

# FRI0261 SKIN CANCER IN A COHORT OF SYSTEMIC LUPUS ERYTHEMATOSUS

M. Taraborelli<sup>1</sup>, C. Genitori<sup>2</sup>, I. Cavazzana<sup>3</sup>, M. Fredi<sup>3</sup>, A. Tincani<sup>4</sup>, P. Calzavara Pinton<sup>2</sup>, F. Franceschini<sup>3</sup>. <sup>1</sup>Internal Medicine Unit, Mellino Mellini Hospital, Chiari (Brescia); <sup>2</sup>Dermatology Unit and Chair, University and Spedali Civili di Brescia; <sup>3</sup>Rheumatology Unit, Spedali Civili di Brescia; <sup>4</sup>Rheumatology Unit and Chair, University and Spedali Civili di Brescia, Brescia, Italy

**Background:** Conflicting results about the prevalence of skin cancer in Systemic Lupus Erythematosus (SLE) have been reported in the literature [1,2].

**Objectives:** The aim of this study was to retrospectively evaluate the prevalence of malignancies, with a particular focus on skin cancers, in a cohort of SLE patients followed in a single Center.

**Methods:** All the SLE patients classified according to the ACR and SLICC criteria, attending the Rheumatology and Clinical Immunology Unit of Spedali Civili, Brescia, were retrospectively evaluated. Clinical and laboratory data were obtained from clinical charts. Diagnoses of skin cancers (melanoma and non-melanoma: basaloma, squamous cell carcinoma) and other malignancies were recorded together with the time elapsed from diagnosis of SLE. Univariate analysis was performed to compare characteristics of patients with (K+) and without (K-) cancer. We also compared the prevalence of cancer in our population to that reported in the Italian general population (from the Italian National Institute of Statistics, ISTAT, report 2014).

**Results:** In a cohort of 511 SLE patients (92% females, 95% caucasian) regularly followed from 1972 to 2016 (mean age at diagnosis 31 years±13 and median follow-up 12 years, range 1–40) we detected 51 cases (9.9%) with a history of malignancy: melanoma was reported in 3 (0.5%), non melanoma skin cancer (NMSC) in 11 (2%) and other malignancies in 38 cases (7.4%). Table I reports the comparison between patients with and without cancer. Patients with cancer, as well as cases with NMSC and non cutaneous malignancies, showed a higher age at disease onset ( $p<0.0001$ ;  $p=0.002$  and  $p<0.0001$  respectively) and higher SLE damage ( $p<0.0001$ ;  $p=0.019$  and  $p<0.0001$  respectively) compared with patients without malignancies. Patients with melanoma showed the same age at SLE onset, but a higher prevalence of discoid lupus ( $p<0.0001$ ) and oral ulcer history ( $p=0.02$ ). No difference in serological SLE features or in disease activity were detected between groups. The prevalence of melanoma in our cohort (0.5%) was only slightly higher than the one reported in the northern Italian general population (0.2%), while the prevalence of NMSC (2%) resulted to be significantly higher than that reported in the same population (prevalence of spinocellular and basocellular cancer 0.1% and 0.5% respectively).

Table I Characteristic of Systemic Lupus Erythematosus patients with and without cancer

