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Background: Infectious disease is one of the leading causes of mortality in systemic lupus erythematosus (SLE). Among these infections, invasive fungal infection (IFI) carries high mortality rate (25-70%), but the literature of IFI in SLE is limited.

Table 1. Independent risk factors of IFI in patients with SLE^a

	Candidiasis		Cryptococcosis		Aspergillosis	
	HR (95% CI)	P value	HR (95% CI)	P value	HR (95% CI)	P value
Age>50	1.77 (1.27-2.47)	<0.001				
Diabetes mellitus	1.65 (1.16-2.35)	0.006				
End-stage renal disease	1.76 (1.29-2.41)	<0.001				
Stroke	1.77 (1.26-2.47)	<0.001	1.96 (1.09-3.53)	0.024		
Mycophenolate mofetil	2.72 (1.60-4.61)	<0.001			4.02 (1.32-12.26)	0.015
Cyclosporin					4.94 (1.61-15.10)	0.005
Cyclophosphamide	1.50 (1.07-2.10)	0.019				
Intravenous steroid	28.19 (21.17-37.52)	<0.001	63.51 (36.10-111.71)	<0.001	34.80 (15.09-80.24)	<0.001

^a All factors with $P < 0.05$ in univariate analysis were selected for Cox multivariate analysis. CI, confidence interval; HR, hazard ratio.

Figure 1. Incidence rate and incidence rate ratio of invasive fungal infection

Figure 2. Kaplan-Meier curve of invasive fungal infection-free status in SLE versus non-SLE group.

Objectives: To investigate the epidemiology and risk factors of invasive fungal infection and its subtypes, including candidiasis, aspergillosis, and cryptococcosis, in SLE patients.

Methods: All patients with newly diagnosed SLE between 1997-2012 were enrolled from Taiwan National Health Insurance Research Database, with an age- and sex-matched non-SLE control group in a ratio of 1:10. IFI was identified by ICD9 codes¹ from discharge record and validated by use of systemic anti-fungal agents. The incidence rate (IR), incidence rate ratio (IRR), cause mortality rate of IFI and its subtypes were compared. A Cox multivariate model with time-dependent covariates was applied to analyse the independent risk factors of IFI.

Results: A total of 269 951 subjects (24 541 SLE and 245 410 control) were included. There were 445 episodes of IFI in SLE group. Candida was the most common pathogen (52.8%), followed by cryptococcus and aspergillus. The IR of IFI in SLE was 20.83 per 10,000 person-years with an IRR of 11.1 (95% CI 9.8-12.6) compared to the control (figure 1). Kaplan-Meier curve also disclosed a lower IFI-free survival in SLE (figure 2). The all-cause mortality rate was similar between SLE and the control (26.7 vs 25.7%). In SLE, treatment with mycophenolate mofetil (HR=2.24, 95% CI 1.48-3.37), cyclosporin (HR=1.65, 95% CI 1.10-1.75), cyclophosphamide (HR=1.37, 95% CI 1.07-1.75), oral daily dose of steroid>5 mg prednisolone (HR=1.26, 95% CI 1.01-1.58), and intravenous steroid therapy (HR=29.11, 95% CI 23.30-36.37) were identified as independent risk factors of IFI. Similar analyses were performed for subtypes of IFI. Distinctive risk factors were found between different subtypes of IFI (table 1).

Conclusion: SLE patients have a higher risk of IFI. Intravenous steroid therapy is the most important risk factor of IFI. This study provides crucial information for risk stratification of IFI in SLE.

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FRI0550 CAN CYTOKINE GENE POLYMORPHISMS BE USEFUL FOR THE THERAPEUTIC CHOICE IN JAPANESE PATIENTS WITH RHEUMATOID ARTHRITIS?

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Background: Rheumatoid arthritis (RA) is a common autoimmune disease. It is characterized by systemic synovitis with bone erosion and joint cartilage degradation(1). Production of autoantibody is important for autoimmune disease. Cytokines play crucial roles in its pathogenesis(2). SNP distribution varies between races. Few studies have examined SNP targeted at Japanese patients. The analysis of cytokine gene polymorphisms is important factor of pathophysiology and treatment.

Objectives: This analysis was aimed to investigate the association between cytokine gene polymorphisms and autoantibody and therapeutic response in Japanese RA patients.

