced age. The relative risk (RR) of developing a CTD over 13 years for ANA positive individuals is 1.78 (95% confidence interval -1:1.6-2.73; p=0.0001). The RR of developing a CTD for individuals with high-titer ANA is 12.26 (95% CI 2.52-59.62; p=0.0001). No cases of SSc were observed during the follow-up period using this low-sensitivity approach.

Conclusions. Prevalence of serum ANA and anti-ENA may be higher than reported when a general unselected population is investigated with sufficient power. Serum positivity for autoAbs confers a significant risk of developing an autoimmune disease when subjects are observed for a long period of time.

PS272
OSTEOPOROSIS AND FRACTURE RISK IN OUTPATIENTS WITH SYSTEMIC SCLEROSIS

V. Codullo, F. Inverardi, S. Breda, L. Bogliolo, F. De Nard, G. Cagnotto, R. Caporali, C. Montecucco

IRCCS Pollicinico San Matteo, Unit of Rheumatology, Pavia, ITALY.

Background/Purpose. Osteoporosis (OP) is a frequent complication of a number of chronic inflammatory diseases. Only Rheumatoid Arthritis (RA) is included in the FRAX algorithm to calculate fracture risk but also Systemic Sclerosis (SSc) is considered in the calculation tool (http://www.shef.ac.uk/FRAX). A routine SSc evaluation (according to EUSTAR) was performed as well. Age- and BMI-matched early RA (ACR/EULAR 2010 criteria) patients were enrolled as controls. Methods. The general population of a Northern Italian area was randomly selected 1:4 and enrolled in 1999 in a clinical epidemiology study and 71% of resident subjects (age 18-75) participated to the study (mean age 42, female/male 1:1.5). Subjects were blindly tested for ANA and anti-ENA including anti-Scl70 and anti-CENP-B using commercially available indirect immunofluorescence and ELISA. Administrative data were then analyzed to determine if study subjects had developed SSc following the 13 years. Results. Serum ANAs were detected by IF in 18.1% (titre≥1:80) and 5.7% (titre≥1:160) of tested samples and the pattern was speckled in 52.2% of cases and centromeric in 0.3%. The prevalence of anti-Scl70 was 1.45% and anti-CENP-B 0.5% by ELISA. In all cases, prevalence rates were higher in women but predominance was lower than classically reported for CTD. The predictive value of autoantibodies was obtained from the analysis of copyamptex exemptions, even if this approach does not account for 11% of the population with total expense waiver for low income or advanced age. The relative risk (RR) of developing a CTD over 13 years for ANA positive individuals is 1.78 (95% confidence interval -1:1.6-2.73; p=0.0001). The RR of developing a CTD for individuals with high-titer ANA is 12.26 (95% CI 2.52-59.62; p=0.0001). No cases of SSc were observed during the follow-up period using this low-sensitivity approach.

Conclusions. Prevalence of serum ANA and anti-ENA may be higher than reported when a general unselected population is investigated with sufficient power. Serum positivity for autoAbs confers a significant risk of developing an autoimmune disease when subjects are observed for a long period of time.

Table 1.

<table>
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<tr>
<th>Type of systemic sclerosis</th>
<th>Limited (n=178)</th>
<th>Diffuse (n=56)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sclerodactyly</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(n=149)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acrosclerosis</td>
<td>64 (39.5)</td>
<td>44 (75.8)</td>
</tr>
<tr>
<td>(n=29)</td>
<td>39.5</td>
<td>44 (75.8)</td>
</tr>
<tr>
<td>Females, %</td>
<td></td>
<td></td>
</tr>
<tr>
<td>42 (25.6)</td>
<td>36 (64.2)</td>
<td>0.06</td>
</tr>
<tr>
<td>Age at diagnosis, years</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>5.5 (1)</td>
<td>1.9 (0.8)</td>
</tr>
<tr>
<td>Duration of Raynaud before diagnosis, years median (SD)</td>
<td>9.2 (3.4)</td>
<td>5.5 (1)</td>
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<tr>
<td>Anti-Scl70</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anti-centromere</td>
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<td>44 (75.8)</td>
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<tr>
<td>Antibodies, %</td>
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<td></td>
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<td></td>
</tr>
<tr>
<td>Nucleolar ANA</td>
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<td>37.7</td>
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| 17.3 (0.01)               | 0.018         | 19 (0.8)      | 0.008

Conclusion. These results appear to confirm that extension of skin involvement within limited SSc may identify two different subsets with clinical and serological characteristics. Indeed, Type 2 as defined by Barnett appears to have intermediate characteristics. Other characteristics did not reach statistical differences.

TABLE I.

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Conclusion. These results appear to confirm that extension of skin involvement within limited SSc may identify two different subsets with clinical and serological characteristics. Indeed, Type 2 as defined by Barnett appears to have intermediate organ involvement, and serology may be more similar to the diffuse type.

TABLE I.
PS274

CORRELATION AMONG WHOLE BLOOD VISCOSITY, HEMATOCRIT AND CAPILLAROSCOPIC PATTERNS IN SYSTEMIC SCLEROSIS

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1Rheumatology Research Unit, Magna Graecia University, Catanzaro, ITALY; 2AO Pugliese-Ciaccio, Catanzaro, ITALY.

Background. Microvascular alterations represent the pathophysiologic hallmark of systemic sclerosis (SSc). As known, hemorheological features such as blood viscosity strongly influence vessels tone, structure and function through interaction of blood with the endothelial surface. Previous investigations reported an impaired rheological profile in SSc patients. The present study was aimed to investigate whether alterations in blood viscosity contribute to microvascular damage in subjects with SSc.

Methods. 16 women who met the ACR criteria for scleroderma and 16 healthy controls were recruited for this study. Hematocrit (Ht), hemoglobin (Hb), fibrinogen, erythrocyte sedimentation rate (ESR) were measured by standard methods. Whole blood viscosity (WBV) was calculated according to the formula: (0.12. haematocrit) + 0.17. (plasma proteins - 2.07). Nailfold videocapillaroscopy (NVC) was performed in each participant as reported elsewhere. Afterwards, patients were distributed into two groups based on the presence of late or early/active pattern. Variables among these groups and controls were compared using either ANOVA or Kruskal-Wallis test.

Results. Overall mean age of patients was 57.5±12.2 years, while mean disease duration was 8.1±6.3 years. Significant inverse correlations were found between Ht (r=-0.53, p=0.027), Hb (r=-0.63, p=0.027), WBV (r=0.54, p=0.031) and NVC patterns. In the case control analysis, patients showing ‘late pattern’ had significant lower Hb concentration, Ht and WBV than control group and ‘early/active’ patients.

Conclusion. Our study demonstrates an inverse association among WBV, HB, Ht and capillaroscopy patterns providing further evidence about the effects of hemorheology on vascular properties in SSc patients. The possible mechanisms responsible for these findings can be only hypothesized. Blood viscosity and hematocrit strongly influence shear stress, that is the frictional force that flowing blood generates tangentially to the endothelial surface. Wall shear stress is an important regulator of the nitric oxide synthesis and strongly influences vessel tone and angiogenesis. It is likely that low hematocrit and WBV, through a reduction in shear stress, contributes to capillaries loss in SSc.

References

Table. Clinical characteristics and hemorheological parameters of subjects.

<table>
<thead>
<tr>
<th></th>
<th>Late</th>
<th>Early/Active</th>
<th>Group ANOVA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>8</td>
<td>8</td>
<td>16</td>
</tr>
<tr>
<td>Age (years)</td>
<td>58.8±15.8</td>
<td>55.0±8.7</td>
<td>54.3±15.1</td>
</tr>
<tr>
<td>RP duration (years)</td>
<td>15.8±11.0</td>
<td>12.2±11.0</td>
<td>-</td>
</tr>
<tr>
<td>Disease duration (years)</td>
<td>11.0±9.0</td>
<td>7.2±5.2</td>
<td>-</td>
</tr>
<tr>
<td>Hematocrit (%)</td>
<td>36.3±4.5*</td>
<td>41.0±3.2</td>
<td>42.0±2.5</td>
</tr>
<tr>
<td>Hemoglobin (g/dL)</td>
<td>10.7±1.4*</td>
<td>12.8±1.4</td>
<td>13.4±1.2</td>
</tr>
<tr>
<td>Fibrinogen (mg/dL)</td>
<td>392±55</td>
<td>340±92</td>
<td>352±82</td>
</tr>
<tr>
<td>ESR (mm/h)</td>
<td>44.5±28.5</td>
<td>40.8±20.5</td>
<td>17.9±11.5</td>
</tr>
<tr>
<td>Whole blood viscosity (CP)</td>
<td>3.5±0.5*</td>
<td>4.0±0.4</td>
<td>4.2±0.3</td>
</tr>
</tbody>
</table>

ANOVA Tukey post hoc test, *p<0.01 group ‘Late’ vs control; p=0.03 group ‘Late’ vs group ‘Early/Active’. **p=0.02 group ‘Late’ vs control.

PS275

AUTOANTIBODIES IN SYSTEMIC SCLEROSIS MAY PREDICT DISEASE SEVERITY, COMPLICATIONS, AND MORTALITY: A SINGLE EUSTAR CENTER (842) EXPERIENCE

A. Balbir-Gurman1, Y. Braun-Moscovici1

1B. Shime Rheumatology Unit, Rambam Health Care Campus, The Bruce Rappaport Faculty of Medicine, Technion, Haifa, ISRAEL.

To assess the association between scleroderma (SSc) specific autoantibodies (Abs, antinuclear (ANA), anti-topoisomerase (ATA), anti-centromere (ACA)), clinical features, and mortality in SSc patients registered at our EUSTAR site (842).

In 219 out of 230 registered SSc patients clinical or laboratory data were available. According to Abs profile patients were divided: ATA+ (37%), ACA+ (34%), and ANA+ (29%, ATA negative and ACA negative). There was no difference in gender or nationality between subgroups. ACA+ patients were significantly older and had the longest disease duration. Diffuse SSc was significantly more often in ATA+ and ANA+ patients. Rodman skin score was lowest in ACA+ and highest in ATA+ patients. ATA+ and ANA+ patients had higher incidence of arthritis and sclerodactyly. ATA+ patients had more often digital ulcers (DU), gangrene, and CK elevation. Digestive system was involved equally in all patients. Above 50% of ATA+ and 26% ANA+ patients had significant pulmonary fibrosis (PF). PF was rare and mild in ACA+ patients. Heart involvement was reported in 12% of ATA+ and 6.8% of ACA+ patients. ATA+ and ACA+ patients had similarly high incidence of pulmonary hypertension (PAH, pulmonary artery pressure more than 45 mm Hg on ECHO-Doppler): 22.9% and 20.5%. Ten patients developed renal crisis (RC): 5 ATA+ and 5 ANA+. During follow-up 43 patients died (24%): 35% with higher mortality in ATA+ (24.1% and lower in ANA+ (11.8%). Among ATA+ patients 25% died from PF, 15% from heart, digestive system, and SRC each; among ACA+ patients 43.8% died from PAH and 31.3% from heart involvement; among ANA+ patients 8.7% died from PAH, 13/4% from heart failure, 8.4% from SRC. 41.6% of patients died from cancer: 66% of ATA+ and 50% of ACA+.

In SSc patients Abs profile is associated with different clinical features. ATA positivity was associated with diffuse SSc, arthritis, complicated DU, and risk for severe lung, heart, and kidney involvement. Presence of ACA+ was associated with severe PAH but not with PF or SRC. ANA+ patients had often SSc-overlap syndromes, severe skin, joint and muscle involvement, multiple DU, PF, GIT involvement, and SRC. Awareness regarding malignancy should be high, especially among ATA+ and ACA+ SSc patients.

PS276

SSC-OVERLAP SYNDROMES: A DISTINCT CLINICAL SUB-GROUP WITH SIGNIFICANT DIFFERENCES IN DISEASE PROGRESSION COMPARED TO LSSC AND DSSC PATIENTS


1Dept. of Dermatology, Cologne University Hospital, Cologne, GERMANY; 2Dept. of Dermatology, Medical University of Graz, Graz, AUSTRIA; 3Dept. of Rheumatology, Asklepios Clinic Altona, Hamburg, GERMANY; 4Dept. of Internal Medicine, Division of Rheumatology, University of Heidelberg, Heidelberg, GERMANY; 5Dept. of Rheumatology, University of Erlangen, Erlangen, GERMANY; 6Dept. of Dermatology, University of Tubingen, Tubingen, GERMANY; 7Dept. of Rheumatology, Clinic of Rheumatology of Aachen, Aachen, GERMANY; 8Dept. of Dermatology, University-Hospital Carl-Gustav Carus, Dresden, GERMANY; 9Dept. of Dermatology, Munich University of Technology, Munich, GERMANY; 10Dept. of Rheumatology, University of Tubingen, Tubingen, GERMANY.

Background. SSc-Overlap syndromes are a very heterogeneous and remarkable subgroup of SSc-patients, who present at least two connective tissue diseases (CTD) at the same time, usually with a specific autoantibody status. Objectives: To determine whether patients, classified as SSc-overlap syndromes, represent a distinct SSc subgroup with a disease course different from patients with limited (SSc) and diffuse cutaneous SSc (dSSc). Methods. The data of 3240 prospectively included patients, registered in the database of the German network for systemic sclerosis and followed between 2003 and 2013, were analyzed. The following statistical methods were used: Kaplan-Meier analysis, logistic regression and chi-square test.
**PS277**

**SYSTEMIC SCLEROSIS-RELATED AUTO-ANTIBODIES ARE MARKERS OF NEW CLINICAL ASSOCIATIONS IN A COHORT OF 328 BRAZILIAN PATIENTS**

C.M. Silva, A.B. Bortoluzzo, V.S. Viana, G.S. Pasto, E.P. Leon, E. Bonfá, P.D. Sampaio-Barros

*Division of Rheumatology, Universidade de São Paulo, São Paulo, BRAZIL; Insper Institute of Education and Research, São Paulo, BRAZIL.*

**Background.** Systemic Sclerosis (SSc) shows a heterogeneous clinical presentation, characterized by marked skin and internal organ fibrosis and vascular dysfunction, associated with immunological abnormalities. A varied panel of SSc-related auto-antibodies has been described, and there is a growing interest to establish their prevalence and clinical associations in populations of different ethnicities.

**Objective.** To evaluate the frequency and the putative associations of a panel of SSc-related auto-antibodies with demographic and clinical features in a large SSc cohort.

**Methods.** We analyzed serum of 328 consecutive SSc adult patients attended at the Scleroderma Outpatient Clinic of a tertiary referral university hospital in Brazil. Clinical and demographic data were obtained through a review of the electronic register database. SSc-related auto-antibodies were determined by indirect immunofluorescence, ELISA, and immunoblotting.

**Results.** ANA positivity was 88% and anti-Ro/SSA was positive in 96 patients (29%). Anti-Scl-70 was present in 92 (28%), anticentromere (ACA) in 83 (25%), anti-Scl-70 in 54 (16.9%), anti-Ro (24.7%), La (11.0%), as well as Jo-1 (4.1%) and Ku-antibodies (3.8%).

**Conclusions.** These data support the concept, that SSc-overlap syndromes should be regarded as a separate SSc subset, distinct from ISc and dcSSc.

**PS278**

**THE AUTOANTIBODY PROFILE OF THE WAIKATO HOSPITAL SYSTEMIC SCLEROSIS COHORT (WHSSC COHORT)**

W. Chang1, A. Schollum1, R. Campbell1, T. Sole2, J. Petrie1, M. Empson1, D. White1, 2, K. Solanki1, 2

1Rheumatology Department, Waikato Hospital, Hamilton, NEW ZEALAND; 2Rheumatology Department, Tauranga Hospital, Tauranga, NEW ZEALAND; 1QE Health, Rotorua, NEW ZEALAND; 2Auckland University, Auckland, NEW ZEALAND; 3Waikato School of Medicine, Hamilton, NEW ZEALAND.

**Introduction.** Systemic Sclerosis (SSc) is a heterogeneous autoimmune connective tissue disease (CTD). The two subtypes of SSc are limited cutaneous systemic sclerosis (lcSSc) and diffuse cutaneous systemic sclerosis (dcSSc). SSc can overlap with other CTD and is called systemic sclerosis overlap syndrome (SOS). Association of specific autoantibodies with the subtypes and specific phenotypes is well recognized with some geographic and ethnic variation.

So far the autoantibody profiles in SSc have not been assessed in the New Zealand population.

**Objective.** To characterize the autoantibody profile of the WHSSc cohort.

**Methods.** Sixty patients had the autoantibody profile checked within allocated time. The SSc was defined per ACR criteria.

Autoantibodies were tested with Euroline (IgG) Systemic Sclerosis Immunoblot. Antibodies to Scl-70, CENP-A, CENP-B, RNA Polymerase III (RP-11 and RP155), Filibrillarin (U3-RNP), NO R90, NO R90, Th-To, PM-Scl 100 and 75, Ku, Ro52 and P6DFR were tested.

**Results.** 60 patients were reviewed (56 females) with median age 61 (range 29-81) years. Cohort consisted of 54 Europeans, 2 Indians, 2 Maoris, 1 Tongan and 1 Southeast Asian. 41 had lcSSc, 15 dcSSc and 4 SOS. Of lcSSc, 31 (75.6%) were positive for CENP-A and CENP-B, 12 (29.3%) for Ro-52, 5 (12.2%) for RP11 and RP155, 4 (9.8%) for Scl-70, 1 (2.4%) for Th-To. Of 15 dcSSc patients, 7 (46.7%) were positive for RP11 and RP155, 4 (26.7%) for Scl-70, 4 (26.7%) for Ro-52, 2 (13.3%) for Ku and 1 (6.7%) each for NO R90 and Fib. In the 4 SOS group, 1 was positive for CENP-A and CENP-B, 1 for Ro-52 and 1 for Ku.

Both Maori patients with lcSSc were positive for CENP-A & B. 2 of 5 Indian patients had dcSSc but no detectable autoantibodies.

**Discussion.** 27.6% of dcSSc patients had anti-Scl-70 antibodies. This is less than the French group (35%) but similar to UK and US prevalence (22%). There was a higher prevalence of CENP-A & B in our lcSSc group (75.6%). Anti-RP11 & RP155 prevalence was 20%, similar to Denmark (22%), but different from France (9.4%), UK (12%), Spain (16%) and USA (25%). There was a higher prevalence of anti-Ro52 (28.3% vs quoted 10%) with increased co-existence of anti-Ro52 with anti-RP11 & RP155 (33%) in our cohort RP11 & RP155, Scl-70 and anti-CENP-A and CENP-B were mutually exclusive except for one.

**Conclusion.** This is the first study to look at the autoantibody profile of SSc patients in New Zealand. Our findings support the suggestion that antibody prevalence vary geographically and ethnically. There possibly are different (yet undetected) antibodies in local Indian ethnic group.

