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Myositis and SSc: Clinical highlights 2019

OP0062

IDENTIFICATION OF SIX DERMATOMYOSITIS SUBGROUPS USING PRINCIPAL COMPONENT ANALYSIS-BASED CLUSTER ANALYSIS

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Background: Dermatomyositis (DM) is a heterogeneous disease with a wide range of clinical manifestations. Bohan and Peter suggested four subtypes of DM: idiopathic DM, juvenile DM, DM associated with cancer, and DM associated with other connective tissue diseases. Different DM subtypes have distinct clinical manifestations, responses to therapy and prognoses.

Objectives: The aim of the present study was to identify the clinical subtypes of DM by applying cluster analysis.

Methods: We retrospectively reviewed the medical records of 720 DM patients and selected 21 variables for analysis, including clinical characteristics, laboratory findings, and comorbidities. Principal component analysis (PCA) was first conducted to transform the 21 variables into independent principal components. Patient classification was then performed using cluster analysis based on the PCA-transformed data. The relationships among the clinical variables were also assessed.

Results: We transformed the 21 clinical variables into 9 independent principal components by PCA and identified 6 distinct subgroups. Cluster A was composed of two sub-clusters of patients with classical or moderate DM. Cluster-B patients were older and had malignancies. Cluster C was characterized by interstitial lung disease (ILD), skin ulcer, and minimal muscle involvement. Cluster D included patients with prominent lung, muscle, and skin involvement. Cluster E contained DM patients with other connective tissue diseases. Cluster F included all patients with myocarditis and prominent myositis and ILD. We found significant differences in treatment across the six clusters, with clusters C, D, and E being more likely to receive aggressive immunosuppressive therapy.

Conclusion: We applied cluster analysis to a large group of DM patients and identified six clinical subgroups, underscoring the need for better phenotypic characterization to help develop individualized treatments and improve prognosis.

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Fig. 1

Dermatomyositis Unsupervised combination of the Dermatomyositis Patients into Distinct Clusters

Fig. 2

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OP0063

SAFETY OF MYCOPHENOLATE MOFETIL TREATMENT IN SYSTEMIC SCLEROSIS IN REAL LIFE: REPORT FROM A SINGLE CENTER LARGE COHORT OBSERVATIONAL STUDY

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Background: Mycophenolate mofetil (MMF) has been increasingly used in the treatment of early diffuse cutaneous Systemic Sclerosis (dcSSc) and SSc-associated interstitial lung disease (SSc-ILD), and a recent Randomized Controlled Trial confirmed its efficacy and safety in SSc-ILD. However, the safety of this drug in the long term use has not been assessed in a real life setting.

Objectives: We aimed to analyze the period prevalence and the type of adverse events (AEs) associated to MMF treatment in a single center large cohort.

Methods: Charts of all SSc patients meeting the 2013 ACR/EULAR classification criteria consecutively visited at our outpatient clinic from January 1st 2017 to December 31st 2017 were retrospectively analyzed. Demographics, clinical, serological, functional, imaging data, treatments, and AEs were recorded. Patients were subgrouped according to the immunosuppressant (IS) taken during the observation period (e.g. MMF, azathioprine- AZA, or cyclophosphamide- CYC, no IS). The period prevalence of AEs was calculated and correlations of between AEs and patient features were investigated by univariate and multivariate analyses.

Results: Two-hundred and thirty-seven patients were included (92.4% were females, aged 56.4±11.3 years, with a median disease duration of 17 years, range 1-60). Among them, 85 (35.9%) were taking MMF, 34 (14.3%) AZA or CYC, 118 (49.8%) had no current IS treatment. Prevalence of the dcSSc subset was higher in the MMF group (34.1% versus 17.6% in the AZA/CYC group and 5.9% in the no IS group; p<0.05), while prevalence of ILD was similar in the MMF and in the AZA/CYC group and higher than the no IS group (89.4% and 82.3% versus 41.5%; p<0.05 for both), as well as the prevalence of the anti-topoisomerase I antibody positivity (60.7% and 52.9% versus 26.3%; p<0.05). Both patients treated with MMF and AZA/CYC had more frequently concomitant low-dose glucocorticoid (GC) therapy than patients without IS (76.5% for both groups versus 39%; p<0.05). In regard of total AEs, their prevalence was higher in the MMF group (71.7% versus 67% in the AZA/CYC group and 49% in the no IS group; p<0.05 MMF vs no IS). In particular, patients treated with MMF had a higher prevalence of total infectious AEs (55.7% versus 30.4% in the AZA/CYC group and 27.6% in the no IS group; p<0.05), predominantly airway infections (41.2% of all infectious AEs). Given so, we investigated the correlations of the infectious AEs in the MMF group with ILD, smoking history, and concurrent GC. However, we didn't find any significant association with these variables. When we looked for correlations of infectious AEs in the MMF group with other disease features, we found that they were correlated with the duration of the disease (median= 4 years; r=0.25; p=0.02) and with the presence of digital ulcers and/or pitting scars (r=0.22; p=0.03). No AE required hospitalization and resolved after treatment suspension.