Variable	All n. 511	K+ n. 51	K- n. 460	melanoma n. 3	NMSC n. 11	Other tumors n. 38
Male sex, n (%)	40 (8)	1 (1.9)	39 (8.4)	0 (0)	0	1 (2.6)
Mean age at diagnosis (years), (SD)	31.4 (12.7)	41 (14.48)	32 (12.1)	21 (1.5)	43 (18)	43 (12.6)
Mean disease duration, years (SD)	16.31 (9.53)	18 (22)	16 (9.3)	20 (4.5)	15 (11.7)	18 (11.5)
Mean SLEDAI-2K at inclusion (SD)	11.6 (6.02)	12.18 (5.81)	11.6 (6)	17.33 (8.96)	10.3 (2)	12.2 (6)
Mean last SLICC (SD)	1.5 (1.6)	3 (1.85)	1 (1.5)	3.67 (2.8)	2 (1.5)	3 (1.85)
Discoid lupus (%)	32	3 (5.8)	29 (6.3)	3 (100)	0 (0)	3 (7.8)
Acute cutaneous lupus (%)	270 (53)	24 (47)	246 (53.4)	3 (100)	5 (45.4)	17 (44.7)
Photosensitivity (%)	246/502 (49)	21 (41.1)	225 (48.9)	1 (33.3)	5 (45.4)	16 (42.1)
Glomerulonephritis (%)	160 (31)	13 (25.4)	147 (31.9)	1 (33.3)	2 (18.1)	10 (26.3)
Arthritis (%)	298 (58)	34 (66.6)	264 (57.3)	3 (100)	9 (81.8)	23 (60.5)
Oral ulcers (%)	170 (33)	12 (23.5)	158 (34.3)	3 (100)	0 (0)	9 (23.6)
Chronic alopecia (%)	47 (9.2)	5 (9.8)	39 (8.4)	1 (33.3)	1 (9)	3 (7.8)
Fernus (%)	81 (16)	10 (19.6)	71 (15.4)	0 (0)	4 (36.3)	6 (15.7)
Pericarditis (%)	63 (12)	5 (9.8)	58 (12.6)	0 (0)	2 (18.1)	3 (7.8)
Leucopenia (%)	134 (26)	14 (27.4)	120 (26)	3 (100)	5 (45.4)	7 (18.4)
Lymphopenia (%)	73 (14)	7 (13.7)	66 (14.3)	1 (33.3)	2 (18.1)	5 (13.1)
Thrombocytopenia (%)	91 (18)	9 (17.6)	82 (17.8)	1 (33.3)	1 (9)	7 (18.4)
Deep vein thrombosis/pulmonary embolism (%)	43 (8.4)	4 (7.8)	37 (8)	0 (0)	1 (9)	4 (10.5)
Anti-dsDNA (%)	439 (86)	43 (84.3)	396 (86)	3 (100)	10 (90.9)	31 (81.5)
Anti-ENA (%)	297 (58)	27 (52.9)	270 (58.6)	2 (66.6)	5 (45.4)	20 (52.6)
Antiphospholipid syndrome (%)	70/509 (13.7)	8 (15.6)	62 (13.4)	0 (0)	2 (18.1)	6 (15.7)
Lupus anticoagulant	115/326 (35.3)	14 (27.4)	136 (29.5)	1 (33.3)	3 (27.2)	10 (26.3)
aCL (IgG and/or IgM)	186/458 (40.6)	26 (50.9)	204 (44.3)	0 (0)	6 (54.5)	19 (50)
anti-B2GPI (IgG and/or IgM)	156/413 (37.8)	25 (49)	222 (48.2)	2 (66.6)	3 (27.2)	20 (52.6)

**Conclusions:** Non-melanoma was the most common skin cancer observed in our SLE cohort. Its prevalence appeared to be higher than that reported in the general population. SLE patients with melanoma showed a higher frequency of cutaneous lupus history compared with other SLE patients.

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# FRI0262 CLINICAL, LABORATORY AND IMMUNOLOGICAL CHARACTERISTICS OF 413 PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS IN SOUTH KOREA: A MULTICENTER RETROSPECTIVE COHORT STUDY

E.-K. Park<sup>1</sup>, S.-G. Lee<sup>1</sup>, J.-H. Park<sup>1</sup>, S.-M. Kwon<sup>1</sup>, D.H. Sohn<sup>2</sup>, Y. Kim<sup>3</sup>,

G.-T. Kim<sup>3</sup>, Y.-S. Suh<sup>4</sup>, H.-O. Kim<sup>4</sup>, J.-W. Lee<sup>5</sup>. <sup>1</sup>Internal Medicine, Pusan National University School of Medicine, Pusan National University Hospital, Busan; <sup>2</sup>Microbiology and Immunology, Pusan National University School of Medicine, Yangsan; <sup>3</sup>Internal Medicine, Kosin University College of Medicine, Busan; <sup>4</sup>Internal Medicine, Gyeongsang National University School of Medicine, Gyeongsang National University Changwon Hospital, Changwon; <sup>5</sup>Internal Medicine, Busan St. Mary's Hospital, Busan, Korea, Republic Of

**Background:** Epidemiologic studies have described clinical characteristics of patients with systemic lupus erythematosus (SLE) in Middle Eastern Asia and Western countries and marked ethnic and geographic differences in the prevalence, severity and outcome of SLE have been reported. However, data from Northeast Asia countries including South Korea are lacking.