**PS279**

**HIGH PREVALENCE OF ANTI-THYROID ANTIBODIES IN A NEW ZEALAND COHORT OF PATIENTS WITH SYSTEMIC SCLEROSIS**

K. Solanki1, M. Al-Majmoei1, A. Schollum1, T. Sole2, J. Petrie1, D. White1, 2

1Waikato Hospital, Hamilton, NEW ZEALAND; 2Waikato Clinical School, Hamilton, NEW ZEALAND; 3Midmore Hospital, Auckland, NEW ZEALAND; 4Tauranga Hospital, Tauranga, NEW ZEALAND; 5QE Health, Rotorua, NEW ZEALAND.

**Background.** Autoimmune thyroid disease is common and affects 1% of general population with thyroid antibodies being found in up to 15% of healthy subjects. Autoimmune conditions tend to cluster.

**Objectives.** We hypothesized that Systemic Sclerosis (SSc), being an autoimmune disorder was associated with higher prevalence of thyroid autoantibodies.

**Method.** Our SSc Clinic patients were prospectively tested for the thyroid autoantibodies as part of their assessment. 75 patients with SSc and 10 patients with Overlap Syndrome (SOS) were randomly chosen. The anti-thyroglobulin (anti-Tg) and anti-thyroid peroxidase (anti-TPO) antibodies were tested utilizing SERODIA-ATG and SERODIA-AMC Haemagglutination tests respectively. Data was analyzed in SPSS (Chi square analysis).

**Results.** Our cohort comprised 76 females (89.5%), 53 (61.6%) patients had limited cutaneous Systemic Sclerosis (lcSSc) (4 males), 22 patients (25.6%) had
They were treated with therapist-guided exercises twice a week for 1 hour, three times in a year for 5 weeks. At T1 patients showed improvement in the TUG and 6MWt tests and the parameters of capillaroscopic examination with a potential significant predictive value for the development of UCTD (apical limb width, capillary width and capillary length) showed no tendency to be larger, as in those who develop CTDs, in any of the patients. These encouraging findings suggest that clinical remission might be a realistic end point of UCTD treatment and Prednisone MR may be effective for both induction and maintenance of remission in these patients, also improving compliance to the programme of therapist-guided rehabilitation exercises.

**PS281**

**NEUTROPHIL-LYMPHOCYTE AND PLATELET-LYMPHOCYTE RATIOS IN SYSTEMIC SCLEROSIS**

S. Yoldas, B. Gundugdu, A. Yildirim, S. S. Koca
First University Faculty of Medicine Department of Rheumatology, Elazig, TURKEY.

**Introduction.** Inflammatory process and autoimmunity affect the haemopoetic system and alter the counts and figures of peripheral blood cells in chronic inflammatory diseases. The indices of the complete blood cell count (CBC) analysis such as mean platelet volume (MPV), neutrophil-lymphocyte ratio (NLR), and platelet-lymphocyte ratio (PLR) are reported to be associated with a variety of cardiovascular and oncological diseases. Therefore, the aim of the present study was to evaluate the potential association of these indices on the disease course of systemic sclerosis (SSc) which is a connective tissue disease characterized by widespread fibrosis.

**Method.** The study included 39 patients with SSc and 51 patients with systemic lupus eritematosus (SLE) as patient controls, and 50 healthy controls (HC). The patients were fulfilling the established criteria. Modified Rodnan skin score (MRRS), Valentini disease activity index and Medsger disease severity scale in the SSc patients and SLE disease activity index (SLEDAI) and Systemic Lupus International Collaborating Clinics/American College of Rheumatology (SLICC/ACR) damage index in the SLE group were assessed. Routine laboratory analyses were applied by the standart methods. NLR and PLR were calculated. One-way ANOVA, post-hoc Tukey test and chi-square test were applied to statistical analysis.

**Results.** When compared to the HC group, the neutrophil counts were higher in the SS group and the lymphocyte counts were lower in the SLE group (Table I). Correspondingly, the NLR was higher in the SSc and SLE groups than in the HC group (p<0.008 and p<0.001, respectively). The platelet counts and MPV were similar among the study groups. However, when compared to the HC group, PLR was higher in the SLE group (p<0.001), while it was not higher in the SSc group (p=0.104). 93.8% of the SSc patients had limited cutaneous subtype. NLR, PLR and MPV in patients with the positive for anti-nuclear, anti-centromer or anti-Topo I antibodies were not significantly different from the patients negative ones (p<0.05 for all). Moreover, they were not correlated with the MRRS, disease activity index and severity scale (p>0.05 for all). Further studies are needed to explain the precise roles of NLR and PLR in SSc.

<table>
<thead>
<tr>
<th><strong>Table I. The demographics and laboratory parameters in the study groups.</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>HC</strong> (n=55)</td>
</tr>
<tr>
<td>Mean Age (years)</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
</tr>
<tr>
<td>Mean disease duration (years)</td>
</tr>
<tr>
<td>Haemoglobin (g/dL)</td>
</tr>
<tr>
<td>WBC (10^3/μl)</td>
</tr>
<tr>
<td>Neutrophil (10^3/μl)</td>
</tr>
<tr>
<td>Lymphocyte (10^3/μl)</td>
</tr>
<tr>
<td>NLR</td>
</tr>
<tr>
<td>PLR</td>
</tr>
</tbody>
</table>
| **HC:** healthy controls; SLE: systemic lupus erythematosus; SSc: systemic sclerosis; BME: body mass index; WBC: white blood cell count; NLR: neutrophil-lymphocyte ratio; MPV: mean platelet volume; PLR: platelet-lymphocyte ratio *p<0.001; **p<0.01 when compared to the HC group. **p<0.05 when compared to the SLE group.**
The aim of this study was to evaluate functional T cell subsets in patients with early SSc (eSSc) in basal conditions and after iLOPROST treatment.

**Patients and Methods.** A total of 7 previously untreated female patients with early SSc (7±1.8 years from diagnosis) were included in this study. The diagnosis of SSc was made according to the American College of Rheumatology classification criteria. All patients were treated i.v. with 100 mcg of iLOPROST 3 times a day for 5 days. The analysis of T cell subsets, including Th1, Th2, Th17, quiescent CD8+ (CD8+CD38-HLADR-) and activated CD8+ (CD8+CD38+HLADR+) was carried out on peripheral blood samples by 8-color flow cytometry. Patients were studied first in basal condition and after 5 days of therapy. Fifteen healthy males were studied as controls.

**Results.** Our results showed: a) Low basal absolute values of CD4+ T cells in patients with eSSc (mean 776.5/mL, range 424.8/mL-1520.4/mL) vs control group (mean 1048.1/mL, range 642.2/mL-1863.8/mL); b) Lower values of percent and absolute CD4+Th17+ cells in the eSSc group, mean 7.66% and 12.59% (range 4.2% - 12.1% vs 2.7% - 20.3%, p<0.05) and mean 53.92/mL vs 123.1/mL (range 26.34/mL – 87.47/mL vs 45.44/mL-257.8/mL, p<0.05), respectively; c) Reduced baseline quiescent CD8+T cells values and increased activated CD8+T cells after treatment (baseline mean quiescent CD8+ cells: 86.71% and 494.7/mL vs post therapy mean CD8+ cells: 74.54% and 478.3/mL, basal activated CD8+ cells: 1.86% and 13.4/mL vs after treatment activated CD8+ cells: 2.41% and 18/mL, respectively).

**Conclusion.** The literature data on T cell regulatory subsets in eSSc are scanty. Our approach included the phenotypic evaluation of CD4+Th17+ cells using CC36 and CXC3R1, so that our measured levels may be higher than those used in preclinical IL17 evaluation. The low baseline level of CD4+Th17+ cells may be related to the very early phase of the disease, whereas the increase in activated CD8+ cells can be related to the anti-inflammatory and anti-fibrotic effects of ILOPROST.

**Table I. Clinical data of patients (NDA: No Data Available).**

<table>
<thead>
<tr>
<th>Sex</th>
<th>F</th>
<th>F</th>
<th>F</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>50</td>
<td>75</td>
<td>75</td>
</tr>
<tr>
<td>Scleroderma</td>
<td>diffuse</td>
<td>limited</td>
<td>limited</td>
</tr>
<tr>
<td>Raynaud’s phenomenon</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
</tr>
<tr>
<td>Fingertip necrosis</td>
<td>yes</td>
<td>no</td>
<td>yes</td>
</tr>
<tr>
<td>Calciosis</td>
<td>NDA</td>
<td>NDA</td>
<td>NDA</td>
</tr>
<tr>
<td>Telangiectasia</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
</tr>
<tr>
<td>Osseous palisade hypomobility</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
</tr>
<tr>
<td>Sclara syndrome</td>
<td>NDA</td>
<td>yes</td>
<td>yes</td>
</tr>
<tr>
<td>Arthralgia</td>
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<td>no</td>
<td>no</td>
</tr>
<tr>
<td>Pulmonary fibrosis</td>
<td>mild</td>
<td>severe</td>
<td>mild</td>
</tr>
<tr>
<td>Pulmonary hypertension</td>
<td>No</td>
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<td>no</td>
</tr>
<tr>
<td>Renal disease</td>
<td>yes</td>
<td>no</td>
<td>yes</td>
</tr>
</tbody>
</table>

**PS284**

**DISTRIBUTION OF BODY MASS INDEX AND METABOLIC SYNDROME IN PATIENTS WITH SYSTEMIC SCLEROSIS: STUDY OF A SINGLE ITALIAN CENTRE**


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**Background.** Obesitas is now considered as a mild, long-lasting inflammatory disease associated with an increased cardiovascular (CV) risk. Systemic Sclerosis (SSc) and other rheumatic diseases have been associated with increased CV risk, but despite an increasing interest regarding the prevalence and the effects of obesity and metabolic syndrome in these patients, conclusive data are lacking.

**Objectives.** To evaluate the prevalence of overweight, obesity and metabolic syndrome (MS) in a cohort of patients with SSc.

**Methods.** Body mass index (BMI) was assessed in 296 SSc patients. BMI was categorized into 4 classes, i.e. <25 kg/m^2 (underweight), 18-25 kg/m^2 (normal weight), 25-30 kg/m^2 (overweight), and >30 kg/m^2 (obese). Levels of total cholesterol, HDL-cholesterol, triglycerides, fasting glucose were evaluated, as well as the presence of arterial hypertension and diabetes mellitus. Metabolic syndrome was defined according to the American Heart Association/Updated NCEP criteria (1). We considered central obesity as a BMI>24 kg/m^2 for women and BMI>25 kg/m^2 for men (2).

**Results.** In the SSc cohort (58.2% female, age 58±14.2 years, mean disease duration 11.4±8.6 years) the mean BMI was 24.4±4.8 and the prevalence of obesity was 10.4%. According to BMI, 136 SSc patients (46.1%) were normal-weight, 125 (42.2%) were overweight, 31 (10.4%) where obese, while only 4 (1.3%) were underweight. The analysis of individual cardiovascular risk factors highlighted that 50 patients (16.9%) presented hypertegric/lebericidemia, 107 (36.1%) had low HDL-cholesterol levels and/or were taking a specific treatment for lipid abnormalities and 25 (8.4%) had arterial hypertension. The prevalence of metabolic syndrome was 14.2%. The prevalence of obesity and MS was comparable in patients with diffuse and limited cutaneous disease. Considering the immunological autoantibodies profile and the organ involvement no differences emerged in the prevalence of obesity and MS. Nineteen (6.4%) patients of our cohort presented myocardial involvement, but only 3 of them had a MS and none of them was obese.

**Conclusions.** SSc-patients have a lower prevalence of both obesity and MS with respect to the general population as well as to patients with other rheumatic diseases such as rheumatoid arthritis, according to available data (3,4). The weight of well-known CV risk factors and of specific disease abnormalities leading to the SSc micro- and macrovascular damage, has to be further defined.

**References**

PS285
COMpromise of forearm bone mass in patients with systemic sclerosis: association with disease duration, range of motion, quality of life and systemic bone involvement
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Introduction. Skin thickening associated with forearm and hand joint involvement can contribute to functional disability, with consequent disease and worsening of bone loss in patients with systemic sclerosis (SSc).

Objective. To evaluate prognostic factors that can contribute to forearm bone loss in patients with diffuse cutaneous SSc.

Methods. Prospective study analyzing 38 female patients with the diagnosis of SSc attended at the scleroderma outpatient clinic of the University of São Paulo (May 2012-May 2013). Patients were interviewed about disease symptoms and examined regarding modified Rodnan skin score (mRSS), measurement of total passive range of motion (ROM) of wrists and fingers joints, Health Assessment Questionnaire (HAQ), nailfold capillaroscopy, bone mineral density (BMD by DXA) and high-resolution peripheral quantitative computed tomography (HR-pQCT) of distal forearm.

Results. Mean age was 40.18±7.27 years and mean disease duration was 8.23±4.96 years. Clinical and laboratory findings revealed intestinal lung disease in 79%, esophageal hamotopit in 63%, and anti-Scl70 antibody in 53% of patients. Modified Rodnan skin score was 6.4±2.7 and nailfold capillaroscopy score was 5.48±1.24. Osteoporosis was found in 39%, and BMD of left forearm with T-score<−2.5 was present in 13% of patients. Left forearm BMD was negatively correlated (Pearson) with disease duration (r=−0.328; p=0.043); HAQ (mainly eating: r=0.323; p=0.047); radius trabecular structure [trabecular separation (r=−0.369; p=0.006)] and positively with: ROM of left hand fingers thumb (r=0.350; p=0.031); index (r=0.351; p=0.030); middle (r=0.372; p=0.021); ring (r=0.354; p=0.028); little (r=0.258; p=0.117); ROM of right hand fingers thumb (r=0.342; p=0.035); index (r=0.359; p=0.026); middle (r=0.325; p=0.046); ring (r=0.320; p=0.049); little (r=0.338; p=0.037); BMD of L1-L4 (r=0.781; p<0.0001); BMD of femoral neck (r=0.571; p=0.0002); BMD of total hip (r=0.779; p<0.001); trabecular bone volume/ tissue volume (r=0.645; p<0.0001), trabecular thickness (r=0.624; p<0.0001); trabecular volumetric bone density (r=0.647; p<0.0001) and cortical radius thickness (r=0.632; p<0.0001). There was no correlation between left forearm BMD with mRSS and nailfold capillaroscopy.

Conclusion. Forearm bone involvement was associated with disease duration, impairment in daily living activities (eating), ROM of hands and involvement of trabecular and cortical bone.

PS286
Levels of vitamin D, PTH and calcium in patients with systemic sclerosis in limited and diffuse forms
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Introduction. The importance of the vitamin D in patients with Systemic Sclerosis (SSc) has been reported in some studies, but its role is not yet well established. Recently it was concluded that vitamin D deficiency is very common in patients with SSc.

Objectives. Conduct a prospective comparative study related with the dosage of vitamin D 25 (OH) D3, ionized calcium and parathyroid hormone (PTH) among female patients who have SSc in limited and diffuse forms.

Methods. Case-control study between March 2012-2013, with 32 patients followed up at Rheumatology ambulatory, with a diagnosis of Systemic Sclerosis. The study included female patients with a mean age of 44.4 years, both limited and diffuse forms, living in the same city, during mild winter, to assess dosage of vitamin D by a competitive method based on steroid use and labeled binding protein; parathyroid hormone and ionized calcium. According to the consensus of the Endocrine Society of 2011, the reference ranges for deficiency, insufficiency and sufficiency of vitamin 25 (OH) 1D3 were <20ng ml , 20-30ng/mL and >30ng/mL, respectively. Criteria for exclusion: patients on supplementation of calcium and vitamin D, intestinal or renal involvement or presence of malignancy bone disease and osteoporosis or osteopenia confirmed by bone densitometry.

Results. Of the 32 patients who were evaluated, 13 (40.6%) have diffuse form and 19 (59.4%) limited form. Regarding the dosage of vitamin 25 (OH) D3 in patients with diffuse form, we founded 6 (46%) patients with deficiency, 3 (23%) with insufficiency, and 4 (31%) with sufficiency. In the limited form group, we found 7 (36.8%) patients with deficiency, 11 (58%) with insufficiency, and 1 (5.2%) with sufficiency. Considering together limited and diffuse forms, 12 (38.7%) patients had deficiency, 14 (43.7%) had insufficiency and 5 (16.1%) had sufficiency. With regard to PTH and ionized calcium values were normal in all forms.

Discussion. Studies evidenced a high prevalence of vitamin D deficiency in these patients. More studies are necessary to identify the exact role of vitamin D in different manifestations of the disease, including pulmonary artery hypertension, disease activity and the presence of pulmonary fibrosis.

Conclusion. Decreased levels of vitamin D were found in 26 of 32 patients with SSc in this study. It was more prevalent in limited form than diffuse form of SSc. These findings may be important hereafter, correlating with some aspects of the disease and perhaps a perspective of treatment.

PS287
Bone mineral density in patients with systemic sclerosis
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Studies of bone mineral density (BMD) in patients with systemic sclerosis (SSc) showed its decreasing in comparison with healthy control. Prevalence of low bone mass and severity of BMD decreasing differ significantly between patients from different countries and vary from 17% in China (Mok CC, et al, 2012) to 77% in Spain (Rios-Fernández R, et al, 2012). Aim. To assess BMD and frequency of osteoporosis (OP) in patients with SSc in Russia.

Methods. In case-control study BMD was evaluated in 52 postmenopausal women with SSc (16 – diffuse and 36 – limited form), mean age 57.6±7.1yrs and mean disease duration 11±8 yrs. Forty four healthy postmenopausal women (mean age 59.2±6.6yrs) served as control. BMD was measured at the lumbar spine (LS), femoral neck (FN) and total hip (TH) by DXA (Hologic 4500A). BMD decreasing was determined according to WHO criteria. Results. BMD was significantly decreased in SSc women in comparison with control group: in LS – 0.844±0.090 vs 0.861±0.092 g/sm2 (p=0.025); in FN – 0.670±0.128 vs 0.736±0.112 g/sm2 (p=0.037), and in TH – 0.801±0.160 vs 0.884±0.124 g/sm2 (p=0.03). Frequency of OP in SSc group was significantly more often than in control group (59% vs 11%, p=0.001). PS288
Bone microarchitecture assessment by trabecular bone score, in patients with systemic sclerosis
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Current data on bone mineral density (BMD), in patients with Systemic Sclerosis (SSc) is discrepant. Trabecular Bone Score (TBS) is a novel software application for bone quality assessment, in addition to BMD measurement. Aim. To examine the micro architectural bone status by TBS in SSc patients and its relation to the bone mineral density and clinical features of the disease. Methods. The cross sectional study included 40 female SSc patients. The parameters of lumbar spine BMD and total body were examined by X-ray absorptionimetry (DXA) on Hologic Discovery device, TBS analysis was carried out by Insight TBSS® - Medimaps. Demographic data and clinical characteristics of SSc patients
were collected from the EULAR Scleroderma Trials and Research (MEDS EU-STAR) database. SSc activity was determined using Valentine’s questionnaire (SSAS). We examined the correlation between the TBS and demographic and clinical features.