Methods: This study subjects consisted of 100 RA patients and 50 healthy controls. We extracted data on patient sex, age, disease duration, rheumatoid factor (RF), anti cyclic citrullinated peptide (anti-CCP) antibody and therapeutic response including methotrexate (MTX) and biological DMARDs. Genomic DNA was isolated from peripheral blood, these were genotyped for TNFα, TGFβ₁, IL-6, IL-10 and IFNγ polymorphisms. We analyzed these data using a chi-square test.

Results: IL-10 (-819 C/T and -592 C/A) revealed that there were significant decrease in the frequency of IL-10 (-819) CC genotype and (-592) CC genotype as compared to controls in RA patients. Genotyping of IL-10 showed that there was significant decrease ACC/ACC genotype (Table 1).

IFNγ (+874 A/T) revealed that there was significant decrease in the frequency of TT genotype as compared to controls (Table 1).

No significant differences in TNFα, TGFβ₁ and IL-6 genotypes and alleles frequency were observed between RA patients and control.

TGFβ₁ (+869 A/T) in patients with anti-CCP antibody positive revealed that there was significant decrease in the frequency of TT genotype as compared to patients with anti-CCP antibody negative (Table 2).

No significant association between RF and any cytokine gene polymorphism.

Analyzing cytokine gene polymorphisms could be useful for treatment with MTX and biological DMARDs.

Conclusion: IL-10 (-819 C/T, -592 C/A) and IFN γ (+874 A/T) polymorphism might be related to RA in Japanese population. In addition, TGF β_1 (+869 A/T) polymorphism might be associated with the production of anti-CCP antibody. These results suggest that the analyzing cytokine gene polymorphisms may offer promise as useful factors in the choice of treatment for Japanese RA patients.

Table 1.

Cytokine GT* & alleles	RA (n=100)	Controls (n=50)
IFN γ +874		
A/T	21.0% (21/100)	16.0% (8/50)
T/T	0% (0/100)	6.0% (3/50)
A/A	79.0% (79/100)	78.0% (39/50)
A allele	89.5% (179/200)	86.0% (86/100)
T allele	10.5% (21/200)	14.0% (14/100)
IL-10		
Genotypes		
ACC/ACC (Lo)	5.0% (5/100)	22.0% (11/50)
ACC/ATA (Lo)	43.0% (43/100)	32.0% (16/50)
ATA/ATA (Lo)	46.0% (46/100)	40.0% (20/50)
GCC/ACC (Int)	3.0% (3/100)	1.0% (1/50)
GCC/ATA (Int)	2.0% (2/100)	2.0% (2/50)
GCC/GCC (Hi)	0% (0/100)	0% (0/50)
IL-10 -819 (C/T)		
C/C	89.0% (89/100)	24.0% (12/50)
C/T	45.6% (46/100)	36.0% (18/50)
T/T	45.6% (46/100)	40.0% (20/50)
C allele	31.0% (62/200)	42.0% (42/100)
T allele	69.0% (138/200)	58.0% (58/100)

* : genotype

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Table 2.

Cytokine GT* and alleles	RA (n=100)	ACPA-positive (n= 70)	ACPA-negative (n= 30)	Controls (n= 50)
TGF β_1 +869				
T/C	52.0% (52/100)	60.0% (42/70)	33.3% (10/30)	52.0% (26/50)
C/C	28.0% (28/100)	20.0% (14/70)	46.7% (14/30)	22.0% (11/50)
T/T	20.0% (20/100)	20.0% (6/30)	20.0% (6/30)	26.0% (13/50)
T allele	46.0% (92/200)	50.0% (70/140)	36.7% (22/60)	52.0% (52/100)
C allele	54.0% (108/200)	50.5% (70/140)	63.3% (38/60)	48.0% (48/100)

* : genotype

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FRI0551 PERFORMANCE OF THE 2019 AMERICAN COLLEGE OF RHEUMATOLOGY/EUROPEAN LEAGUE AGAINST RHEUMATISM SYSTEMIC LUPUS ERYTHEMATOSUS CLASSIFICATION CRITERIA

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Background: Systemic lupus erythematosus (SLE) is a heterogenous autoimmune disease, with increased morbidity and mortality, often diagnosed in advanced stages. The recently published 2019 American College Of Rheumatology/European League Against Rheumatism (ACR/EULAR) classification criteria for SLE are weighted, hierarchically clustered criteria developed to increase reliability and the identification of early SLE.