**Objectives:** To investigate demographic, clinical, laboratory and immunological characteristics and prognosis of patients with SLE in South Korea.

**Methods:** We retrospectively evaluated 413 SLE patients (380 female, 33 male, mean age 40.6 years) diagnosed at 3 tertiary rheumatology centers in South Korea from 1992 to 2016 by reviewing medical chart. All patients fulfilled 1997 revised American College of Rheumatology classification criteria for SLE and were ethnically Korean.

**Results:** The mean (±SD) age at disease diagnosis was 30.9 (±12.8) years and the median (IQR) disease duration was 108 (60–168) months. The commonest clinical manifestations in our patients were arthritis (59.1%), fever (49.9%), malar rash (48.4%), alopecia (43.8%) and oral ulcer (35.1%). The frequency of major organ involvement was as follows: biopsy-proven lupus nephritis (40.7%), neuropsychiatric involvement (19.4%), secondary anti-phospholipid antibody syndrome (6.1%) and lupus pneumonitis (1.7%). Class IV (41.1%) was the most common type of lupus nephritis followed by class V (15.5%). Regarding hematologic abnormalities, the cumulative incidence of leucopenia was 74.3%, thrombocytopenia 46.5%, lymphopenia 45.1% and hemolytic anemia 8.7%. Antinuclear antibodies were detected in 97.8%, anti-Sm in 38.4%, anti-dsDNA IgG in 56.5%, anti-cardiolipine IgG in 27.4%, anti-cardiolipine IgM 11.8%, lupus anticoagulant in 23.2%, anti-Ro in 62.3%, anti-La 30.2% and anti-RNP in 47.9%. Twenty (4.8%) patients died during median follow-up of 84 months and the 5-year and 10-year survival rates were 96.9% and 95.5%, respectively (Figure 1). The major causes of death were infection (35%) and diffuse alveolar hemorrhage (20%). In multivariable Cox regression models, male (HR=8.68,  $p<0.001$ ), age at diagnosis  $\leq 16$  years (HR=3.33,  $p=0.033$ ), serositis (HR=3.04,  $p=0.018$ ) and thrombocytopenia (HR=3.23,  $p=0.041$ ) were associated with poor survival, while SLE patients with hydroxychloroquine use showed better survival (HR=0.11,  $p=0.001$ ).

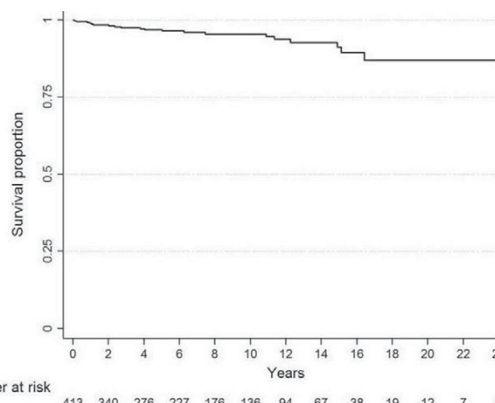


Figure 1. Kaplan-Meier survival curve of 413 patients with systemic lupus erythematosus

**Conclusions:** Compared with data from other countries, the higher prevalence of hematologic manifestations and positive anti-Ro antibody were prominent feature of South Korean SLE patients. Overall survival rate in our patients was better than that in other populations.