Results. The average age of the patients (N=40) was 57.22 (36 - 73.2±6.9 years, postmenopausal 37/40, menopause duration: 10.00 (1-26.85) years, duration of disease 9.06 (1-26±6.8) years. Diffuse disease subtype (dSSc) had 19/40 (47.5%), limited (lSSc) 21/40 (52.5%) pts, 4/40 had fractures (10%), glucocorticoids (GC) users were 10/40 (25%), current smoking was recorded in 10/40 (25%), ATα +18 / 40 (45%), ACA +19 / 40 (47.5%). The most frequent clinical features were: Raynaud phenomenon (100%), sclerodactyly (98%), digital ulcers (81.5%), esophageal reflux (80.3%), joint contractures (78.8%), etc. Average disease activity by SSAS = 6.5. Lumbar spine BMD was 1.03±0.321g/cm², TBS 1.36±0.034, calcium content 2.25±0.03 kg. There was no statistically significant correlation between the BMD, BMC and TBS. TBS values were inversely correlated with the age and use of GC in the treatment (r=-0.330, -0.385, p=0.03), while positively correlated with SSc activity, presence of digital ulcerations and calcinosis (r=0.342, 0.341, -0.367, respectively; p<0.05).

Conclusions. The TBS values are not associated with BMD parameters in SSc patients. Lower TBS is associated with age and the use of steroids in the treatment. Higher TBS values are associated with the presence of digital ulcers, calcinosis and higher disease activity.

PS289

SEXUAL DYSFUNCTION AND LOWER URINARY TRACT SYMPTOMS IN 74 PATIENTS WITH SYSTEMIC SCLEROSIS

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Objective. To estimate the frequency of lower urinary tract symptoms (LUTS) and sexual dysfunction in patients with systemic sclerosis (SSc) and correlate these symptoms with clinical and functional parameters including disability and quality of life.

Patients and methods. SSc patients fulfilling the American College of Rheumatology and/or the Leroy and Medsger criteria, received by mail self-administered questionnaires assessing for clinical symptoms, LUTS using Urinary Symptom Profile (USP) scale, sexual dysfunction using Feminine Sexual Function Index (FSFI), International Indication for the Erectile Function (IEF-5), disability using Health Assessment Questionnaire (HAQ) and McMaster Toronto Arthritis Patient Preference Disability Questionnaire (MACTAR), anxiety and depression using Hospital Anxiety and Depression scale (HAD) and quality of life using the Short Form Health Survey (SF-36).

Results. 74 patients (61 females) were included. The most frequent LUTS were overactive bladder (n=11, 84.6%) and dysuria (n=8, 61.5%) in males and overactive bladder (n=52, 85.3%) and incontinence (n=39, 49.2%) in females. Thirty two females were sexually active, 20 (62.5%) of whom presented sexual dysfunction with a mean ± SD FSFI score of 16.3±6.2; the most compromised domains being mean ± SD arousal (2.5±1.4) and mean ± SD desire (2.6±1.3). Sexual disorders were associated with a lower disease duration (p=0.01) and a higher depression (p=0.04) and anxiety (p=0.05) score. Dysuria was indirectly correlated with sexual disorders in women (r=-0.48). Seven of 8 men (87.5%) had erectile dysfunction, with a mean ± SD IIEF-5 score of 16±5.3.

Conclusion. LUTS are more frequent in SSc patients than in the general population. The most frequent symptom is overactive bladder. Sexual disorders are similarly frequent in French SSc women than in Canadian.

PS290

ANTI-NUCLEAR AUTOANTIBODIES IN 200 IRANIAN PATIENTS WITH SYSTEMIC SCLEROSIS: CORRELATION WITH CHARACTERISTIC CLINICAL FEATURES

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Objectives. To investigate correlation of different antinuclear antibodies (ANA) in patients with systemic sclerosis and its clinical features.

Methods. Sera of 200 patients with systemic sclerosis (SSc) were analyzed by an indirect immunofluorescence (IF) technique with Hep-20-10 liver (monkey) cells as a substrate. Specific ANA such as anti-centromere antibodies (ACA), anti-topoisoensamera(TOPO), anti-RNA Polymerase III (Pol 3), anti-Pm-Scl/Pm’(Scl) and anti-Histone were examined by IFA. The frequency of clinical features associated with a specific antibody (ab) group was reported cumulatively over the follow-up period. We compared frequency of specific clinical features across different auto-antibody types.

Results. We detected ANA in sera of 91.5% of the patients (ACA:11.5% ; anti-TOPO:78%; anti-Pol3:11%; anti-Pm-Scl:3.5%; anti-Histone: 4.5%). ACA was related to a high prevalence of Raynaud’s phenomenon as first symptom, esophageal reflux, lung fibrosis in HRCT of chest and low prevalence of diarrhea. Anti-TOPO abs were associated with higher prevalence of diffuse subtype of SSc, digital ulcer/gangrene, pulmonary fibrosis, calcinosis and reduction of pulmonary diffusion (DLCO<60%). Patients with anti-pol3 were older at time of first symptom had more diffuse subtype, showed significant relation to Raynaud’s phenomenon and had less pulmonary fibrosis. Positive anti-Pm-Scl ab correlated with younger age at disease onset but not with specific clinical features. Positivity for anti-Histone was associated with pulmonary fibrosis.

Conclusions. Anti-i-TOPO abs showed higher prevalence and correlation with diffuse disease subtype. Age at disease onset associated with anti-Pm and anti-Pm/Scl ab positivity. The anti-TOPO abs was showed high prevalence as previously described in a group of Iranian SSc patients.

Key words. Systemic sclerosis. Auto-antibodies.

PS291

SEVERITY OF NAILFOLD CAPILLARY MICROSCOPY CORRELATE WITH BONE MINERAL DENSITOMETRY BY ULTRASONOGRAPHY AND RODNAN SKIN SCORE IN SSc PATIENTS

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Systemic Sclerosis is characterized by autoimmunity and vasculopathy leading to tissue fibrosis, osteopenic syndrome might be an important complication of complexed pathogenesis in SSc.

Objective: to perform bone ultrasonography assessment in SSc Patients and to correlate with capillaroscopic findings and the pattern of skin thickness. Methods: BMD by bone ultrasonography of every patients, all digits capillaroscopy and clinical data were carefully analyzed in 44 consecutive SSc patients fulfilling Leroy and Medsgder criteria.

Results: we include 44 post-menopausal consecutive women (average age 58.6 years) with an average duration of disease 8 years; 22 pts(50%) were diffuse SSc, 40% with digital ulcers, 18% smokers, 58% were treated with glucocorticoids and 9% suffered from fractures earlier.75% presented T-score <-1.0 (osteopenic) and 25% were osteoporotic. Nail fold capillaroscopic pattern was found Late in all osteoporotic patients (100%). In 35 osteopenic patients nail fold capillaroscopic pattern was found active in 20 pts (60,6%), Early in 10 pts (30,3%), Late in 3 pts (9,1%).Another association was found between both lower BMD, Late capillaroscopic pattern and modified Rodnan Skin Score >18. Our study point to a significant role of capillaroscopy in osteoporotic SSc pts and in evaluating the role of capillaroscopy in discriminating between osteoporotic and osteopenic SSc pts. We did not observe any association between bone fragility and age, duration of disease, smoking, glucocorticoid therapy or some other feature of disease. Conclusion Capillaroscopic study was indicative regarding the clinical pathological context with a specificity 100% scleroderma pattern late in all osteoporotic pts. According to data we believe that evaluation of SSc pts with BMD searching for bone fragility is a priority.

PS292

CALCINOSIS PREFERENTIALY AFFECTS THE THUMB COMPARED TO OTHER FINGERS IN PATIENTS WITH SYSTEMIC SCLEROSIS

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Background. Systemic sclerosis (SSc)-related calcinosis (which is well demonstrated on plain X-rays), frequently affects the fingers, and can be a major source
of pain and disability. Although Raynaud’s phenomenon often spares the thumb, clinical experience suggests that conversely the thumb is frequently affected by calcinosis. We set out to investigate the hypothesis that in patients with SSC, thumbs are more commonly affected than other digits by calcinosis.

Methods. Hand radiographs from patients with SSC from a single tertiary referral centre were selected for analysis on the basis that at least one area of calcinosis was identified. Each finger on both hands of each patient was assigned a severity score on a 0 to 3 scale (0 = no calcinosis, 3 = most severe); scores were then analysed. The scoring was completed twice, including and excluding the metacarpals.

Results. Hand X-rays of 68 patients with SSC (90% female, median age 62 years [range 55-68], 81% limited cutaneous and 19% diffuse cutaneous) showed calcinosis. When metacarpals were excluded, the overall trend in scores across digits for both hands suggested that there was decreasing severity from the thumb to the little finger (finger 5). There were a particularly large number of 3 scores for thumbs on right hands (15%) compared to left hands (4%). A Friedman test of difference in median scores across fingers (testing for an overall difference between fingers) was statistically significant for both left hands and right hands (both p<0.0001). Post-hoc tests of the difference in paired medians between thumbs and other fingers showed, for left hands, significant differences in severity between the thumb and fingers 3, 4 and 5 and for right hands, significant differences between the thumb and each of the other fingers. For example, for right hands the median difference in calcinosis scores between the thumb and finger 5 was 1.6 (95% confidence interval [CI] 1.0 to 2.0, p=0.0001), and between the thumb and finger 2 the median difference was 0.5 (95% CI 0.0 to 1.5, p=0.037). When the analysis was repeated for scores including the metacarpals, the same broad trends were apparent.

Conclusions. 1. The thumb is affected by calcinosis more than other digits, followed by the index finger. 2. This observation provides insight into the pathogenesis of SSC-related calcinosis, which may relate more to repetitive trauma than to ischaemia.

PS294  
CORRELATION BETWEEN CHRONIC WIDESPREAD PAIN OR FIBROMYALGIA AND ACTH AXIS ALTERATIONS IN PATIENTS WITH LOCALISED AND DIFFUSE SYSTEMIC SCLEROSIS

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Objective. The aim of this study was to evaluate the prevalence of FM and CWP in SSC patients, and the correlations between the adrenocorticotropic hormone (ACTH) axis alterations and clinical and laboratory parameters.

Methods. We enrolled 40 consecutive outpatients fulfilling the American College of Rheumatism (ACR) criteria for SSC. All of the patients were evaluated in terms of disease activity, inflammation markers, the presence of antibodies, and disease duration.

They were all classified as having FM on the basis of the 1990 and 2010 ACR FM criteria.

Conclusion. CWP in SSC patients correlates with the clinical manifestations of the disease, but not with serum levels of cortisol or ACTH. Moreover, skin fibrosis assessed through mRSS seems to be inversely related to pain V AS score, suggesting a possible protective effect in nociception.

PS295  
INFLUENCE OF GENDER, ETHNICITY AND AGE AT ONSET IN THE CLINICAL PRESENTATION OF SYSTEMIC SCLEROSIS IN A LARGE BRAZILIAN COHORT OF 1017 PATIENTS

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Background. Although systemic sclerosis (SSc) is a systemic connective tissue disease characterized by female predominance, male adult patients are frequently associated with higher disease severity. There are no data assessing these variables in a Brazilian population with heterogeneous genetic background.

Objective. To characterize SSc clinical presentation according to gender, ethnicity and age at onset in a large cohort of Brazilian patients.

Methods. Retrospective study analyzing demographic variables in a cohort of 1017 patients with SSc from the Scleroderma Outpatient Clinic of two referral University centres in Brazil in the period between 1990 and 2012. Clinical and demographic data were obtained through chart review from 1990 to 2000, and through an electronic register database after 2001. Regarding ethnicity, patients were considered as white (with European ancestry), African-Brazilians (including mullatos/mestizos, i.e., originating from the mixture of white and black individuals, and black patients of unmixed ancestry), and Asian descendants.

Influence of gender, ethnicity and age at onset on the clinical presentation of systemic sclerosis in a large Brazilian cohort of 1017 patients.
Systemic sclerosis (SSc) is an autoimmune disease characterized by vascular dysfunction, microangiopathy and macrovascular damage. Aortic pulse wave velocity (aPWV) is known to be a reliable indicator of arterial stiffness and a useful prognostic predictor of cardiovascular events. Objective. The aim of this study was to evaluate aPWV alterations in a series of SSc patients. Methods. A total of 33 patients diagnosed with SSc (30 females and 3 males, mean age 51.81 years) were included in the study. We determined parameters of aortic stiffness - pulse wave velocity (PWV) and augmentation index (Aix) in all subjects using Arteriograph device (Tensio Med Ltd., Budapest, Hungary). In our cohort more than half had a limited SSc (60.6%) and 51.5% had an elevated aPWV. 10 out of 33 patients had one or more classic cardiovascular risk factors, 30% with limited SSc and only 7.69% (1 patient) with diffuse SSc, while patients had higher age at diagnosis (p=0.003) and telangectasias (p=0.002). Patients with juvenile SSc were associated with diffuse SSc (p=0.001), calciﬁcation (p=0.001), and myositis (p=0.026), although they were also associated with lower frequency of interstitial lung disease (p=0.050), pulmonary hypertension (p=0.035), interstitial lung disease (p=0.050), pulmonary hypertension (p=0.035), esophageal (p=0.005), and joint (p=0.047) involvement. Conclusion. Male gender and African-Brazilian ethnicity presented distinct clinical features characterized by major organ involvement, while juvenile SSc was associated with lower frequency of visceral involvement.

PS296

ARTERIAL STIFFNESS IN SSC PATIENTS - A SINGLE CENTRE EXPERIENCE

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Background. Systemic sclerosis (SSc) is characterized by endothelial dysfunction, microangiopathy and macrovascular damage. Aortic pulse wave velocity (aPWV) is known to be a reliable indicator of arterial stiffness and a useful prognostic predictor of cardiovascular events. Objective. The aim of this study was to evaluate aPWV alterations in a series of SSc patients. Methods. A total of 33 patients diagnosed with SSc (30 females and 3 males, mean age 51.81 years) were included in the study. We determined parameters of aortic stiffness - pulse wave velocity (PWV) and augmentation index (Aix) in all subjects using Arteriograph device (Tensio Med Ltd., Budapest, Hungary). In our cohort more than half had a limited SSc (60.6%) and 51.5% had an elevated aPWV. 10 out of 33 patients had one or more classic cardiovascular risk factors, 30% with limited SSc and only 7.69% (1 patient) with diffuse SSc, but with no proof of microangiopathy correlated with these comorbidities. These patients also had an elevated average of aPWV (10.99), significantly higher compared to those with no C-V risk factors (9.12), 18.18% of patients with limited SSc had no C-V risk associated and high aPWV, respectively 12.12% of those with diffuse disease. Also, in the group with no CV risk, patients had a higher Aix (9.11 vs 1.94).

Conclusion. As expected, patients with high aPWV were classified as having limited SSc and also had conventional cardiovascular risk factors. Aortic pulse wave velocity be easily measured by non-invasive, user-friendly tool and can be used as a marker of damage, still further prospective studies are required for better validation of this method.

PS297

JUVENILE SCLERODERMA INTERNATIONAL NETWORK (JUSINET) DATABASE: A RELIABLE INSTRUMENT FOR CLINICAL RESEARCH IN JUVENILE SCLERODERMIA SYNDROMES

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Background. The conduct of Clinical Research in rare diseases, such as Juvenile Systemic Sclerosis (JSSc) and Juvenile Localized Scleroderma (JLS), requires an adequate number of patients and a fruitful collaboration between international centers. The clinical management of young patients suffering from these diseases is also often difficult to achieve in an effective and shared matter.

Objective. We propose a web-based registry (www.jusinet.org) to prospectively collect data on demographic, epidemiological, clinical, and laboratory features of patients with JSSc and JLS from adult and paediatric rheumatology centres and to educate physicians to a more standardized approach to these conditions. The purpose is to provide a well-characterized cohort of scleroderma patients according to the current classification criteria and collect adequate information enabling to uniform clinical assessment and diagnostic tests, to stimulate clinical and basic research projects.

Methods. The Database was evaluated by some international experts who provided us with valuable advice for improvement. JUSINET has an administrative structure including a Database Executive Committee (DEC), which evaluates the progress of the project and discusses management issues. The Database Coordinator (DC) assisted by a Research Assistant (RA), and a Database Manager (DM, statistician) form the Local Administrative Structure (LAS). In order to verify the performance of JUSINET at national and international level, four centers in Italy, one in Slovenia, Argentina and Turkey, have tested and validated the system including all patients cases. Compilers were required to express their opinion on 3 variables, clarity of information, ease of data entry and completeness of information, for each section of the database. The 324 opinions expressed for the 22 sections of JUSINET, in a range between 1-5, reached a mean value of 4.62. The mean time to enter a new patient data was 14 minutes for JSSc, and 8 minutes for JLS; to update data was 8 minutes for JSSc and 5 minutes for JLS.

Conclusions. The JUSINET Database represents a valuable instrument to better characterize patients childhood onset scleroderma and facilitate research on pathogenesis and treatment of this relatively rare condition. It also provides a simple and reliable tool for the daily clinical management of these patients.
Background. Systemic sclerosis (SSc) is a heterogeneous autoimmune disease which affects predominantly women. SSc is subclassified by the extent of skin involvement into diffuse cutaneous (dcSSc) and limited cutaneous systemic sclerosis (lcSSc). The main difference between the two types of systemic sclerosis is the rate of disease progression, the severity of skin and visceral involvement along with a few characteristic phenotypic differences. It has a variable course and a guarded prognosis.

The association between autoantibodies (immunoglobulins) and the two major subsets of SSc is well known. Anti-centromere antibodies (ACA) are highly specific for limited cutaneous systemic sclerosis (lcSSc) and anti-topoisomerase 1 (scl70) antibodies are highly specific for diffuse cutaneous systemic sclerosis (dcSSc) which carries a poorer prognosis. However, the role of the above autoantibodies in the pathogenesis of SSc remains elusive.

There is a paucity of literature on the association between isotypes of autoantibodies and their clinical implications.

Objective. We aimed to evaluate the significance of immunoglobulin isotypes and their association with clinical features in our cohort of patients with SSc.

Method:

- Patients with SSc and SSc-Overlap Syndrome (SOS) were identified from the Waikato Systemic Sclerosis database and the most recent immunoglobulin and complement levels recorded.
- Diagnosis of Systemic Sclerosis was established as per 1980 ACR criteria in all cases.
- Immunoglobulin and complement levels were estimated by Nephelometry (Beckmann Immage).
- Association of Ig levels with SSc subtype and SOS was assessed with one way analysis of variance (ANOVA) & a receiver operating characteristic curve was generated for the significant result.

Results. The cohort comprised of 78 female and 10 male patients (60 lcSSc, 20 dcSSc and 8 SOS).