Conclusion: The period prevalence of AEs recorded during MMF treatment appeared as high as 71.7% in our real life setting. Even though we did not record any serious AE, our analysis suggests a close monitoring of this therapy in SSC.

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OP0064

EVIDENCE-BASED CONSENSUS RECOMMENDATIONS FOR THE IDENTIFICATION AND MANAGEMENT OF INTERSTITIAL LUNG DISEASE IN SYSTEMIC SCLEROSIS

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Background: Interstitial lung disease in systemic sclerosis (SSc-ILD) occurs frequently and carries a high burden of morbidity and mortality. To date, there are no existing guidelines for screening, diagnosis and management of SSc-ILD that would aid early recognition and treatment and improve the care of these patients.

Objectives: To develop expert consensus recommendations for the identification and management of SSc-ILD.

Methods: Based on the results of a comprehensive systematic literature analysis conducted in line with NICE/CRD and IQWiG guidelines and PRISMA methodology, evidence-based statements on SSc-ILD risk, screening, diagnosis, treatment and follow-up were developed. A modified Delphi process was then used to establish consensus statements for the identification and management of SSc-ILD. Briefly, an expert panel of 27 European-based pulmonologists, rheumatologists and internists with experience in treating SSc-ILD was established. Between July and November 2018, the panel took part in 3 rounds of online surveys, a face-to-face discussion and a WebEx meeting to establish consensus-based recommendations for the management of SSc-ILD. Statements were categorised by topic: risk factors (including biomarkers); screening; diagnosis; assessment of severity; treatment initiation; treatment options; disease progression; treatment escalation; other management options. Panelists indicated their level of agreement with proposed statements on a scale of 1 (strong disagreement) to 7 (strong agreement), and consensus was considered achieved when ≥80% either disagreed (score of 1–3) or agreed (score of 5–7) with a statement. Based on panel feedback, statements that did not reach consensus were modified and re-voted in later rounds.

Results: At the close of the Delphi process, the panel agreed on the following:

1. Risk factors: The presence of anti-topoisomerase I antibodies, male gender and diffuse cutaneous SSc all increase risk for ILD
2. Screening: All SSc patients should undergo screening for ILD, using HRCT and lung function testing. Frequency of screening using HRCT should be guided by risk of developing ILD, in combination with clinical symptoms and lung function
3. Diagnosis and assessment of severity: Use of HRCT to diagnose SSc-ILD and assess severity, with supporting findings from lung function testing and clinical assessment, is also recommended
4. Treatment initiation and options: All patients with severe or progressive SSc-ILD should be considered for pharmacotherapy, with mycophenolate mofetil and cyclophosphamide recommended as treatments. Patients not receiving treatment should be followed closely for signs of disease progression
5. Disease progression: Indicators of progression include sustained decline in lung function, worsening of clinical symptoms, and change in extent and/or pattern of fibrosis on HRCT
6. Treatment escalation: Patients with inadequate treatment responses should be considered for treatment escalation. Suitability for lung transplant should be evaluated early, especially for patients diagnosed with advanced disease. Autologous haematopoietic stem cell transplant may be considered in carefully selected patients

Conclusion: These evidence-based expert consensus recommendations, developed using a modified Delphi process, provide important guidance for the identification and management of SSc-ILD.