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# FRI0263 SYSTEMIC DISEASE ACTIVITY PROGRESSION IN A LARGE COHORT OF PRIMARY SJÖGREN'S SYNDROME: A LONG-TERM FOLLOW-UP DATA BASED ON THE ESSDAI SCORE

L. Quartuccio, S. Zandonella Callegger, S. Gandolfo, C. Fabro, S. De Vita. Rheumatology Clinic, Udine Hospital Santa Maria della Misericordia, Udine, Italy

**Background:** Primary Sjögren's syndrome (pSS) is a chronic slowly progressive

autoimmune disease, which mainly affects the salivary and lachrymal gland function. However, it is an autoimmune systemic disease with a widespread spectrum of systemic manifestations, which are now captured by validated scores (1).

**Objectives:** The aim of this retrospective study is to evaluate the disease course in a long-term follow-up, by focusing on the accrual of the systemic activity of the disease over time.

**Methods:** 254 patients suffering from pSS were studied. Mean (standard deviation) age at diagnosis was 52 (13) years. They were 235/254 (92.5%) females. Patients' chart were reviewed in order to compare the baseline ESSDAI score, ie calculated at the diagnosis, with the total ESSDAI accrual, by verifying the new onset ESSDAI domain and/or the worsening in already active ESSDAI domains in the whole available follow-up.

**Results:** The observation covered 9,1 (6,9) years of follow-up from the diagnosis to the last follow-up visit. The median (range) baseline ESSDAI was 4 (0-31), while the total ESSDAI score accrual up to the last visit was 7 (0-43) ( $p<0,0001$ , by Wilcoxon). The onset of new ESSDAI domains and/or worsening of already active ESSDAI domains was shown in 136/254 (53.5%) patients, accounting for a total amount of 210 onsets of new domains or worsening in the already active domains [9,1 (95% CI 5,2-27,7) events/100 patients/year]. There was no difference between patients with baseline ESSDAI score  $<5$  and patients with baseline ESSDAI score  $\geq 5$  (56/103, 54.4% vs 66/121, 54.5%). In only 15/135 (11.1%), the biologic domain was the sole ESSDAI domain, which was worsened or newly recorded. Finally, the ESSDAI domains, which more frequently raised or worsened in the follow-up were haematological (42/210, 20%), biological (37/210, 17.6%), articular (37/210, 17.6%), lymphadenopathy (28/210, 13.3%), and peripheral nervous system (15/210, 7.1%).

**Conclusions:** Primary Sjögren's syndrome is not a benign disease, a half of patients showing an increasing disease activity, and probably damage, in terms of new onset or worsening of already existing manifestations, even when the disease activity is low at the onset. Importantly, clinically relevant changes over time are much more frequently observed than only biological changes, thus suggesting the need of a careful follow-up by experts, as well as the unmet need of effective treatments, according to disease activity and damage.

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**FRI0264 EPIDEMIOLOGIC PROFILE OF ERECTILE DYSFUNCTION IN SLE: A MULTI-CENTER STUDY IN LATIN AMERICAN PATIENTS**

J. Merayo-Chalico<sup>1</sup>, A. Barrera-Vargas<sup>1</sup>, S. Morales-Padilla<sup>1</sup>, R. Reyna-De la Garza<sup>1</sup>, R. Vázquez-Rodríguez<sup>1</sup>, M. Sotomayor<sup>2</sup>, D. Gómez-Martín<sup>1</sup>, J. Alcocer-Varela<sup>1</sup>, C. Abud-Mendoza<sup>3</sup>, M. Martínez-Martínez<sup>3</sup>, I. Colunga-Pedraza<sup>4</sup>, C. Uriarte-Hernández<sup>5</sup>, I. Acosta-Hernández<sup>6</sup>, D. Fajardo<sup>7</sup>, C. García-García<sup>8</sup>, D. Padilla-Ortiz<sup>9,10</sup>. <sup>1</sup>Immunology and Rheumatology; <sup>2</sup>Urology, Instituto Nacional de Ciencias Médicas y Nutrición "Salvador Zubirán", Mexico City; <sup>3</sup>Rheumatology, Hospital Central "Dr. Ignacio Morones Prieto", San Luis Potosí; <sup>4</sup>Rheumatology, Hospital Universitario "Dr. José e González", Monterrey, Mexico; <sup>5</sup>Internal Medicine, Hospital Metropolitano "Vivian Pellas", Managua, Nicaragua; <sup>6</sup>Rheumatology, Instituto Salvadoreño del Seguro Social, San Salvador, El Salvador; <sup>7</sup>Rheumatology, Instituto Mexicano del Seguro Social, Guadalajara; <sup>8</sup>Departamento de Reumatología, Hospital General de México "Dr. Eduardo Liceaga", Mexico City, Mexico; <sup>9</sup>Internal Medicine, Hospital Universitario de la Samaritana; <sup>10</sup>Internal Medicine, Hospital Militar Central, Bogotá, Colombia