The mean immunoglobulin levels in the three groups are as tabulated.

Conclusion: We have demonstrated that the IgG levels were significantly higher in dcSSc than other subtypes (ROC for IgG as above). This is consistent with previous work by Tamby MC et al who showed higher (but not significant) mean IgG & IgA levels in patients with anti-scl70 positive dcSSc compared to lcSSc.

No significant difference in complement levels and the three groups were found. An IgG level of 11.85 g/L had a sensitivity of 85% and specificity of 72% (Positive Likelihood Ratio of 3.04) in the diagnosis of dcSSc.

References


<table>
<thead>
<tr>
<th>Table I. The mean immunoglobulin levels in the three groups are tabulated.</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean (g/L)</td>
<td>SD</td>
<td>95% CI</td>
<td></td>
</tr>
<tr>
<td>IgG Level (NR=7.0-16g/L)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IgG</td>
<td>11.1</td>
<td>3.82</td>
<td>10.1-12.1</td>
</tr>
<tr>
<td>IgA</td>
<td>14.8</td>
<td>5.46</td>
<td>12.2-17.3</td>
</tr>
<tr>
<td>IgM</td>
<td>12.5</td>
<td>3.78</td>
<td>9.3-15.7</td>
</tr>
<tr>
<td>IgG Level (NR=8.4-40g/L)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IgG</td>
<td>2.5</td>
<td>1.25</td>
<td>2.2-2.9</td>
</tr>
<tr>
<td>IgA</td>
<td>2.8</td>
<td>1.36</td>
<td>2.1-3.4</td>
</tr>
<tr>
<td>IgM</td>
<td>2.9</td>
<td>1.52</td>
<td>1.6-4.1</td>
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<tr>
<td>IgG Level (NR=0.4-2.5g/L)</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>IgG</td>
<td>1.5</td>
<td>0.9</td>
<td>1.3-1.8</td>
</tr>
<tr>
<td>IgA</td>
<td>1.2</td>
<td>1.03</td>
<td>0.76-1.7</td>
</tr>
<tr>
<td>IgM</td>
<td>1.9</td>
<td>0.89</td>
<td>1.3-1.7</td>
</tr>
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</table>

Association of Ig levels with SSc subtype and SOS were assessed with one way analysis of variance (ANOVA) & a receiver operating characteristic curve was generated for the significant result.
Is about retrospective study on the review of patients’ restrictive cardiomyopathy (2), pulmonary hypertension complicated with right heart failure (2), pseudo- obstruction (2) at the origin of a syndrome of severe dyspnea during physical and emotional effort, observed in 8 patients complicating by ulcerations (3) and stenosis (2). We observed 4 amputations (2), calcinosis (4). The systemic manifestations are dominated by Raynaud’s phenomenon (3), a sclerodactyly (5), cutaneous ulcerations (7) ischemic digital necrosis (1), a silicosis exposure (1) and a tymectomy for myasthenia (1). The cutaneous involvement is an almost universal manifestation. Skin changes include non-pitting oedema, sclerosis, telangiectasias and hypo and hyperpigmentation (known commonly as “Salt and Pepper skin” or pseudovitiligo) and the accompaniment of pruritus.

Aim. To analyze clinical profile of the systemic sclerosis (SSc) observed in male patients.

Patients and Methods. Is about retrospective study on the review of patients’ cases observed in specialized consultation and hospital stay in an internal medicine department from January, 1997 till December, 2011. All patients SSc referred to the ACR criteria and appropriate investigations allowing the data analysis. Results. 150 patients on a troop of 117 patients (12%); the average age is of 31.2 years, range (19.5-59). The diagnosis delay is established about 15.2 months. It is about 50% of patients in the first 5 years (30% in the first 5 years; 20% in the first 10 years; 10% in the first 15 years). The mean delay of diagnosis is 17.5 months. The mean duration of disease is 150 months. The male SSc is rare (12%) and sever with high mortality (26%). The diffuse restrictive lung disease is the dominant manifestation. The cardiovascular causes constitute the second cause of morbi-mortality and appears mostly associated to an embolic event. The associated autoimmune diseases are various and often infra-clinical so its justify to be detected by the appropriate investigations (biological, morphological, histological explorations...).

There is a significant association between the presence of salt and pepper skin and cirrhosis, SSc subtype was assessed using the chi-squared test (or Fisher’s exact test where numbers were small). Student’s t-test was used for between group comparison of mean mRSS. No association was found between pruritus or salt and pepper changes and the skin pigmentation with SSc subtype was assessed using the chi-squared test (or Fisher’s exact test where numbers were small). Student’s t-test was used for between group comparison of mean mRSS.

Results. Demographics: 87 patients were reviewed as in the table below. Salt and Pepper Skin and SSc Subtypes: Presence of salt and pepper skin changes was associated with dcSSc subtype, X2=47.9, p=0.001 with the positive likelihood ratio of 8.83 (PPV 74.0%; NPV 96.5%). In addition, the presence of salt and pepper skin changes was also associated significantly with pruritus, X2=9.07, p=0.004.

Conclusion. There is a significant association between the presence of salt and pepper skin and cirrhosis, SSc subtype and pruritus. The presence of pruritus is associated with higher mean mRSS. There was no gender differences noted in these respect.

Table.

<table>
<thead>
<tr>
<th>Subtype</th>
<th>Females (Mean age, SD)</th>
<th>Males (Mean age, SD)</th>
<th>Subtotal</th>
</tr>
</thead>
<tbody>
<tr>
<td>lcSSc (mean age 58.80 yrs)</td>
<td>58 (58.9, 12.8)</td>
<td>6 (58, 14.7)</td>
<td>64</td>
</tr>
<tr>
<td>dcSSc (mean age 33.74 yrs)</td>
<td>19 (54.3, 10.9)</td>
<td>4 (48.8, 18.2)</td>
<td>22</td>
</tr>
<tr>
<td>Total</td>
<td>77</td>
<td>10</td>
<td>87</td>
</tr>
</tbody>
</table>
The frequency of abnormal electrophysiological findings was 63%. The frequency of polyneuropathy (defined as abnormality in 2 or more nerves) was 52%. The skin involvement evaluated by modified Rodnan skin score was highly variable between SSc patients with or without PN (p=0.05). No significant differences were found for the distribution of age, disease duration, autoantibody profile, estimated sPAP, hemoglobin and creatinine levels between SSc patients with or without PN. Severity of joint/tendon involvement was different between SSc patients with or without PN (p=0.02). Activity score according to Valentini was higher in SSc patients with PN than in the SSc patients without (p<0.05). The prevalence of PN is relatively high in SSc and occurs more frequently in patients with greater skin and joint/tendon involvement and high disease activity. Larger, prospective studies using the more sensitive tools as well as pathologic studies of nerve, including cutaneous innervation, are needed to further assess the characteristics and etiology of the neuropathy in SSc.
PS308

JOINT INVOLVEMENT IN SYSTEMIC SCLEROSIS AND ITS RELATIONSHIP WITH AUTOANTIBODY TO ANTI-CYClical CITRULLINATED PEPTIDE

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Introduction. The presence of anti-cyclic citrullinated peptide antibodies (anti-CCP) has a high specificity for the diagnosis of rheumatoid arthritis (RA). Different cross-sectional studies estimated the point prevalence of anti-CCP antibodies in patients with systemic sclerosis (SSc), which ranged from 1% to 15%.

Objectives. To investigate joint involvement in SSc and its relationship with autoantibody to anti-cyclic citrullinated peptide.

Patients and Methods. One hundred fifty (150) patients attending the rheumatology department at Ben Aknoun Hospital, as part of a prospective study and fulfilling the ACR and/or LEOPR and Medger criteria for systemic sclerosis were evaluated. Joint involvement was determined by clinical, radiological and ultrasound examination. All autoantibody analyses were performed in the Lab of Beni Messous hospital. The presence of anti-CCP IgG was evaluated with commercially available enzyme-linked immunosorbent assay (ELISA) kit. The test was used following the procedures suggested by the manufacturer. The samples were classified as negative (<5 units), positive (≥5 units).

Results. The analysis of results was performed by the Epidata database. The presence of anti-CCP was not associated with clinical, radiological and ultrasound examination. Positive anti-CCP was found in only 7% of patients. The presence of anti-CCP was found in sera of 9.4%.

Conclusion. Anti-CCP was positive in 16.5% patients with arthritis and in 4.5% patients without arthritis (p=0.01). Anti-CCP was positive in 33.3% of patients with erosive arthritis and in 7.7% of patients without erosive arthritis (p=0.01), in 71.4% of patients with overlap syndrome SSc-RA (p=0.05).

A statistically significant association was found between anti-CCP positivity and the presence of arthritis (p=0.01), erosive arthritis (p=0.01) and overlap syndrome (p<0.05). High titres of anti-CCP antibodies were found in patients having an overlap syndrome SSc–RA. The presence of anti-CCP antibodies was not associated with intestinal lung disease and pulmonary arterial hypertension.

Conclusion. Anti-CCP antibodies were associated with the presence of arthritis, erosive arthritis and overlap syndrome. The finding of high titres of anti-CCP antibodies may help to define the diagnosis of overlap syndrome SSc–RA.

PS309

22 YEARS EXPERIENCE OF PATIENTS WITH SYSTEMIC SCLEROSIS ON HOME PARENTERAL NUTRITION

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Introduction. Patients with systemic sclerosis (SSc) may develop significant gastrointestinal involvement (GI). When severe, this can lead to intestinal failure (IF) requiring home parenteral nutrition (HPN). However, few outcome data are reported for these patients.

Objective. To review the characteristics and outcomes of all patients with SSc who had received HPN.

Methods. Records were reviewed of all patients with SSc who required HPN, at a national IF centre, between 1990 and 2012. Disease characteristics and survival/outcome data were evaluated.

Results. 25 patients (5 male, median age: 55 (range 24-76) with SSc received HPN (37,200 catheter days). Mean time from SSc onset to HPN was 113 months (range 14-393). All had small intestinal involvement. 80% had proven bacterial overgrowth. 44% had experienced at least one episode of pseudo-obstruction. 16% had a small intestinal resection.

Prior to HPN initiation, 6 patients failed a naso-enteric feeding trial. 10 patients had a gastro-intestinal tract (GIT) requirement. 7 of 10 received enteral feeding for less than 1 year. The remaining 9 patients commenced HPN directly, without enteral tube feeding, because of the severity of their dysmotility/associated co-morbidity.

Only 2 patients were weaned off HPN (after 8 and 29 months) following successful medical optimisation. After 1 year, median body mass index rose from 18.5 to 21.3.

3 patients received HPN for more than 10 years. The cumulative survival on HPN after 1, 5, and 10 years were 75%, 37% and 23% respectively.

No patients died from HPN-related complications. 16 died from causes related to their SSc. 1 died from malignancy. 8 patients survive, 7 of whom remain on HPN (median duration: 40 months, range 9-178).

9 patients were trained to manage their central venous catheters and self-administer HPN. 16 patients relied on others for their HPN administration. Reported catheter complications included non-thrombotic occlusion (0.7/1,000 catheter days), sepsis (0.19/1,000 catheter days) and central venous thrombosis (0.11/1,000 catheter days). The sepsis rate for all HPN patients, at the same IF centre, is 0.39/1,000 catheter days. No one developed IF-associated liver disease.

Conclusion. The largest reported series of patients with SSc requiring HPN, which is life-saving in patients with severe bowel involvement. Our data shows that HPN offers a safe means of nutritional support for patients with severe SSc-related GI involvement, but that SSc-related mortality remains high. Patients with SSc had a low catheter-related sepsis rate. Additionally, the majority relied on others for their catheter care.
**IC SCLEROSIS**

**PS312**

**OBESETY: A NEW ASPECT OF MALNUTRITION IN SYSTEMIC SCLEROSIS**

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**Objective.** Systemic Sclerosis (SSc) is a rare connective tissue disease characterized by small vessel vasculopathy, autoantibody production and excessive collagen deposition in the skin and internal organs.

Demunition is present in SSc patients from 15% to 56%, according to the diagnostic method; many factors may contribute to the development of nutritional impairment, including gastrointestinal involvement and psychobehavioral aspects. The aim of this study is to evaluate the prevalence of malnutrition in a cohort of SSc patients and to identify subgroups at elevated risk for disease progression.

**Methods.** 93 SSc patients were enrolled at Day Hospital of San Luigi Hospital (TO). Nutritional status was assessed by a combination of anthropometric, biochemical parameters and specific scores as MUST (Malnutrition Universal Screening Tool), INM (Intraluminal Nutritional Assessment), NRI (Nutritional Risk Index), MI (Maastricht Index). Food intake was assessed by a 24-h recall.

**Results.** Overall, BMI (Body Mass Index) ranked 10 patients (11%) as underweight and 44 (47%) as overweight/obese. These conditions were not associated to the main clinical characteristics.

The nutritional tools identified 18-60% of patients at high risk of malnutrition: 18% using MUST, 31% INM, 60% NRI, 39% MI. None of the score was associated to the main disease characteristics, gastrointestinal involvement included. Moreover, NIN, NRI and MI ranked patients as malnourished and did not show significant differences in BMI values. All the six patients affected by pulmonary hypertension were identified as malnourished, as the patients with ulcer by INM.

Biochemical parameters did not show any significant difference across the groups, except for haemoglobin and B vitamin, despite being in normality range.

**Conclusion.** The risk of malnutrition in SSc is high-moderate, particularly evaluating this shape in its wider meaning. It appears as not associated to disease activity, gastrointestinal involvement, psychobehavioral aspects or nutritional intake. Patients affected by ulcers or pulmonary hypertension could be at high risk, but further studies are needed to define this association. Our results show that, contrary to what we thought, a high proportion of patients are obese, according to BMI growth pattern of Italian population. Obesity increases the risk of cardiovascular disease in healthy subjects. SSc patients have an increased risk for cardiovascular disease, likely due to inflammatory and fibrotic mechanisms affecting the macrovasculature and microvasculature. Obesity, in this population, could be an aggravating element which worths to be corrected.
PS314

ESOPHAGEAL ABNORMALITIES IN VERY EARLY SYSTEMIC SCLEROSIS: A CASE SERIES

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Introduction. The esophagus is affected in up to 90% of patients with systemic sclerosis (SS), and generates symptoms in half of them. Alterations of esophageal motility and lower esophageal sphincter hypotonicity trigger gastroesophageal reflux disease (GERD) that is more severe than in patients without SS, and has been related to lung disease.

Objective. To determine if esophageal abnormalities are present in patients with very early systemic sclerosis (VESS).

Methods. We retrospectively analyzed 17 patients with SS. Clinical features, high-resolution esophageal manometry (HREM), barium esophagogram (BE), esophagogastrroduodenoscopy (EGD), serum antibodies, pulmonary function tests and high-resolution CT scans (HRCT) were analyzed. Patients with VESS were analyzed separately and compared with patients with limited systemic sclerosis (LSS) and sine scleroderma systemic sclerosis. (sSSc).

Results. Four patients with VESS were identified. All were asymptomatic and had normal EGD. Only 1 had evidence of gastroesophageal reflux on BE. However the HREM showed lower esophageal sphincter hypotonicity (HLES) in 3 of them (3/4), one of which also had weak peristaltic waves with large peristaltic defect (WPWLd). HRCT showed no esophageal dilatation, air-fluid level of pulmonary infiltrates in this group.

Interstial lung infiltrates 0/4 0 11/13 84.6 0.006
Fluid level in Esophagus 0/4 0 6/13 46.1 ns 0.237
Esophageal dilatation HRCT 0/4 0 12/13 92.3 0.002
GER on BE 1/4 25 8/10 80 0.005

Conclusion. Despite a small number of patients, the VESS group seems to have asymptomatic esophageal involvement, and poor evidence of alterations in UDE and BE. The HREM seems to be more adequate to detect early esophageal alterations. This group could not show structural alterations in the esophagus at the EGD and HRCT whereas in SSL/SESS are more prevalent clinical findings due to esophageal muscles dysfunction and structural alterations.

Discussion. Comparing the VESS group with SSL/SESS group these patients seems to have asymptomatic esophageal involvement, and poor evidence of alterations in UDE and BE. The HREM seems to be more adequate to detect early esophageal alterations. This group could not show structural alterations in the esophagus at the EGD and HRCT whereas in SSL/SESS are more prevalent clinical findings due to esophageal muscles dysfunction and structural alterations.

Table I. Results.

<table>
<thead>
<tr>
<th>VESS Group</th>
<th>LSS/SSSS</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients / N</td>
<td>%</td>
<td>Patients / N</td>
</tr>
<tr>
<td>Female</td>
<td>4/4</td>
<td>12/13</td>
</tr>
<tr>
<td>Age (years)</td>
<td>61 (43-69)</td>
<td>50 (28-73)</td>
</tr>
<tr>
<td>Time of disease (years)*</td>
<td>1</td>
<td>9.5 (3.6-15.5)</td>
</tr>
<tr>
<td>Symptoms of GERD</td>
<td>0/4</td>
<td>13/13</td>
</tr>
<tr>
<td>GER on BE</td>
<td>1/4</td>
<td>25</td>
</tr>
<tr>
<td>Abnormal EGD</td>
<td>0/3</td>
<td>0</td>
</tr>
<tr>
<td>Altered HRCT</td>
<td>3/4</td>
<td>75</td>
</tr>
<tr>
<td>Esophageal dilatation HRCT</td>
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<td>0</td>
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<td>Fluid level in Esophagus</td>
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<td>0</td>
</tr>
<tr>
<td>Interstitial lung infiltrates</td>
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</tr>
</tbody>
</table>

Fisher exact test for categorical variables and U-Mann-Whitney for continuous variables.

*Mean (95% Confidence Interval; GERD: gastroesophageal reflux disease; BE: barium esophagogram; EGD: esophagogastrroduodenoscopy; HREM: high-resolution esophageal manometry; HRCT: high-resolution CT scans.

PS315

SMALL INTESTINAL BACTERIAL OVERGROWTH IN PATIENTS WITH SYSTEMIC SCLEROSIS, CLINICAL DATA RELEVANCE

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Background. Gastrointestinal involvement is frequent in systemic sclerosis (SSc), occurring in 75 to 90% of patients with diffuse or limited cutaneous SSc. Small bowel involvement in SSc occurs in 17 to 57% of patients. The intestinal migrating motor complexes are reduced or absent, predisposing to small intestinal bacterial overgrowth (SIBO). Malabsorption syndrome is related to SIBO. The aim of the study was to investigate frequency of SIBO in relevance with age, of SSc onset, organ manifestation and disease classification.