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options or bond holdings in a for-profit corporation in Apellis, Grant/research support from: Received funds from BI advisory board participation and conference travel. Received research funding and/or consulting fees or other remuneration from GSK, UCB, AstraZeneca, Roche, Bayer, Biogen Idec, Cipla, Prometic, and Sanumed, Consultant for: Toby Maher has received consultancy or speakers fees from Apellis, AstraZeneca, Bayer, Biogen Idec, Boehringer Ingelheim, Galapagos, GlaxoSmithKline R&D, Indalo, Pliant, ProMetic, Roche, Samumed, and UCB; and has received consultancy fees from Galeto, Edward E Philpot Employee of: Employee of IQVIA, Ali Ashrafzadeh Employee of: Employee of IQVIA, Oliver Distler Grant/research support from: Prof. Distler received research funding from Actelion, Bayer, Boehringer Ingelheim and Mitsubishi Tanabe to investigate potential treatments of scleroderma and its complications, Consultant for: Prof. Distler has/had consultancy relationship within the last 3 years with Actelion, AnaMar, Bayer, Boehringer Ingelheim, ChemomAb, espeRare foundation, Genentech/Roche, GSK, Inventiva, Italfarmaco, IQVIA, Lilly, medac, MedImmune, Mitsubishi Tanabe Pharma, Pharmacyclics, Novartis, Pfizer, Sanofi, Serodapharm and UCB in the area of potential treatments of scleroderma and its complications. In addition, he had/had consultancy relationship within the last 3 years with A. Menarini, Amgen, Abbvie, GSK, Mepha, MSD, Pfizer and UCB in the field of arthritides and related disorders

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OP0065

THE VERY EARLY DIAGNOSIS OF SYSTEMIC SCLEROSIS (VEDOSS) PROJECT: PREDICTORS TO DEVELOP DEFINITE DISEASE FROM AN INTERNATIONAL MULTICENTRE STUDY

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Background: Early identification of patients is of key importance for the management and treatment of inflammatory rheumatic diseases.

Objectives: The aim of the VEDOSS project (1) is to determine through an at-risk population the predictive factors for the progression toward a definite systemic sclerosis (SSc).

Methods: VEDOSS investigators prospectively recruited patients with Raynaud phenomenon (RP), with or without anti-nuclear antibodies (ANA) for this longitudinal, observational study. Fulfilling the 2013 classification criteria at baseline was an exclusion criterion. Patients with primary Raynaud syndrome were recruited as controls. Patients had an annual assessment according to EUSTAR standards to determine organ involvement and severity. The endpoint was defined as fulfilment of the 2013 classification criteria. The time to fulfilling 2013 classification criteria was evaluated with Kaplan-Meier analysis, and predictors of evolution were determined by univariate and multivariate Cox regression.

Figure 1. A matrix was built to show the PPV of various variables alone or in combination to predict subsequent progression of VEDOSS patients toward definite SSc after 3 years

	alone	Disease specific atb	scleroderma pattern on NVC	puffy fingers
	PPV%	PPV%	PPV%	PPV%
Disease specific atb	70.2		82.2	94.1
scleroderma pattern on NVC	75.0	82.2		77.8
puffy fingers	78.9	94.1	77.8	

Results: 735 patients with RP were recruited into the study. The sample is distributed as follows: i) 237 patients (143 with follow up) RP/ANA negative (ANA/pRP) as the control group, ii) 498 patients (401 with follow up) RP/ANA positive (ANA+/pRP): 87 had puffy fingers (PF), 199 had anti-centromere antibodies (atb) positive, 45 had anti-topoisomerase I atb positive and 182 had nailfold videocapillaroscopy (NVC) abnormalities at baseline. Out of 401 ANA+/pRP patients, 7.4% within 1 year, 29.3% within 3 and 44.1% within 5 years satisfied the 2013 classification criteria. Out of the 143 ANA/pRP patients, none (0%) within 1 year, 4.6% within 3 years, and 4.6% within 5 years satisfied SSc criteria. After adjustment for age, the following baseline parameters were identified as independent predictors for progression into definite SSc by multivariate analysis: puffy fingers (OR=3.4 [2.0;5.6]), anti-centromere atb (OR=2.6 [1.6;4.1]) and anti-topoisomerase 1 atb (OR=3.1 [1.6;5.8]), and NVC abnormalities (OR=1.9 [1.3;2.9]) The presence of PF had a positive predictive value (PPV) of 79% and combination of PF + specific auto-antibodies showed 94% PPV to satisfy ACR/EULAR 2013 criteria within 5 years (figure 1).

Conclusion: the data show that patients with very early SSc develop definite, classification criteria fulfilling SSc within 5 years of follow up. The VEDOSS study