**Background:** Although systemic lupus erythematosus (SLE) has a higher prevalence in women, the disease usually has a more aggressive course in men. Information regarding erectile function in men with SLE is quite scant.

**Objectives:** The aim of this study was to describe the prevalence of erectile dysfunction (ED), as well as associated demographic and clinical features, in men with SLE, by means of a systematic, standardized evaluation.

**Methods:** We performed a transversal study in eight tertiary care centers in Latin America. We included male patients  $\geq 16$  years who fulfilled  $\geq 4$  ACR criteria for SLE, and who had regular sexual activity in the previous 6 months. Patients with other rheumatic diseases (except for APS), chronic viral infections and late-onset SLE were excluded. All patients answered the IIEF-5 Questionnaire, which has been validated in Spanish. Other relevant demographic, clinical and serological characteristics were documented. We included two control groups: the first one was made up by healthy men and the second by men with autoimmune diseases different from SLE (non-SLE group).

**Results:** We included 279 subjects (174 SLE, 55 non-SLE and 50 healthy controls). The prevalence of ED in SLE group 68% (vs 22% in healthy group,  $p=0.001$ ). The mean age of patients with ED in the SLE group was  $36.1\pm 1.03$ , while in patients without ED it was  $32.5\pm 1.27$  ( $p=0.022$ ). Whereas there was no difference regarding ED prevalence between SLE patients and the non-SLE group (68 vs 60%,  $p=0.25$ ), patients with other autoimmune diseases were 10 years older ( $46.3\pm 1.60$  years,  $p=0.001$ ).

Among SLE patients with and without ED, the presence of persistent lymphopenia ( $\leq 1000$ cells/mcl at three consecutive times,  $p=0.006$ ), the prednisone dose

( $9.3\pm 1.2$  vs  $5.3\pm 1.2$ mg,  $p=0.026$ ), as well as the SLICC damage score ( $1.2\pm 0.1$  vs  $0.8\pm 0.1$  points,  $p=0.026$ ), were significantly different. Comorbidities and other demographic, serological and treatment variables were not different between those groups. Multivariate analysis showed the following independent risk factors for ED in SLE patients: persistent lymphopenia (OR 2.79 CI95% [2.79-5.70],  $p=0.001$ ) and corticosteroid use (any dose) in the previous year (OR 2.15 CI95% [1.37-3.37],  $p=0.001$ ). Only 7% of patients had been questioned about their sexual function in the previous three visits to the rheumatologist; also, 81% of subjects considered it would be appropriate to be asked about their sexual function.

**Conclusions:** Regardless of comorbidities, treatment (excluding steroids) and type of disease activity, SLE patients have a high prevalence of ED, especially considering most patients are young and sexually active. Rheumatologists should be aware of the relevance of this problem in male SLE patients and should ask about this issues in regular visits.

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**FRI0265 CYTOKINES AND CORRELATIONS WITH PATIENT REPORTED OUTCOMES IN SYSTEMIC LUPUS ERYTHEMATOSUS AND POPULATION CONTROLS**

S. Pettersson<sup>1,2</sup>, H. Idborg<sup>3</sup>, S. Eketjäll<sup>4</sup>, I. Gunnarsson<sup>3</sup>, E. Svenungsson<sup>3</sup>. <sup>1</sup>Rheumatology unit, Karolinska University hospital; <sup>2</sup>Department of Neurobiology, Care Sciences and Society, Karolinska Institutet; <sup>3</sup>Rheumatology unit, Department of Medicine, Karolinska Institutet and Karolinska University Hospital, Stockholm; <sup>4</sup>Cardiovascular and Metabolic Diseases, Innovative Medicines and Early Development Biotech Unit, AstraZeneca, Integrated Cardio Metabolic Centre (ICMC), Karolinska Institutet, Huddinge, Sweden