Methods. 37 (9 male, age range 57-77 years, median 61 years) patients with SSc were examined. SSc patients, according ACR criteria, underwent hydrogen breath testing. After 12 hours fasting end-expiratory air was collected by means of QUNTRON GaSampler two-bag system with T-value (Quinton Instrument Company, Milwaukee, WI, USA). After collection of baseline sample, patient ingested substrate (75g of glucose of 10g of lactulose) and subsequent samples were collected in 20 minutes intervals for a total of 4 hours. Breath samples were analyzed by special gas chromatograph QUNTRON Microlyzer DP Plus (Quinton Instrument Company, Milwaukee, WI, USA). Data on type and severity of scleroderma involvement, actual medication, TLCO, echocardiography, weight loss were recorded.

Results. 14 (37.8%) patients have positive SIBO test. Patients with SSc had higher age p<0.037, time of onset of first SSc symptom (p<0.05) using T-test. There was no significant difference between the scleroderma type, frequency of pulmonary arterial hypertension, digital ulcers, Rodnan skin score. Patients with SSc had a significantly high frequency of TLCO decrease (p<0.005).

Conclusion. The SIBO is frequent finding in SSc. The results of this study suggest that SIBO in SSc patients is associated with age, disease duration and interstitial lung disease. These findings should be of interest to clinician and investigator alike.

PS316

SYSTEMATIC EVALUATION OF ESOPHAGEAL AND ANORECTAL DAMAGE IN SYSTEMIC SCLEROSIS: PRELIMINARY RESULTS

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Introduction. Esophageal and anorectal damages are common in scleroderma and are often associated. Since 2008, Health French High Authority made recommendations and suggested the creation of functional tests based on symptoms (1). However, in clinical practice, it seems that if the esophageal examination is regularly prescribed, anorectal evaluation is rarely offered. In the literature, when lower gastro-intestinal abnormalities is documented, an esophageal concomitant disease is always described (2, 3). Nevertheless, this involvement was often unrecognized and unexplored so that early detection of anorectal disorders in these patients could prevent the occurrence of pelvic floor disorders and disabling symptoms. The main purpose of our study is to systematically detect esophageal and anorectal damage in scleroderma by high resolution esophageal manometry (MOHR) and anorectal high resolution three-dimensional manometry (MHR3D).

Patients and Methods: All patients followed for systemic scleroderma or CREST syndrome in one department of internal medicine of the University Hospital of Marseille were included. Symptomatic and quality of life self-administering questionnaires have been given and a 10 and a limited damage (CREST syndrome). Combined high and low manometric dysfunction was found in 6 patients : 5 with symptoms of both high (4 Gastroesophageal reflux disease (GERD) and dysphagia, only one GERD ) and low (3 constipation and incontinence, 1 incontinence alone, 1 constipation alone) and 1 asymptomatic patient. Quality of life (physical
and mental) of 2 symptomatic patients was impaired. An isolated esophageal manometric dysfunction was found in 4 patients with 3 symptomatic (1 GERD and dysphagia, 2 GERD only). Of these 3 patients, two reported an alteration of the overall quality of life. On immunological results, 4 patients had anti-Scl 70 and 13 patients anti-centromere B positive profile.

**Conclusion.** These preliminary results confirm that the anorectal disease appears closely linked to esophageal involvement. Its screening, as for the esophageal damage, appears necessary to limit the occurrence of disabling symptoms such as fecal incontinence.

**PS317**

**TRANSLATION, CROSS-CULTURAL ADAPTATION, AND VALIDATION OF THE UNIVERSITY OF CALIFORNIA, LOS ANGELES SCLERODERMA CLINICAL TRIAL CONSORTIUM GASTROINTESTINAL TRACT INSTRUMENT 2.0 INTO THE DUTCH LANGUAGE**

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**Objective.** To translate and adapt the University of California, Los Angeles Scleroderma Clinical Trial Consortium Gastrointestinal Tract Instrument 2.0 (UCLA SCTC GIT 2.0) into Dutch and validate it among Dutch systemic sclerosis (SSc) patients.

**Methods.** First, the UCLA SCTC GIT 2.0 questionnaire was translated and adapted according to international guidelines. The resulting Dutch GIT 2.0 was, in combination with the SSc Health Assessment Questionnaire (SHAQ) and Short Form-36 (SF-36) administered to SSc patients participating in a standard medical examination. The frequency of GIT symptoms in SSc patients and confirmed medical diagnoses related to GIT were extracted from the medical records. Internal consistency was determined by calculating Cronbach’s alpha. To determine the reliability, the questionnaire was re-administered with an interval of two weeks to a subgroup of patients and the intraclass-correlation coefficient (ICC) was computed. Spearman correlation coefficients between GIT scores, SF-36 and SHAQ were computed. GIT scores were compared among patients with and without previous gastrointestinal examinations and/or diagnoses.

**Results.** Eighty-nine patients with a mean age of 53.6 (SD 12) years, and predominantly female (76%) were included. The median total GIT score was 0.17 (Cronbach’s alpha 0.921). The test-retest reliability of the total GIT score was good (ICC 0.749). Overall, the GIT total scores correlated significantly with the SHAQ visual analogue scale intestinal complaints and the SF-36. Significant differences between GIT total and subscale scores of patients with and without previous gastrointestinal examinations and diagnoses were present.

**Conclusion.** The Dutch GIT 2.0 questionnaire showed good internal consistency, construct validity and test-retest reliability.

**PS318**

**GIT MANIFESTATIONS OF SYSTEMIC SCLEROSIS AS THE MOST FREQUENT. IS IT THE MOST IRRITANT TOO?**

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**Introduction.** Gastrointestinal (GIT) manifestation of scleroderma (SSc) is a common complication, with major impact on quality of life and morbidity, (UCLA) Scleroderma Clinical Trial Consortium GI Tract Instrument (UCLA SCTC GITI) was developed to measure gastrointestinal tract disease in SSc. Patients and Methods. Twenty eight patients of (SSc) recruited from two rheumatology clinics in Sohag and Assut university hospitals, all patients completed UCLA SCTC GITI, a self-administered questionnaire with 7 scales and an overall quality of life. On immunological results, 4 patients had anti-Scl 70 and 13 patients anti-centromere B positive profile.

**Results.** Twenty female and 8 male patients, with mean disease duration 9.3 years, mean age 46 years, 19 patients were dcSSc, and 9 patients were lcSSc. Mean questionnaire scores showed that patients have a wide range of GI symptoms, 85.7% of patients reported upper and 75% lower GI symptoms, and 3.57 % of patients reported no symptoms. There was no association between disease subtype and GI symptoms.

With reclassification of the patients’ symptoms under the UCLA SCTC GITI to “Non- to Mild”, “Moderate” and “Severe-to- Very severe”, 78.6 % were reported as severe to very severe category, 14% were mild, while 7% were non to mild symptoms, these reports showed positive correlation with the barium swallow and upper endoscopy.

**Conclusion.** The frequency of GIT symptoms in SSc patients whether upper or lower is high. UCLA SCTC GITI focused questionnaire is an effective way to assess not only gut symptoms but also severity of the gut involvement.

**PS319**

**CHARACTERIZATION OF SYSTEMIC SCLEROSIS PATIENTS FOLLOWED IN A SYSTEMIC IMMUNE MEDIATED DISEASES CLINIC - 4 YEAR RETROSPECTIVE ANALYSIS**

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**Background.** Systemic sclerosis (SSc) is a rare autoimmune disease, characterized by fibrosis of skin and internal organs and obliterator vasculopathy.

**Aim.** To characterize patients with SSc in a systemic immune mediated diseases clinic.

**Methods.** Retrospective analysis of patients with SSc, followed in our clinic, between June 2009 and November 2013.

**Results.** Forty patients were identified (37 female, 3 male), mean age of 52 (±15) years. The mean disease duration was 10 (±11) years, and the mean age of Raynaud’s Phenomenon (RP) beginning was 43 (±23) years. 9 patients had diffuse SSc, 9 limited SSc, 9 mixed connective tissue disease (MCTD), 8 overlap syndrome, 3 very early SSC, 1 SSC sine scleroderma and 1 CREST syndrome. 87% fulfilled the ACR/EULAR 2013 criteria. 92.5% were ANA positive, 35% anti-centromere positive, 25.7% anti-U1-RNP positive and 20.6% anti-Scl70 positive. RP was the first clinical manifestation in 65% of the patients, followed by polyarthrosis in 25%. Peripheral vascular involvement was frequent: 82.5% with RP, 37.5% with digital ulcers (DU) - active DU in 1 patient. Nailfold capillaroscopy revealed an early pattern in 26% of the patients, an active pattern in 25%. Follow-up data were often a late pattern in 24% (patients with a late pattern had a prolonged mean disease and RP duration compared to the early pattern). Cutaneous involvement was limited in 42.5% and diffuse in 25%. Gastrointestinal involvement was frequent with 57.5% of the patients with oesophageal dysmotility. 45% had interstitial lung disease (ILD) on high resolution thoracic scan (67% usual interstitial pneumonia pattern and 33% non-specific interstitial pneumonia pattern). 35% had a decrease in diffusing capacity of carbon monoxide, in lung function tests. According to the scoring system proposed by Wells for evaluation of ILD in SSC, 67% had a limited disease and 33% an extensive disease. 17% had pulmonary hypertension (evaluated by pulmonary artery pressure on echocardiogram), 30% of them with MCTD. 2 patients had scleroderma renal crisis. The preferred immunosuppressor strategies were cyclophosphamide (30%), methotrexate (23%), azathioprine (20%) and biologics (13% - 3 tocilizumab, 2 rituximab). The most used vasodilator therapies were calcium channel blockers (34%), endothelin receptor antagonists (20%) and prostacyclin analogs (15%).

**Conclusions.** Our patients had a high prevalence of vascular involvement and ILD, which explains the high percentage of treatment with cyclophosphamide and endothelin receptor antagonists. Both capillaroscopy and Wells scoring system for ILD in SSc were useful for a better characterization of the disease. We also highlight the significant percentage of patients under biologic therapeutics.

**PS320**

**CHARACTERIZATION OF INTERSTITIAL LUNG DISEASE IN A COHORT OF SYSTEMIC SCLEROSIS PATIENTS - 4 YEAR FOLLOW-UP DATA**

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**Background.** Interstitial lung disease (ILD) is a frequent manifestation of systemic sclerosis (SSc), associated with significant morbidity and mortality. Its early recognition and intervention in clinical practice, whether defining its presence or ascertaining its severity, is still not standardized.

**Objectives.** To characterize interstitial lung disease in SSc patients.

**Methods.** SSc patients with interstitial lung disease followed in our clinic for a 4 year period of time were retrospectively analyzed.

**Results.** Forty subjects were included, with mean age of 53±16 years and mean duration of disease since first manifestation of SSc of 9±10.3 years. Of these, 9 had mixed connective tissue disease (MCTD) and 8 had an overlap syndrome. 18
was unable to block fibroblast activation at a concentration of 0.04 μg/ml. The concentration (2.5 μg/ml). Imatinib mesylates was less efficient than dasatinib and the lowest concentration dasatinib tested (0.04 μg/ml) inhibited PDGF-BB-induced activation, with the exception of anti-centromere (ILD in 10%). There were no differences in the mean disease duration between those with and without ILD, neither between those with limited and extensive disease.

**Conclusions.** In this cohort, there was a relevant proportion of patients with ILD and no changes in lung volumes on PFT. In order to rigorously evaluate lung involvement, semi-quantitative methods, such as the one used, are practical and effective. NSIP pattern in LCT seems to be associated with a less extensive disease and to MCTD. Mean duration of disease does not seem to be associated with ILD or its severity.

**PS321**

**THE TYROSINE KINASE INHIBITOR DASATINIB EFFICIENTLY BLOCKS PDGF-INDUCED ORBITAL FIBROBLAST ACTIVATION: A POTENTIAL NOVEL THERAPEUTIC AGENT IN FIBROTIC DISEASE?**

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Fibrosis is a leading cause of morbidity and mortality in the Western World. The hallmark of fibrosis is abnormal and exaggerated fibroblast proliferation and deposition of extracellular matrix components. In Graves’ disease (GD), autoantibodies directed against the thyroid stimulating hormone receptor activate the thyroid gland, resulting in hyperthyroidism. The orbital tissues are frequently affected in GD, referred to as Graves’ Orbitopathy (GO). Excessive orbital fibroblast activity, driven by locally produced platelet-derived growth factor (PDGF), plays a central role in GO which is similar to fibrotic diseases involving other organ systems such as idiopathic pulmonary fibrosis and systemic sclerosis. So far, treatment options are limited. The effects of small-molecule tyrosine kinase inhibitors (TKIs) imatinib mesylate and nilotinib to block aberrant tyrosine kinase activity in fibrotic disease models have been explored by researchers, including ourselves. However, results were variable and these compounds are associated with adverse effects like peri-orbital edema and peripheral artery occlusion. The second-generation TKI dasatinib displays a higher IC50 for the PDGF receptor and ABL tyrosine kinases and may therefore be a more promising compound. The aim of this study is to compare the pro-fiblastic and therapeutic effect of imatinib mesylate and dasatinib on PDGF-BB-induced proliferation, hyaluronan, IL-6, IL-8 and CCL2 production by orbital fibroblasts. Orbital fibroblasts were obtained from orbital tissue of four GO patients and five healthy controls. Pro-fiblastic effect was evaluated by overnight pre-incubation with TKI before PDGF-BB (50 ng/ml) stimulation for 24 hours, while TKI was added together with PDGF-BB for estimation of therapeutic effects. Proliferation was assessed by colorimetric assay, and hyaluronan and cytokine production were measured by ELISA. Dasatinib dose-dependently inhibited PDGF-BB-induced orbital fibroblast proliferation, hyaluronan, and cytokine production much more efficiently than imatinib mesylate in the pro-fiblastic setting, reaching statistical significance from a concentration of 0.04 μg/ml. Under therapeutic conditions, lowest concentration dasatinib tested (0.04 μg/ml) inhibited PDGF-BB-induced orbital fibroblast activation as efficient as in the pro-fiblastic condition, with the exception of IL-8 production that was only reduced at the higher dasatinib concentration (2.5 μg/ml). Imatinib mesylates was less efficient than dasatinib and was unable to block fibroblast activation at a concentration of 0.04 μg/ml. The strong anti-fibrotic effects of dasatinib in our study may provide a basis for its introduction in treatment of GO and its clinical implications may be extended to other fibrotic diseases as well. Further clinical studies are warranted to evaluate its potential clinical effects.

**PS322**

**UPDATE ON THE JUVENILE SYSTEMIC SCLEROSIS INCEPTION COHORT. WWW.JUVENILESCLERODERMA.COM**

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**Background.** Juvenile systemic sclerosis (jSSc) is an orphan autoimmune disease. Currently just retrospective data is existing without a standardized assessment of the organ involvement. Our project is the first projects, where prospectively and with a standardized assessment data of early jSSc patients are collected.

**Objectives.** To learn about the evolution of juvenile systemic sclerosis.

**Methods.** Patients with less than 18 months of disease duration, after the first Non-Raynaud symptomatic, are prospectively assessed, using the proposed standardized patient assessment protocol.

**Results.** Up to now 23 patients were enrolled, the mean follow up of the patients in the cohort are 3 months. Seventeen of the 23 patients were female. The mean age at the onset of Raynaud symptom was 11.1 years, the youngest 4.2 years old. The mean age at the onset of the non-Raynaud symptomatic was 11.6 years. 15 of the 22 have diffuse subtype, 5 of them have an overlap symptomatic. At the time of the inclusion the mean modified Rodnan Skin Score was 19.9, ANA positive were 19, and 6 of them were anti-Scl 70 positive. None of them was anticentromere positive. 19 of them have Raynaud’s, 15 of them have capillary changes and 7 of them already ulcerations.12 of them have cardiopulmonary involvement, 10 of them have interstitial lung disease. Two of them have renal involvement. Eight of them have gastrointestinal involvement, and 5 of them oesophageal involvement. Nineteen of them have musculoskeletal involvement.

**Conclusion.** We present the data on the first 23 prospectively assessed patients with jSSc. The current recruitment data confirms that pediatric patients are different from the adult patients. We are only at the first phase of this project and hope to recruit up to 50 patients and follow them prospectively over the next 5 years at least.

**PS323**

**SYSTEMIC SCLEROSIS IN OVERLAP WITH RHEUMATOID ARTHRITIS: A RATHER FREQUENT ASSOCIATION IN SCLERODERMA PATIENTS**

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**Background.** Patients with systemic sclerosis (SSc) may sometimes simultaneously have consistent disease features of another connective tissue disease (CTD). These patients may represent disease subsets with distinct prognosis and management options. Musculoskeletal symptoms are a common complaint in SSc patients and the existence of a SSc overlap with rheumatoid arthritis (RA) has been cited in the literature. Our aim was to define in a cross-sectional study the clinical particularities of patients with SSc who also satisfy classification criteria for RA.

**Methods.** In a single-center cohort of patients with SSc, as defined by the 1980 ACR classification criteria or SSc we identified 11 subjects (9%) also satisfying the 1988 ACR classification criteria or SSc we identified 11 subjects (9%) also satisfying the 1988 ACR classification criteria. Those patients who identified in the literature. We present the data on the first 23 prospectively assessed patients with jSSc. The current recruitment data confirms that pediatric patients are different from the adult patients. We are only at the first phase of this project and hope to recruit up to 50 patients and follow them prospectively over the next 5 years at least.
less skin involvement as assessed by the modified Rodnan skin score (4.2±6.3 vs. 11.4±8.9 in controls), greater musculoskeletal involvement including higher tender and swollen joint counts, and more severe hand involvement as shown by higher finger contracture counts (9.3±6.5 vs. 5.3±6.0) and higher finger-to-palm distance on maximal finger flexion (28±23 vs. 13±15 mm), all p<0.01 by Mann-Whitney U test. There was a tendency towards lower prevalence of the SSC diffuse cutaneous subset and less peripheral vascular involvement (telangiectasiae, digital ulcers, digital scars) in SSC-RA overlap patients vs. SSC patients, without reaching statistical significance. Demographic data, intestinal lung disease and SSC-associated GI involvement were similar between groups. Methotrexate treatment was significantly more frequent in SSC-RA patients (54.5% vs. 5.7%, p<0.01 by Fisher's exact test).

Conclusion. Patients with SSC-RA overlap may have milder skin fibrosis, less vascular involvement but more severe hand musculoskeletal damage than patients with SSC who do not satisfy RA classification criteria. These findings should be confirmed on a larger SSC cohort.

PS324
EVOLUTION OF SYSTEMIC SCLEROSIS OVERLAP SYNDROME
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Objective. To study evolution and outcome of SSC-RA and SSC-PM/DM.

Material and methods. There were 100 pts SSC overlap syndrome: 68 SSC-PM/DM and 32 SSC-RA (17 male, 83 female; mean age 45±14.4; disease duration 2-10 years; follow-up 10 years).

Results. 71% pts has had SSC-PM/DM and SSC-RA within the first three years of disease and in 40% of them during the 1st year after onset. The first symptoms of pts were Raynaud's syndrome, edema hands, arthralgia and rare isolated joint and musculoskeletal involvement (7% and 2%). All pts were treated corticosteroids and 74% of them received cytotoxic (methotrexate 48%; cyclophosphamide 10%; azathioprine 5%), hydroxychloroquine 11%, D-penicillamine 7%.

Identified two variants of evolution: I- favorable 79%; II unfavorable 21% (include deaths 10%). The favorable evolution was observed in pts with onset before 40 years, the relative stabilization of the process - from the onset of the disease before the age of 25 years, an unfavorable outcome - in pts with age of onset of the disease for more than 40 years, where pts SSC-PM/DM prevailed.

The peripheral symptoms SSC-RA has not progressed for 10 years and has decreased: skin induration (ISSc/dSSc 97%/3% and 100%/0%), hyperpigmentation (34% and 9%), flexion contractures (81% and 72%), arthritis (100% and 78%), rheumatoid nodules disappeared. Rainaud's syndrome was less expressed. However, clinical features SSC increased: telangiectasias (37.5% and 47%), calcinosis (31% and 47%), ostosclerosis (25% and 28%), conduction blocks (53% and 56%) and arrhythmia (9% and 19%), interstitial lung disease (9% and 19%), esophageal involvement (66% and 69%). Decrease of ESR was observed in 1/3 of pts.

The SSC-PM/DM pts has decreased skin induration (lSSc/dSSc 68%/32% and 100%/0%), hyperpigmentation (15% and 18%), interstitial lung disease (12% and 15%), increased telangiectasias (50% and 59%), calcinosis (32% and 56%), ostosclerosis (23.3% and 26%), conduction blocks (53% and 57%) and arrhythmia (15% and 18%), interstitial lung disease (12% and 15%), esophageal involvement (78% and 88%). Decrease of ESR was observed in 2/3 of pts.

Conclusion. Adverse prognostic factors of SSC overlap syndrome: age of onset after 40 years, rapidly progressive acute with generalization of the process and features of the PM in the first year of the disease, late diagnosis of the disease and inadequate therapy.

PS325
ASSOCIATION BETWEEN SYSTEMIC SCLEROSIS AND SJÖGREN'S SYNDROME
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Background. Systemic Sclerosis (SSc) is an autoimmune disease characterized by vasculopathy, inflammation, and fibrosis that can lead to loss of organ function. It is frequently associated to other autoimmune disease. This present report aims to describe the clinical presentation, immunological features and outcome of patients with the association SSc and Sjögren's syndrome (SS).

Patients and methods. We retrospectively investigated 102 patients with SSc and 133 patients with SS hospitalized in our internal medicine department from 2000 to 2012. All patients fulfilled ACR criteria for SSc and the American-European Consensus Group criteria for SS. Only patients with the 2 diagnoses were included. Demographic, clinical and serologic characteristics were analyzed.

Results. We identified 15 women with SSc and SS. The mean age of onset of SSc and SS was respectively 53.6 years (range:29-74) and 54 years (range:29-74). Diagnosis of SSc was prior to SS in 8 cases (53.3%), they were concomitant in 4 patients. Thirteen patients were classified as diffuse SSc and 2 others as limited SSC. All patients had sicca syndrome (xerophthalmia et xerostomia). Grade 3 or 4 sialoadenitis was detected in all patients. Raynaud’s phenomenon was constant and giant capillaries were noted in 9 patients. Only 3 patients had digital ulcers. Rheumatologic involvements were as follows: arthralgia (n=11), arthritis (n=1), calcinosis (n=1). Electromyogram showed myositis in 3 patients and peripheral neuropathy in 3 others. Interstitial lung disease was found in 8 patients with a decreased forced vital capacity in 5 of them. Cardiac ultrasonography showed pulmonary arterial hypertension in 2 patients and pericardial effusion in 1 case. All patients were positive for AAN [ACA (n=7), ScI70 (n=4), SSA (n=6), SSB (n=3)]. All autoimmune diseases were found in 3 diffuse and 2 limited cases. The outcome was favorable in 7 cases; while we noted stabilization in 4 and improvement in 2. Two patients were lost to follow-up.

Conclusion. SSc and SS are connective tissue disorders with different pathogenic mechanisms. However, they have several common manifestations, particularly sicca syndrome, rheumatologic involvement, interstitial lung disease and Raynaud’s phenomenon. In our report, the association does not seem to impair SSC’s clinical course. Similar results have been reported in other studies.

PS326
SJÖGREN'S SYNDROME IN SYSTEMIC SCLEROSIS
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Background. The clinical manifestations of systemic sclerosis are very divers both in the amount and in the clinical signs and symptoms. The clinical prognosis and the quality of patients’ life with systemic scleroderma depend mostly on the possession of Sjögrens syndrome. The majority of the scientist who studied the problem with the Sjögrens syndrome in the patients with systemic sclerosis emphasizes the high level of difficulty of prognosis for this syndrome.

Objectives. tracking the factors that contribute to the development of Sjögrens syndrome in the patients with systemic sclerosis.

Methods and methods. 150 patients with systemic sclerosis where examined, of which only 6 were males. The average age of the subjects included in the examination was 42.3 ages. The average duration of the disease – 13.6 ages. 121 (80.7%) from the patients manifested SS in a limited form while 29 (19.3%) had the diffuse form of the disease. The lag phase of Sjögrens syndrome was established according to the diagnostic criteria of SICCA (Sjögren’s Interna
tional Collaborative Clinical Alliance), proposed in 2012. The clinical dates of the patients within the examination were analysed according to the statistical disparity analysis.

Results. Sjögrens syndrome was diagnosed in 28 (18.6%) of the examined patients, of which 20 (71.4%) with a limited form of the disease and 8 (28.6%) with the diffuse one. Sjögrens syndrome’s development was noticed in average at 11.7± 1.2 years from the onset of the disease. Using the static determina
tory analysis, the following factors proved the influence on the development of the Sjögrens syndrome in the patients with systemic sclerosis: the length of the disease of more than 10 years, arthralgia and arthritis in the clinical manifesta
tions of the disease, the presence of interstitial lung disease, the presence of the rheumatoid factor in the blood, a high activity of the base disease (USTAR scale (EULAR Scleroderma Trials and Research Group) higher than 3). Using the same factors the development of the Sjögrens syndrome can be predicted in the patients with systemic sclerosis with an accuracy of 78.2%, and with its absence – 71.6%.

Conclusion. The presence of some factors in the patients with systemic scleroder
cia can predict the development of the Sjögrens syndrome with an accuracy of 78.2%, namely the length of the disease of more than 10 years, arthralgia and arthritis in the clinical manifestations of the disease, the presence of interstitial lung disease, the presence of the rheumatoid factor in the blood, a high activity of the base disease.
In May 2011 a 72 year old man with Systemic sclerosis (SSc) complicated by pulmonary artery hypertension (PAH) and DUs (digital ulcers) came to our observation complaining of dyspnea on exertion. His medical history included Raynaud’s phenomenon (RP) diagnosed in 1988, a definitive diagnosis of SSc in 2002, followed by occurrence DUs on the first, second and third digits of the left foot. He already failed therapy with bosentan (62.5 mg twice daily for the first month, followed by 125 mg twice daily) for marked elevation of hepatic transaminases and with intravenous iloprost (at maximum tolerated dose once monthly) for absence of DUs healing. During this hospitalization the patient underwent diagnostic work-up for PAH, with evidence of severe pulmonary hypertension at right heart catheterization, with a negative vasoactivity test performed by intravenous epoprostenol. He was in WHO class III, and began therapy with warfarin and ambrisentan 5 mg daily, on-label for PAH associated with connective tissue diseases such as systemic sclerosis. After only 3 months of ambrisentan therapy we observed complete healing of DUs (Fig. 1 DU before (a), at 1 month (b) and 2 months (c) after starting ambrisentan). Oral endothelin receptor blockers are a second-line therapy in the treatment of SSc-related DUs; this treatment is able to prevent new DUs and the only randomized clinical trial is limited to bosentan. Ambrisentan, a selective blocker of the ETA receptor, has proven to be effective in SSC-PAH. Preliminary data from a prospective open label, single centre study enrolling 20 patients with DU secondary to SSc treated with ambrisentan revealed the efficacy of this drug on the healing of DUs. A recent study on six SSc patients with DUs and without PAH suggested that ambrisentan might be useful in the treatment of DUs in the case of previous failure of bosentan therapy. There is also a case report concerning the use of selective ETA receptor antagonist sitaxsentan for the treatment of DU, with a complete healing after four months. These data could explain the class-effect mechanism of ETA receptor antagonist drugs. Currently, ambrisentan is an off-label drug for the treatment of DU, but it may be considered an alternative to bosentan, at least in cases of adverse effects. However, there is a need for randomized, double-blind, placebo-controlled trials to further evaluate the efficacy of ambrisentan in the prevention and treatment of DU.

**Fig. 1.**
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Systemic sclerosis (SSc) is an autoimmune disease which involves internal organs. Limphadenopathy is often observed in different connective tissue diseases. In SSc limphadenopathy often coexists with interstitial lung disease (ILD). We present a case report of a patient with the diagnosis of overlap syndrome: polymyositis and SSc. When he was 53 years old the diagnosis of SSc was established. He presented Raynaud’s phenomenon, sclerodactylia, ulcers of the fingers and ScI70 antibodies. The HRCT revealed enlargement of the mediastinal lymph nodes, without coexisting ILD. Other tests confirmed generalized limphadenopa-thy. Branchioscopy, bronchovalveolar lavage (BAL), endobronchial ultrasound (EBUS) biopsy of mediastinal lymph nodes, microbiological tests, cytological study were undertaken to exclude tuberculosis and neoplasia. Immunosuppres-sive treatment was administered. One year later prostatic cancer was diagnosed and one month after finishing radical radiotherapy the symptoms of active inflamma-tive tuberculosis appeared.

Case Report. We report a case of 75 years old woman affected by diffuse systemic sclerosis and digital ulcers refractory to medical therapy. She came to our observation complaining persistent left sided RP with severe ischemic pain (VAS 9-10) and rapidly evolving digital ulcers onto 2nd, 3rd and 4th finger of left hand. The angiogram was performed and revealed a distal ulnary obstructive lesions, radial segmental occlusion with repercussion of the arch handled by intersosseous artery, narrowing of multiple digital arteries. Medical therapy (doprost, low molecular weight heparin, opioid) was started without benefit.

Methods. A diagnostic single shot axillary-brachial plexus block with ropiv-acaine 0.375 30 ml was performed; the block showed immediate effectiveness with pain disappearance (VAS 0) for 12 hours; the left hand also regained temperature and perfusion and return of interdigital flow revealed with continuous waves Doppler. We decided to perform a continuous brachial plexus block. In fusion was started with Ropivacaine 0.2% 5 ml/hr and then reduced to 0.15% because of persistent and limiting motor block; at week 4 after block despite the leucocytoclastic vasculitis has been a manifestation of the infectious process.

Patient was permanently afebrile, skin rash significantly improved, neck lymph nodes - returned to normal size, with decreased dyspnoea. Control labora-tory tests and microbiologic investigations revealed normal value of CRP – 1.1, nor-mal creatinine – 91, sterile urine culture, resorption of pulmonary infiltrates. The final diagnosis of chronicossepsis (not proved microbiologically with evidence of pulmonary and renal infectious foci) with allergic vasculitis was made. Reactive limphadenomagnal and hepatoplenomagnality in this case should be differenti-ated from malignant transformation of Sjögren syndrome in lymphoproliferative disease. The manifested allergic vasculitis may manifest in the context of various conditions some of the major being infections and drugs. In our case, the attempt to start treatment treatment with bosentan one month later after suppression of the infection was well-tolerated from the patient, which led us to conclusion, that the leucocytoclastic vasculitis has been a manifestation of the infectious process.
brisenant. Soon after, she was rushed to the emergency unit because of severe oxygen desaturation with pulmonary edema and pleural effusion. RHC showed remarkable improvement of PAH (mPA 37 to 25 mmHg), but moderate diastolic myocardial dysfunction was apparent by echocardiogram with tissue Doppler imaging.

Case #2. A 75-year-old woman with lcSSc and PAH (WHO-FC II) was treated with sildenafil and beraprost. Hemodynamics had been gradually improved (mPA 35 to 21 mmHg), but her symptoms had never improved. Addition of bosentan resulted in oxygen desaturation with pulmonary congestion. High-resolution CT scan of the chest revealed typical features of pulmonary vено-occlusive disease (PVOD) including centrilobular groundglass opacities, septal lines, and lymph node enlargement.

Case #3. A 72-year-old woman with lcSSc was referred to our hospital because of progressive dyspnea. Diagnosis of PAH with WHO-FC III was made. Treatment with sildenafil and bosentan resulted in improvement of symptoms and hemodynamics. However, her symptoms worsened because of anemia with repeated episodes of gastrointestinal bleeding. Colonooscopy revealed oozing from multiple teleangiectasias, but repetitive endoscopic clipping procedure failed to control bleeding.

A combination therapy of PAH drugs successfully improved PAH, but paradoxically unmasked subclinical other complications of SSc, such as diastolic myocardial dysfunction, PVOD, and bleeding from intestinal telangiectasies. We should be cautious about these adverse effects after increase in the dosage or sequential addition of PAH drugs.

PS334
COEXISTENCE OF SYSTEMIC SCLEROSIS AND SARCOIDOSIS: A CASE REPORT
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Introduction. Sarcoidosis is a Th1-related multisystem granulomatous disease characterized by lymphadenopathy, skin lesions and various internal organ involvement. Systemic sclerosis is a chronic autoimmune disease characterized by skin thickening and fibrosis of various internal organs and vascular abnormality. During the early and active stage of the disease, the presence of Th2-immune response was shown. This presentation reports a female patient presented with symptoms of granulomatous dermatitis, interstitial lung disease and Raynaud’s phenomenon and the association of sarcoidosis with systemic sclerosis.

Case report. A 52-year-old female patient was complaining of Raynaud’s phenomenon, arthralgia, morning stiffness, and dyspnea on exercise was admitted to our rheumatology out-patient’s clinic. Physical examination revealed telangiectasia on the face, reduction in mouth opening, sclerodactyly and pallor phase of Raynaud’s phenomenon and brown-red colored skin lesion on the right pretilial area (Fig. 1). Auscultation of the lung revealed basal crepitant lung craklles in all lungs. Laboratory tests were as follows: ESR 38 mm/h, C-reactive protein: 3.5 mg/dl, RF was negative. Liver and kidney function tests were normal. Routine urine analysis was normal. Serological tests reported nucleon and homogeneous positive ANA, positive anti-Scl70, normal C3 and C4 complements, and anti-CCP, anti-Ro, anti-La, anti-Sm, anti-ribosomal P antibodies were negative. Serum ACE level was 65 U/L (normal values: 8-52 U/L). Fine reticular pattern was captured in lung graph. Chest HRCT reported images of frosted glass and honeycombing in accordance with interstitial AC disease. The patient was presented to a pneumonologist, bronchoscopy, and BAL were performed and mixed-alveolitis was detected. Skin biopsy was performed and non-caseating granulomas, granulomatous dermatitis consistent with sarcoidosis was determined. There were no acid fast bacilli and fungus in Ziehl-Neelsen and PAS histochemistry respectively. The patient was diagnosed as scleroderma and sarcoidosis according to the clinical, laboratory and histological findings. Therapy with corticosteroid 16mg/day, hydroxychloroquine 200mg/day and azathioprine 150mg/day was started. It was noticed on the follow-up pulmonary function tests and DLCO test that dyspnea on exercise was decreased and there was a significant regression in skin lesions. Clinical condition of the patient is stable at the moment and outpatient follow-up is continuing.

Conclusion. Coexistence of sarcoidosis with systemic sclerosis is a rare entity. Th1/Th2 paradigm is one of the most important reasons for this entity. Since each of these syndromes can do similar clinical presentation, the differentiation of actual overlap of syndromes is important in predicting prognosis and planning the treatment.

PS335
RENAL THROMBOTIC MICROANGIOPATHY TRIGGERED BY LUNG CANCER IN LIMITED SSC-A CASE REPORT-
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Background. Scleroderma renal crisis, whose pathophysiology is thrombotic microangiopathy (TMA), is a life-threatening complication of SSc, occurring much more frequently in diffuse type than in limited type. Malignancy, especially lung cancer, can cause TMA as well. Objectives. We report a rare of renal TMA induced by lung cancer in a patient with limited SSc.

Results. A 68-year-old Japanese woman with 30-year history of Raynaud phenomenon began to have her finger tip ulcers 2 months ago. She noticed a right cervical mass a month ago and admitted because of her renal function worsening a month ago. She was diagnosed with limited SSc based on skin sclerosis distal to her wrist and positive anti-centromere antibody. A cervical lymph node biopsy and imaging studies of the chest revealed an advanced lung adenocarcinoma. Renal function gradually worsening, hemodialysis was started.

Conclusion. We speculated that preexisting mild endothelial injury of renal vasculature with SSc was accelerated to the overt TMA by lung adenocarcinoma.
A 56 years old woman presented to our Rheumatologic Clinic. Ischemic lesions scarcely responsive to standard treatment. This is characterized by heart fibrosis and diastolic dysfunction. The mechanism impli- cated is the microcirculation alteration. The abnormal perfusion early detection will allow us to improve quality of life and the prognosis in patients with cardiac involvement in SSC. The algorithm of the screening and the treatment of primiti- ve heart disease in SSc remain to be codified.

**Conclusion.** The primitive heart disease in SSc is rare but a severe situation characterized by heart fibrosis and diastolic dysfunction. The mechanism implicated is the microcirculation alteration. The abnormal perfusion early detection will allow us to improve quality of life and the prognosis in patients with cardiac involvement in SSc. The algorithm of the screening and the treatment of primitive heart disease in SSc remain to be codified.

**PS338**

**DIGITAL NECROSIS IN SYSTEMIC SCLEROSIS NOT ONLY A MICROVASCULAR DISEASE: A CASE REPORT**

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Systemic sclerosis (SSc) is a connective tissue disease characterized by immune system alterations, skin and internal organs fibrosis and diffuse microangiopathy. This latter is responsible for digital ulcers (DU), renal crisis and pulmonary arte- rial hypertension; while macrovascular involvement is less frequently reported in the clinical practice. Here we describe a patient with severe ischemic lesions due to both micro- and macrovascular involvement successfully treated with a combined therapy: systemic vasactive treatment, local medications and angioplasty with distal revas- cularization. A 60 y.o. woman was first diagnosed as SSc in 1996 on the basis of Raynaud’s phenomenon, diffuse skin sclerosis, capillaroscopic scleroderma pattern, anti-Scl70 positivity and interstitial lung disease. In 2012 exertion dyspnea markedly worsened due to pulmonary artery hypertension (mean precapillary pulmonary artery pressure of 48 mmHg at right heart catheterization) treated with bosentan (2) and thomboembolism event (1) despite of an optimized symptomatic therapeutic (diuretics, calcium inhibitors, angiotensin converting enzyme inhibitor drugs anticoagulant...).