**Background:** In open questions patients with systemic lupus erythematosus (SLE) report fatigue as the most distressing symptom. Pro-inflammatory cytokines are generally suggested to contribute to fatigue in chronic diseases, however results are contradictory (1, 2). Patient reported outcome measures (PROMs) quantify patients' experiences of qualities like fatigue and depression, which have great impact on both physical and psychological wellbeing. If PROMs are associated with pro-inflammatory cytokine activity in SLE has not yet been well investigated

**Objectives:** In this study we explored the relationship between a large set of cytokines and self-assessments of fatigue, anxiety, depression and quality of life in a large group of patients with SLE and in matched controls.

**Methods:** In a cross-sectional setting, persons with SLE and age- and gender-matched population controls responded to PROMs, assessing fatigue (Multidimensional Assessment of fatigue Scale), depression/anxiety (Hospital Anxiety and Depression Scale) and health related quality of life (Medical Short Form 36 (SF-36)). 30 cytokines were analyzed (MSD 30-plex cytokine assay). Spearman's rank correlation coefficient ( $r_s$ ) between cytokines and PROMs were calculated.

**Results:** 423 patients, age  $46.6 (\pm 15.3)$  and 315 controls age  $47.5 (\pm 14.6)$  ( $p=0.43$ ) were included. Of 30 analyzed cytokines 20 gave reliable results and were correlated to PROMs. Five of the cytokines (IL-6, TNF- $\alpha$ , IL-15, MCP-1 and MIP-1-beta) correlated best ( $r_s \geq 0.37$ ) with investigated PROMs (table 1). Fatigue correlated with TNF- $\alpha$  ( $r_s = 0.32$ ), IL-15 ( $r_s = 0.31$ ), and MIP-1-beta ( $r_s = 0.32$ ),  $p<0.01$  for all. When summarizing SF-36 results we noted a pattern of stronger correlations between investigated cytokines and the physical component than the mental component. Anxiety and depression correlated, but weakly ( $r_s < 0.25$ ).

Table 1. Correlations between cytokines and patient reported outcomes

	IL-6	TNF- $\alpha$	IL-15	MCP-1	MIP-1 $\beta$
Fatigue	0.28**	0.32**	0.31**	0.29**	0.32**
Anxiety	0.05	0.12**	0.12**	0.06	0.10**
Depression	0.19**	0.25**	0.21**	0.19**	0.21**
Physical Function <sup>§</sup>	-0.38**	-0.41**	-0.37**	-0.42**	-0.42**
Role Physical <sup>§</sup>	-0.29**	-0.38**	-0.32**	-0.35**	-0.34**
Bodily Pain <sup>§</sup>	-0.24**	-0.29**	-0.28**	-0.27**	-0.30**
General Health <sup>§</sup>	-0.37**	-0.45**	-0.37**	-0.40**	-0.38**
Vitality <sup>§</sup>	-0.26**	-0.34**	-0.29**	-0.29**	-0.30**
Social Function <sup>§</sup>	-0.20**	-0.27**	-0.27**	-0.25**	-0.25**
Role Emotional <sup>§</sup>	-0.12**	-0.24**	-0.18**	-0.16**	-0.16**
Mental Health <sup>§</sup>	-0.11**	-0.20**	-0.19**	-0.15**	-0.17**
Physical Component Summary score <sup>§</sup>	-0.39**	-0.43**	-0.38**	-0.42**	-0.41**
Mental Component Summary score <sup>§</sup>	-0.07	-0.16**	-0.15**	-0.10**	-0.11**

\*\*Spearman correlation is significant at the 0.01 level (2-tailed). <sup>§</sup>From SF-36.

**Conclusions:** Most PROMs were positively associated with pro-inflammatory cytokines. Fatigue and PROMs reflecting physical aspect of disease correlated most convincingly, while correlations with mental aspects were weaker.

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