**Conclusion**. The primitive heart disease in SSc is rare but a severe situation characterized by heart fibrosis and diastolic dysfunction. The mechanism implicated is the microcirculation alteration. The abnormal perfusion early detection will allow us to improve quality of life and the prognosis in patients with cardiac involvement in SSc. The algorithm of the screening and the treatment of primitive heart disease in SSc remain to be codified.
The patient had no Raynaud’s phenomenon neither sclerodactyly or telangiectasia. Contemporary to the appearance of bullous skin lesions, she developed dyspnea and dysphagia and the extension of skin induration. From the chest CT scan and spirometry, a restrictive pulmonary pattern was evidenced. BAL was negative for neoplastic cells, cultural exams for common germs and Mycobacterium tuberculosis. An esophageal scintigraphy showed slowed emptying of the esophagus. She was given cyclophosphamide (50 mg bid to take orally) and prednisone (5 mg/ die). In consideration of the lack of response, the steroid therapy was increased at 1 mg/kg/die, with the improvement of skin thickness and dyspnea.

Conclusion. The rapid worsening of the clinical conditions of patient and the bullous lesions, that are a very uncommon presentation of scleroderma cutaneous manifestations, made SSc diagnosis difficult and represented a challenge for physicians. Moreover, these skin lesions may be activity disease index, both cutaneous and visceral. Therefore they should be made known to clinicians so that activity and progression of the disease can be recognized and treated to avoid complications.

PS340
THYROID DYSORDERS IN PATIENTS WITH SYSTEMIC SCLEROSIS: BIOCHEMICAL AND SONOGRAPHIC CHARACTERISTICS

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Background. Previous studies have shown elevated risk for thyroid autoimmune diseases in patients with systemic sclerosis (SSc). Increased risk for thyroid nodules and cancer was demonstrated in other autoimmune disease like systemic lupus erythematosus.

Aim. The aim of our study was to evaluate the thyroid gland in consecutive SSc patients using biochemical and sonographic tools.

Methods. Thyroid-stimulating hormone (TSH), free thyroxine (fT4), antithyroglobulin (aTG; normal range 0.2-3.5 UI per L) and antiperoxidase (aTPO; normal range 0-4 UI per L) autoantibodies as well as thyroid ultrasound were performed to consecutive patients with SSc classified according to the American College of Rheumatology 1980 criteria.

Results. Fifty patients (44F; 6M; age 50.4 ± 14.6 years) with dSSc and lSSc (40; 10) were evaluated. Median duration of the disease was 6.5 years (range 0.5-38 years) with clinical manifestations involving mainly the skin, gastrointestinal tract and musculoskeletal systems (in 90.4%, 82.7%, and 69.2%, respectively). Ten patients were previously diagnosed with hypothyroidism, 2 had hemithyroidectomy, one had procror-induced hypothyroidism and 7 had autoimmune thyroid disease. A third of patients had first degree relatives with autoimmune thyroid disease. TSH level was 2.24±1.18 mIU per L (normal range 0.2-3.4) and fT4 1.28±1.76 (normal range 0.8-2.0 ng per dL). Out of forty thyroid disorder naïve patients 3 had mildly elevated TSH level (5.24±0.76 mIU per L), and 15% and 5% were positive for aTPO and aTG antibodies, respectively. Twenty two patients had 1-6 thyroid nodules, which were >1 cm in 24% of the patients. Two nodules and 2 others were calcified. Overall 6 patients underwent fine needle aspiration procedures: 5 were diagnosed as colloid nodules, and one as papillary carcinoma.

Conclusions. In this screening study no evidence of thyroid autoimmune disease was found in this unique group of patients. Yet, almost half of the patients had thyroid nodules. The clinical significance of these findings is to be determined in long-term studies.

PS341
EXERCISE TRAINING IN SYSTEMIC SCLEROSIS – FIVE SSc PATIENTS FINISHED THE BERLIN MARATHON

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Exercise training can improve aerobic capacity and muscle function in patients with connective tissue diseases e.g. rheumatoid arthritis, inflammatory myositis, systemic lupus and primary Sjögren syndrome. There are only few data concerning the usefulness of exercise training in patients with systemic sclerosis. In 10/2010 we started a 12 months aerobic exercise training program for patients with systemic sclerosis as part of the long term rehabilitation process. 5 patients were enrolled in this uncontrolled single center pilot study, 4 women, age 35 – 48 years, and 1 man age 38 years. 3 patients were ScI+T0, 2 patients ACA+. 3 patients suffered from limited SSc, and 2 patients from diffuse SSc for at least 2 to 4 years.

The individual training program consisted of 3-4 jogging units per week at 50-70% VO2 max and was intensively supervised by two sport scientists from a Swiss Olympic Medical Center in Basel. Exercise training was administered over an 18 month period where participants uploaded their heart rate and GPS data after each training. Baseline tests included clinical evaluation, spiroergometry, lactate threshold testing, capillaroscopy, blood and urine tests, lung function tests, Holter ECG, echocardiography, Raynaud severity analogue scale, and the SF12 Qol test. Tests were repeated every 4 months. After 11 months of exercise training all 5 SSc patients finished the 42,195 km Berlin Marathon with no evidence of adverse events, no changes in muscle enzymes, and no deterioration of the disease.

Results. The most striking results were complete suppression of Raynaud attacks in 4/5 patients. There was also a reduction of finger swellings in 2/5 patients. Both patients could wear rings again. There was a reduction of ANA titer in 4/5 patients. In the other patient with very early SSc ANA and ScI+T0 antibodies became negative during the training period and this result was stable for at least 12 months after the marathon. All patients noticed a reduction of their fatigue syndrome.

We present test results in detail and show a short videoclip with the SSc patients running the 2011 Berlin Marathon.

Conclusion. Professionally supervised exercise training might become a useful adjunct therapy in patients with early SSc but controlled studies are needed.

PS342
SYSTEMIC SCLEROSIS ASSOCIATED TO SYSTEMIC LUPUS ERYTHEMATOSUS

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Objective. The aim of this study was to describe clinical, immunological features and outcome of patients with systemic sclerosis (SSc) and Systemic lupus erythematosus (SLE).

Methods. A retrospective study of patients’ files with SSs, only patients who fulfilled the ACR criteria for both SSc and SLE were included. Demographic, clinical and immunological characteristics were studied.

Results. Twelve Patients have SSc associated to SLE (11.7% of patients with SSc), all of them were female. The average age at the diagnosis of SSc and SLE was respectively 38.33 and 36.08 years. The mean delay between the 2 diagnoses was 40 month. SSc preceded SLE in 5 patients. Five patients had diffuse cutaneous scleroderma and 7 had limited cutaneous scleroderma. Ten patients complained of arthritis and 4 of myalgia. Glomerulonephritis (GN) and pericarditis were both diagnosed in 5 patients. Eleven patients complained of Raynaud’s phenomenon and 3 had digital ulcers. Three patients had interstitial pneumonia and 5 had esophageal involvement. Antinuclear antibodies were positives in all patients; 9 patients had anti-DNA antibodies, 6 had anti-topoisomerase 1 (50%) and one had anti-Pm-scl. Anti-Smith, anti-SSA and anti-RNP antibodies were positives respectively in 7, 5 and 3 cases. All patients were treated by corticosteroids (for GN, pericarditis, myositis, arthralgia or neurological involvement), no scleroderma renal crisis was noted. Eight patients were treated with immunosuppressant agents (GN, interstitial pneumonia or arthralgia). The outcome was good in 9 cases, 2 patients were stables and one died.

Conclusion. Connective tissue diseases may overlap with each other or be associated during the disease course. Serial follow-up for clinical symptoms as well as serological changes is recommended.

PS343
BKVIRUS ASSOCIATED HAEMORRHAGIC CYSTITIS IN A SCLERODERMA PATIENT AFTER CYCLOPHOSPHAMIDE THERAPY

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Introduction. Haemorrhagic cystitis (HC) is characterized by haemorrhage of the bladder mucosa with painful micturation which ranges from microscopic haematuria to clot retention and renal failure. HC is either an early-onset event arising from chemotherapy agents, particularly metabolites of cyclophosphamide (CTX) and/or irradiation, or a late-onset event viral-associated. The majority of these HC are due to reactivation of BKV, but may also arise from cytomegalo virus and adenoviruses. HC-associated reactivation of BKV is a frequently en-
countered condition in immunocompromised haematopoietic stem cell transplant recipients leading to significant morbidity and occasional mortality.

**History.** Years old woman. Beginning of disease in 2011 with polyarthralgias, Raynaud’s phenomenon, digital ulcerations and diffuse skin involvement. Serology testes: positive ANA and anti-ENA (Scl-70). Diagnosis: diffuse cutaneous systemic sclerosis. Staging of disease: HRCT is negative for active alveolitis, barium contrast study is negative for esophageal involvement, echocardiogram is negative for pulmonary hypertension. Due to the rapid progression of the disease it was decided to establish immunosuppressive therapy with CTX iv. The patient has not shown any problem until to infusion of third bolus after which, at a distance of few weeks, is appear HC. Chemical and physical urine examination and urine culture are negative, quantitative search of urine BKV is positive. The ultrasound of the urinary tract has not been documented hydronephrosis. The patient was hospitalized and was placed 3-way catheter for bladder washings. She was obliged to report a dry cough with a pick flow was in normal range. She was obliged to start a immobilization of Tranexamic acid + Hylauronic acid on a weekly basis. Slow but progressive regression of the clinical picture for which no therapy was started with Ciclofibro.

**Discussion.** Polovurmuses (PyV) are small, nonenveloped, circular, double-stranded DNA viruses of the family Polyomaviridae. The first two PyV which were discovered in immunosuppressed patients were: JCY was identified in brain tissue from a patient with progressive multifocal leukenoecephalopathy (PML), and BKV from the urine of a renal transplant. The increased incidence of JCY/ PML in association with the HIV-1 pandemic and the emergence of BKV-associated-nephropathy in association with renal transplantation and HC in bone marrow transplant recipients, highlighted the importance of the host immune system in the control of these latent infections and the pathogenesis of these diseases. For a severe acrosyndrome with pulpal ulcer. She was also complaining about a Raynaud’s phenomenon, digital ulcerations and diffuse skin involvement. Serology testes: positive ANA and anti-ENA (Scl-70). Diagnosis: diffuse cutaneous systemic sclerosis. Staging of disease: HRCT is negative for active alveolitis, echocardiogram is negative for pulmonary hypertension. Due to the rapid progression of the disease it was decided to establish immunosuppressive therapy with CTX iv. The patient has not shown any problem until to infusion of third bolus after which, at a distance of few weeks, is appear HC. Chemical and physical urine examination and urine culture are negative, quantitative search of urine BKV is positive. The ultrasound of the urinary tract has not been documented hydronephrosis. The patient was hospitalized and was placed 3-way catheter for bladder washings. Set treatment with Immunglobulins iv (20 mg daily for 5 consecutive days) for a total of 6-cycles (from December 2011 to September 2012). Bladder instillation of Tranexamic acid + Hylauronic acid on a weekly basis. Slow but progressive regression of the clinical picture for which no therapy was started with Ciclofibro. We present a case of a 40-year-old woman with severe and rapidly progressive dSSc. The initial clinical manifestations were new-onset Raynaud’s, weakness and generalized pain. On the first examination she presented puffy hands since 4 months ago, without skin thickening. Speckled anti-nuclear antibodies were positive with high-titer anti-topoisomerase antibodies. Within 2 months of the beginning of the symptoms, she had a mRSS (modified Rodnan skin score) of 22 and a FVC and DLCO of 93 and 71% of predicted values, respectively. The chest HRCT scan (HRCT) revealed focal ground-glass appearance, predominantly in the lower lobes. She was treated with cyclophosphamide for 6 months. However, a progression of the skin involvement was observed, with a mRSS of 51 and a worsening of the PFT's, with a FVC and DLCO of 70 and 54%, respectively. Her chest HRCT now revealed diffuse ground-glass appearance. Since worsening was observed despite immunosuppressive therapy, she was administered RTX (1 g, 2 weeks apart). She had a good subjective symptomatic improvement. Three months after the RTX infusion, the mRSS had improved to 37 and the FVC and DLCO were of 79 and 78%, respectively. Chest HRCT scan was similar to the one realized in the baseline. Six months after the first RTX infusion, she was re-treated with the same regimen. Three months after the second RTX treatment, mRSS was decreased to 33 and FVC and DLCO reached values of 86 and 78%, respectively. She is now on mycophenolate mofetil as maintenance therapy for 5 months and her clinical situation remains stable.

**Conclusions.** RTX had a beneficial effect in our patient, as indicated by the improvement of mRSS, pulmonary function tests and even the chest HRCT. The clinical improvement of skin thickening and pulmonary function after RTX, which may indirectly support the role of B-cells in the pathogenesis of dSSc, supports the need for formal evaluation of this promising therapy.

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Recently, isolated basal ground glass opacities have been detected bilaterally on chest CT with normal lung volumes and slightly reduced DLCO (65%, and DLCO/VA 74±%). Transthoracic echocardiographic PAPs assessment was near to upper value (33 mmHg) and barium swallow was normal. Thus, a diagnosis of SSc-like undifferentiated connective tissue disease has been made and follow-up planned.

**Discussion.** This is the first description of asymmetric microvascular damage in a hemiplegic patient with new-onset SSc-like disorder. So far, two analogous cases have been described in literature: the former clinically assessed the absence of sclerosis on the parietic limbs; the latter reported the unilateral acroosteolysis on X-ray of the non-paretic hand. In none capillaryscopy was performed. For the first time we have documented the capillaroscopic SSc-like changes of nailfold vessels of the “healthy” limb while sparing the paretic one. The reason of such a “protective” factor is elusive. The mechanobiological dysregulation of dermal fibroblasts in SSc and the abnormal mechanical stimuli such as disuse of parietic limbs is an intriguing yet speculative hypothesis. Besides, evidence supports the mediation of nervous system in inflammatory response. This clinical case points out the possible role of a “cross-talk” between nervous system and microvascular immuno-mediated disorders and suggests areas of research interest for future directions in pathogenetic studies and target therapy advancement for SSc.

**PS347**

**A RARE CASE OF CHRONIC EFFUSIVE-CONSTRICTIVE PERICARDITIS IN LIMITED CUTANEOUS SYSTEMIC SCLEROSIS**

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**Background.** Systemic Sclerosis (SSc) is a heterogeneous autoimmune disease with propensity for internal organ involvement. Mild pericardial effusion is common especially in diffuse cutaneous systemic sclerosis. However significant pericardial effusion with tamponade or constriction is rare. We report a case of a chronic effusive-constrictive pericarditis.

**Case.** A 52 year lady was diagnosed with limited cutaneous systemic sclerosis (lcSSc) whilst living in Australia (then 31 years old) with positive antinuclear antibody (>1280 anticoncetrone pattern), telangietasias, calcinosis, Raynaud’s, sclerodactyly, oesophageal dysmotility. She had penicillamine, omeprazole and (lcSSc) whilst living in Australia (then 31 years old) with positive antinuclear antibody (speckled pattern at 1:640), and positive anti-RNA Polymerase III (anti-RNAP III) antibody screen. She was commenced on escalating doses of captopril. Frusemide, labetalol and amiodipine were required for optimal control. Her pulmonary function tests (PFT) revealed FVC 89%, FEV1 85%, FEV1/FVC ratio 80% and TLCO of 44% predicted; HRCT scan ruled out fibrotic lung disease. Echocardiography (ECHO) revealed pericardial effusion (1.55cm width) with right ventricular systolic pressure of 47.1 mmHg and ejection fraction of 60%.

In mid 2011 her ECHO showed an increase in PcE which progressed to severe degree and required pericardial window by December 2011 her ECHO showed PcE of 1.7cm in diastole (was 1.2 cm in June 2011) and she was beginning to get sympotmatic.

Following this she developed further palpitations, chest pain and shortness of breath and was transferred to our tertiary hospital in January 2012. Clinically she had effusive-constrictive pericarditis. Her transhoracic and transoesophageal ECHO revealed a small PcE (post-pericardial window the pericardial space of 0.9cm) mild RV dysfunction and doppler inflows in MV & TV showed a change of more than 25% with respiration. She proceeded to simultaneous right and left heart catheter studies (figure 1) which confirmed constrictive pericarditis (with normal coronary arteries). Thereafter she had open pericardietomy with improvement in her symptoms. Histological analysis of pericardium ruled out calcified, infective and granulomatous causes.

**Discussion.** We believe our case is one of extremely few cases of SSc presenting with chronic effusive-constrictive pericarditis and the only one reported in lcSSc. Our case also illustrates that significant PcE does occur in lcSSc. Apart from slow worsening of the effusion there was development of constriction with fibrous pericarditis (noted on histology) with a lag in presenting symptoms. Though our patient had calcinosis cutis none was evident in pericardium.

**PS348**

**A RARE PRESENTATION OF SCLERODERMA RENAL CRISIS FOLLOWING SILICONE BREAST IMPLANT RUPTURE**

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**Background.** Systemic sclerosis (SSc) is an autoimmune disorder of unknown aetiology. Exposures to environmental factors may play a role. Silicone breast implants have been postulated as a cause for autoimmune diseases including SSc. This remains unconfirmed.

**Case Presentation.** 47 year old lady developed ridging in her silicone breast implants four years after implantation. Ultrasound confirmed ruptured implants. In 2011 she developed Raynauds which worsened following the silicone breast re-implantation (mid 2012) associated simultaneously with puffiness of her fingers followed thereafter with rapid thickening of the skin over her fingers, forearms, arms as well as chest wall.

In early 2013 she presented with breathlessness. Physical examination and chest x-ray confirmed acute pulmonary oedema. Her NT-proBNP was elevated (>4.000pmol/L). Her blood pressure (BP) was 180/110 mmHg. Her blood tests confirmed acute renal failure with serum creatinine (Scr) 313 micromol/L (NR= <90 micromol/L). She had decreased complement levels, positive antinuclear antibody (speckled pattern at 1:640), and positive anti-RNA Polymerase III (anti-RNAP III) antibody screen.

She was discharged at day 16. Review at 4 weeks confirmed her BP and Scr was stable (149 micromol/L). Repeat PFT and ECHO have been requested to establish the baseline status after stabilization.

**Discussion.** This is the first reported case of dcSSc (and presence of anti-RNAP III antibodies) in a lady with a history of silicone breast implant rupture, presenting with SRC. Autoimmune diseases such as SSc, inflammatory arthritis, human adjuvant syndrome and SLE have been reported following silicone implants.ANA, dsDNA and RF are the commonly reported autoantibodies. Published cases reveal the mean time from silicone implantation to symptom onset was 13.2 years. In our case, the first non-Raynaud developed 9 years after implantation (5 years after rupture).
Bekerecioğlu et al. demonstrated in asymptomatic patients with previous silicone implants a significantly higher concentrations of immunoglobulins (IgG and IgM) and anti-silicone antibodies around the implant suggesting that silicone is not biologically inert. The link between silicone breast implants and SSC is attractive but tenuous on current evidence. There is a biological plausibility. Larger studies are required to see if there is any definite association.

**DUE TO THE SILDENAFIL SEVERE HYPOTENSION WITH ACUTE RENAL FAILURE DUE TO THE SILDENAFIL**

PS349

**A CASE OF SYSTEMIC SCLEROSIS PATIENT THAT HAD SEVERE HYPOTENSION WITH ACUTE RENAL FAILURE DUE TO THE SILDENAFIL**

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A 54-year-old man was re-admitted to severe dizziness and fatigue. At time previous admission, he was diagnosed systemic sclerosis that accompanied severe digital ulcer with gangrene and borderline pulmonary hypertension. He was improved digital ulcer treated with LV antibiotics (Cefazolin) and LV. prostacyclin (Eglandin) and P.O sildenafil (20mg TID), and discharge with P.O medication (Beraprost, Sildenafil 20mg TID). Two weeks after, he felt severe intermittent dizziness and low back contusion at the bus, but initial vital sign was normal blood pressure (120/80 mmHg) rapid rhythm (HR 108), and had not anemia or abnormal finding in complete blood count, chemical, electrolyte. But, he had progressive lowering the blood pressure to 60/40mmhg rapidly in a day. He was discontinued the sildenafil, started vigorous hydration with normal saline, and administered norepinephrine via intra venous. His blood pressure was maintained at the level of 90/70mmHg. But He had showed oliguria and then anuria for 22 hours, and revealed BUN/creatinine 21.7/1.7 IU/L, AST/ALT 111/53 IU/L, Pro-BNP 587.7 IU/L. There was no abnormal heart motion and normal ejection fraction in echocardiographic finding, and normal EKG finding. After anuria state, he had showed large amount urination with 300~60cc/hour on day after, and then massive urination in 5 days 29000cc~323000/day, we performed the vigorously LV hydration for balance of body fluid. Body weight change of patient was just 2kg in first day that the time showed anuria. The 6th hospital day, he had stable vital sign and input-output ratio (3350/2880cc) without LV hydration or norepinephrine, and revealed the BUN/Cr 11.4/0.7 IU/L. After anuria state, he had showed large amount urination with 300~600cc/hour on day after, and then massive urination in 5 days 29000cc~323000/day, we performed the vigorously LV hydration for balance of body fluid. Body weight change of patient was just 2kg in first day that the time showed anuria. The 6th hospital day, he had stable vital sign and input-output ratio (3350/2880cc) without LV hydration or norepinephrine, and revealed the BUN/Cr 11.4/0.7 IU/L.

In conclusion, Ischemic ulcers represent a severe and extremely debilitating condition affecting up to 50% of patients with SSC, most commonly on the hands. This patient had severe involvement of the feet, with gangrene and loss of extensive part of right foot, a rare feature in SSC.

**SYSTEMIC SCLEROSIS WITH EXTREM NECROSIS AND LOST OF PART OF THE FOOT- A CASE REPORT**

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Introduction. The vascular involvement in Systemic sclerosis (SSc) is an early manifestation and represents a central event in the pathogenesis of the disease. Structural and functional abnormalities of blood vessels, include changes in the control of vascular tone, endothelial damage and dysfunction, intimal proliferation of small arteries and arterioles, Raynaud’s phenomenon, digital ulcers, gangrene and amputation of extremities. We describe an important lesion on the foot of a patient with SSC with a very extensive necrosis and lost of three fingers.

Case report. MVOE, female, married, born in Iaperuma - RJ, black, 35 years, housewife, introduced himself to the service of Rheumatology of Gaffrée & Guinle University hospital (RJ). She had diagnosis of Systemic sclerosis (SSc) since 1998. Clinical findings were: Raynaud’s phenomenon, digital ulcers, claw-like hands, fingers and toes acrocyanosis. At February 2009 she developed an enormous ulceration with gangrene of the 1st, 2nd and 3rd right toe, covering the distal extremity of the right foot (Fig. 1). We referred her to surgery for debridement. She was taking the follow medications: captopril, cilostazol, low-dose prednisone (5mg/day), pentoxifylline, nifedipine and aspirin 100 mg/day. It was added sildenafil 50 mg/day and bosentan, but irregularly and for short time. Since September 2010 she had joined regular use of bosentan, initially at a dose of 62.25 mg 12/12hs for four weeks, increasing to 125 mg 12/12hs, with gradual improvement, but maintaining open sore, with smaller diameter and granulation tissue (Fig. 2). Discussion: Digital ulcers are more frequently described in hands than feet. It is not common a so large lesion like this one observed in the patient. New forms of treatment such as phosphodiesterase-V inhibitors and endothelin receptor blockers have proven effective in patients with ischemia of the extremities as a manifestation of SSc.

Conclusion. Ischemic ulcers represent a severe and extremely debilitating condition affecting up to 50% of patients with SSC, most commonly on the hands. This patient had severe involvement of the feet, with gangrene and loss of extensive part of right foot, a rare feature in SSC.

**REFERENCES**

1. thumbnail.png

**Figure 1.** Aspect of the foot of the patient at the onset of the injury.

**Figure 2.** Present aspect of the patient’s foot after two years of treatment.
PS351
AN ALTERNATIVE APPROACH TO THE MANAGEMENT OF A PATIENT WITH SSC-MYOSITIS ASSOCIATED WITH DYSPHAGIA

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Dysphagia commonly occurs in patients with systemic sclerosis (SSc), but is uncommonly due to pharyngeal muscle myositis. Oropharyngeal dysphagia leads to recurrent, potentially life-threatening, aspiration pneumonia. As such, management strategies involve the avoidance of oral nutrition, through temporary percutaneous endoscopic gastrostomy (PEG) placement, whilst the myositis is medically optimised. We present a patient with SSc, myositis-overlap and oropharyngeal dysphagia, who declined PEG placement.

A 44 year old female was referred to our centre for specialist review with a 2 month history of dysphagia to liquids, which she localised to her pharyngeal region. She also reported nasal regurgitation on swallowing liquids. Two years earlier she had been diagnosed with diffuse cutaneous SSc (PM Scl +ve 75/100), associated with pulmonary involvement. This had been preceded by a 6 month history of Raynaud’s phenomenon. Our clinical suspicion was of pharyngeal myositis.

Investigations were performed. Pulmonary function tests (FVC 53%; DLCO 51.4% predicted) and CT thorax showed pulmonary fibrosis. Serum creatinine kinase (CK 1011U/L [reference range 24-170]) and quadriceps muscle MRI confirmed myositis. Videofluoroscopy showed aspiration. Swallowing assessment demonstrated incomplete laryngeal elevation, marked pharyngeal residue and aspiration on swallowing food of all consistencies. Thus, recurrent aspiration from pharyngeal myositis was diagnosed and a multidisciplinary approach presented to the patient. In light of previous success at our centre, placement of a temporary PEG was proposed to reduce the risk of feeding-related aspiration, while the myositis was treated. However, after careful consideration, she declined PEG placement. Instead, she chose to continue on a modified oral diet and take care on swallowing, whilst starting prednisolone and mycophenolate mofetil for her myositis.

To-date, using this approach, she has successfully maintained her weight and has had no serious episodes of aspiration pneumonia. Meanwhile, her myositis has clinically and biochemically (CK 144) improved. However, given her precarious situation, due to her high risk of aspiration whilst immunosuppressed, she remains on close supervision by both gastroenterologists and rheumatologists.

Should her swallowing deteriorate, she is aware of PEG placement. Instead, she chose to continue on a modified oral diet and take care on swallowing, whilst starting prednisolone and mycophenolate mofetil for her myositis.

In summary, this case highlights the possibility of patients with SSc-myositis overlap developing oropharyngeal dysphagia, and describes the success of an alternative management strategy, when PEG placement is declined.

PS352
A MULTI-DISCIPLINARY APPROACH TO THE MANAGEMENT OF A PATIENT WITH RAPIDLY PROGRESSIVE SSC, SEVERE GASTROINTESTINAL INVOLVEMENT AND MALNUTRITION

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Patients with systemic sclerosis (SSc) may rapidly develop malnutrition, associated with morbidity and increased risk of mortality. Thus, when detected, early nutritional intervention is essential. We describe a case highlighting the benefit of a carefully coordinated approach by cross-speciality, multi-disciplinary teams.

A 59 year old female presented with Raynaud’s phenomenon, dry cough, hand swelling and weight loss (5kg over 2-3 months). On examination, she had dilated nailfold capillaries, distal skin thickening, bilateral cracales and proximal muscle weakness. She weighed 65.1kg, body mass index (BMI) of 23.9kg/m2. Investigations showed a raised ESR (40mm/hour), creatinine kinase (214U/L [24-170]) and cardiac troponin (66ng/L [0-14]), but normal full blood count, renal profile and albumin (42g/L). ANA and ENA were negative. Pulmonary function tests showed a restrictive pattern (FVC 1.45 L [49%]; DLCO 80.2% predicted). CT thorax showed basal interstitial changes and a dilated, fluid-filled oesophagus. Quadriceps muscle MRI showed bilateral, multi-focal, low grade myositis. Thus, SSc-myositis overlap was diagnosed. Prednisolone and azathioprine were commenced.

However, 2 months later, she returned with refractory vomiting and diarrhoea. On examination, her abdomen was distended and tympanic. She now weighed 62kg (BMI 22kg/m2). Albumin was low (26g/L). Barium follow-through showed a markedly dilated small bowel. A CT scan revealed considerable colonic bari-um retention. She failed to tolerate a hydrogen breath test. Therefore, rapidly progressive SSc-myositis overlap with extensive small intestinal and colonic involvement, causing pseudo-obstruction and delayed colonic transit, was diag-nosed.

Given this significant gastrointestinal involvement, associated with her rapid weight loss (>10% in <6 months), a combined gastroenterology, rheumatology and dietetic/nutrition support approach was taken. As she failed to tolerate a trial of nasogastric feeding, total parenteral nutrition (TPN) was initiated. Meanwhile, she was empirically treated for small intestinal bacterial overgrowth (cyclical antibiotics). As a result, her gastrointestinal symptoms dramatically improved, whilst her nutritional needs were supported. She discontinued TPN after 2 weeks.

Upon discharge, her weight was maintained on small, frequent meals (low fibre and food fortification) with enteral supplementation.

Now, on days 8, she continues on cyclical antibiotics and a lower dose of prednisolone and has started cyclophosphamide (substituted for azathioprine in view of her pulmonary fibrosis). Albumin (35g/L), creatinine kinase (38U/L) and cardiac troponin (22g/l) have all improved.

In summary, we highlight the need for the prompt, aggressive treatment, of patients with rapidly progressive SSc, by multi-disciplinary teams. In this case, the carefully coordinated inter-speciality multi-disciplinary approach was life-saving.

Angiosarcoma is a rare tumour which consists less than 1% of all soft tissue sarcomas. It most commonly affects elderly men with a poor prognosis. Angio- sarcoma is known to have an association with some conditions such as injury, lymphedema and prior radiation therapy. We report a case of cutaneous angiosarcoma in a 67-year-old woman with limited cutaneous systemic sclerosis (SSc). She noted Raynaud’s phenomenon from decades years before. She admitted our hospital claiming of the rapid growing tumour in the scalp. Clinical examination revealed multiple granulomatous tu-mors up to 8 cm in diameter. Skin sclerosis was observed on her fingers and dorsa of the hands, and also on the face and the scalp surrounding the tumor with salt-and-pepper like depigmentation. A biopsy of the tumor showed a prolif-eration of atypical polygonal tumor cells. Immunohistologically, the tumor cells showed strong immunoreactivity for CD31, vimentin and D2-40. We diag-nosed the tumor as angiosarcoma of the scalp. Although computed tomography revealed lymphadenopathy in the both cervical nodes, no visceral metastasis was evident. We conducted docetaxel monotherapy. As a result, all the tumors including lymph node metastases regressed completely after 9 cycles of weekly and 5 cycles of monthly administration of docetaxel. During the treatment, she devel-oped interstitial pneumonia but recovered by discontinuation of the treatment.

In summary, we highlight the need for the prompt, aggressive treatment, of patients with cutaneous angiosarcoma in a patient with SSc. All three cases developed in an area of sclerodermatous skin. Increasing evidence in-dicates that vascular damage is the primary event in the pathogenesis of SSc. This vascular damage causes the overexpression of the potent angiogenic mediator vascular endothelial growth factor (VEGF) in the skin and circulation of patients with SSc. One of the receptors of VEGF, VEGF receptor-3 has been reported to be upregulated in angiosarcoma. Therefore, we hypothesised that the overexpression of VEGF in angiosarcoma may be one of the mechanisms that leads to the development of angiosarcoma.

Thus, the overexpression of VEGF in SSc could play a causative role in the progression of angiosarcoma. It is important to recognize the association with angiosarcoma and SSc and perform a biopsy when suspicious lesion developed on sclerodermatous skin.
WHEN DOES SYSTEMIC SCLEROSIS IN CHILDHOOD REALLY START? AN ORIGINAL CASE REPORT

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We report the case of a boy who first presented to clinical attention at the age of 4 years old, with an hyperpigmented scleroderma-like skin lesion on the upper left limb. Laboratory findings showed an ANA (titre 1:320 on Hep-2) and anti-Scl70 antibodies positivity. Clinical assessment did not reveal any sign of systemic involvement while the skin lesions were attributed to lichen aureus.

At the age of 8 years, the patient developed a second, hyperpigmented, linear scleroderma-like lesion on the contra lateral arm. The clinical and laboratory assessment showed no systemic involvement but persistence of the autoantibodies abnormalities.

At the age of 13, the patient experienced a Raynaud’s phenomenon followed, one year later, by joint stiffness at the upper limbs. At the age of 15, the patient came to our observation. Clinical examination revealed diffuse induration with bilateral elbows and wrists contractures, the mRodnan skin score was 17/51, digital tip scars and bilateral malleolar ulcerations were also present. On the right arm, a linear hyperpigmented atrophic skin lesion was still evident. The overall organs system revealed a scleroderma active pattern on capillary microscopy, a slow esophageal distal tract transit and a right bundle branch block with right axis deviation. Pulmonary function tests and chest HRCT were normal. Laboratory findings confirmed a positivity of ANA (>1:640), anti-Topoisomerase1 (Scl70) antibodies.

At the best of our knowledge, this is the first report of a patient developing specific autoantibodies positivity several years before the onset of SSC. Indeed, the role of linear scleroderma-like lesions far before the disease onset should be elucidated.

In the large cohort of 127 patients with paediatric onset systemic sclerosis, included in the PRES database, 18 (14.4%) showed the first clinical signs before the age of 4 years. Among these patients, only 2 (11,1%) were male; 94.4% ANA+.

A RARE PRESENTATION OF NECK PAIN WITH RADICULOPATHY IN DIFFUSE CUTANEOUS SYSTEMIC SCLEROSIS

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Background. Systemic sclerosis (SSc) is a chronic multisystem heterogeneous autoimmune disorder of unknown aetiology. Calcinosi is one of the manifestations which may occur in up to 28% cases. It may vary from mild to severe and is not so common in diffuse cutaneous systemic sclerosis (dcSSc). The precise cause and treatment of calcinosi remains elusive.

Case Presentation. 56 year lady with dcSSc (Scl-70 positive) with onset of puffy fingers and skin thickening as 1st non-raynaud manifestation three and half years ago and current problems of severe raynauds (despite Sildenafil), digital pitting, sclerodactyly, joint and tendinopathy (finger to palm test 2cm), usual interstitial pneumonitis and upper gastrointestinal manifestations along with primary nodal osteoarthritis presented with progressive worsening of neck pain with radiation of pain with tingling to lateral aspect of her face and neck without focal weakness or reflex changes around mid 2012.

Light touch sensation was decreased over lateral aspect of neck and over C2-C3 dermatome region without tenderness in her spine. Cervical spine X-ray (Fig. 1) showed degenerative changes and heterotrophic calcification. MRI of brainstem and cervical spine revealed abnormal narrow signal in the left lateral C2 vertebral body involving the articular facet along with extensive calcified mass with severe narrowing of left C2/C3 neural exit foramen as well as encroachment of the lateral aspect of pharynx.

She was referred to neurosurgeon and had CT of head & neck stealth scan (Fig. 2) and angigram as a preoperative workup. Thereafter she had two stage procedures initially the lateral C1-C2 bony mass excision, C2 neural foramen decompression and thereafter the occipitocervical stabilization. She was on cervical hard collar for 6 weeks and mobilized thereafter with resolution of her symptoms.

Histology of the excised mass confirmed calcified material (von Kossa stain) within fibrocollagenous tissue with foreign type giant cell reaction without any evidence of caseating granulomatus inflammation or malignancy.

Discussion. Heterotrophic calcification is known to occur in lcSSc as part of CREST syndrome and tends to occur in soft tissues over areas of trauma or repeated friction like extensor surfaces of phalanges, forearm and around bony prominences. They may occur in unusual sites such as intracerebral and paraspinal (at times leading to serious consequences such as spinal instability given the proximity to facet joints, erosions and even cord compression) and Guyon’s canal leading to nerve entrapment. Very rarely dcSSc patients may have this phenomenon.

Plain X-rays are usually sufficient to reveal calcification, but CT scans allows better definition of calcification around the facet joints as well any erosive changes. MRI is usually undertaken to rule out possible intraspinal extension, cord or nerve compression.

Our lady had dcSSc rather than lcSSc and presented relatively early (compared to greater duration of SSc) with significant symptoms of nerve entrapment in the cervical region secondary to tumorous calcification which is rare and less well recognised complication of SSc.

We would suggest incorporating specific questions regarding any axial discomfort or symptoms of radiculopathy or nerve entrapment in the history and examination of all patients with SSc.
Digital ulcers on toes in patients with systemic sclerosis can be very painful, debilitating and reduce the quality of life significantly. Lack of understanding of the disease and treatment options can lead to unnecessary amputations or other surgical procedures.

In this case we describe a successful combined treatment with local anesthetics and botulinum toxin A.

A 61 year old man with systemic sclerosis of limited type presented treatment refractory digital ulcers on toes. There was a poor response to conventional treatment with nifedipine, tadalafil, sildenafil and iloprost and the patient complained of severe pain and disturbed sleep. A combined treatment as above mentioned prevented a threatening amputation. The treatment was repeated every 12 week. The patient was satisfied with the treatment and expressed a significantly improved quality of life, reduction of pain and healing of wounds.

Using botulinum toxin A combined with local anesthetics to severe digital ulcers in patients with systemic sclerosis could be another option, when other treatments have been ineffective.

The mechanism appears to be related to the paralysis of the blood vessel innervation which improve the availability of oxygen.