Objectives: To compare the sensitivity and specificity of the 2019 ACR/EULAR criteria with the 2012 SLICC criteria in a large single-centre cohort of patients with SLE, diagnosed according to expert opinion.

Methods: Data of SLE patients evaluated in our centre between 1996-2019 have been retrospectively analyzed. The control cohort included patients with positive antinuclear antibodies of other etiology than SLE, evaluated between 2001-2019. The sensitivity and specificity of the 2019 ACR/EULAR and 2012 SLICC criteria were tested using the McNemar test for correlated proportions.

Results: Four hundred and forty-six patients with SLE (413 women, mean $\pm$ SD age 40.5 $\pm$ 12.7 years, disease duration 10.1 $\pm$ 9.2 years) and 67 controls (63 women, mean $\pm$ SD age 50.4 $\pm$ 12.6 years, disease duration 7.6 $\pm$ 6.9 years; 29 systemic sclerosis (SSc), 18 mixed connective tissue disease (MCTD), 15 undifferentiated CTD, 2 rheumatoid arthritis (RA), 2 SSc – RA overlaps and 1 dermatomyositis) were included. The sensitivity of the 2019 ACR/EULAR and 2012 SLICC criteria were similar 85.4% and 83.6 %, respectively (p=0.3). The specificity of the 2019 ACR/EULAR and 2012 SLICC criteria were 70.2 % and 86.6%, respectively (p=0.007). In the SLE group, patients misclassified according to the new 2019 ACR/EULAR criteria were 65, whereas according to the 2012 SLICC criteria were 73; of them, 44 patients did not fulfill any criteria. In the control group, patients misclassified had mainly MCTD (13/20 patients according to the new 2019 ACR/EULAR, and 8/9 according to the 2012 SLICC criteria).

Conclusion: In this real-life cohort, the 2019 ACR/EULAR criteria have a similar sensitivity and lower specificity than the 2012 SLICC criteria, misclassifying especially MCTD patients. These results might be due to the long disease duration in our cohort.

References:

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FRI0552 GLOBAL, REGIONAL, AND NATIONAL BURDEN OF LOW BACK PAIN, 1990-2019: A SYSTEMATIC ANALYSIS FOR THE GLOBAL BURDEN OF DISEASE STUDY 2019

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Background: Low back pain (LBP) has become a major public health problem worldwide although the burden and underlying causes differ across locations and demographic groups.

Objectives: To report the distribution, trend and risk factor in the burden of LBP from the Global Burden of Disease Study 2019 (GBD 2019).

Methods: Based on GBD 2019, decomposition analyses were performed according to gender, age, geography and sociodemographic index (SDI). The number and age standardized rate of incidence, prevalence and disability adjusted life years (DALYs) with 95% uncertainty intervals (UI) were calculated.

Results: In 2019, female patients have a slightly higher number of prevalence (17%), incidence (15%) and DALYs (16%) than male patients. Out of twenty 5-year age group, the number of incidences, prevalence, DALYs peak at 50-54 age group, while the rate of incidence, prevalence, DALYs peaked at 80-84 age group. From 5 SDI regions, the highest number and age-standardized rate of incidence, prevalence, DALYs were observed in middle and high SDI region, respectively. Considering 21 GBD regions, the highest number of incidence, prevalence, and DALYs were observed in East Asia, while the highest age standardized rate of incidence, prevalence and DALYs all found in Central Europe, High-income North America, High-income North America, respectively. In 204 countries and territories, the top 3 highest number of incidence, prevalence and DALYs were from China, India, United States of America. The top 3 highest age-standardized rate of prevalence, and DALYs were Georgia, United States of America, Denmark, while top 3 highest age-standardized rate of incidence were Poland, Vanuatu, Romania.

From 1990 to 2019, globally, the number of incidence, prevalence, DALYs increased by 50%, 47%, 47% to 223,738,363 (95%UI 197,935,799-253,300,243), 569,089,727 (95% UI 505,632,980-641,256,710), 63,533,528 (95%UI 44,883,714-84,975,210), while age standardized rate of incidence, prevalence and DALYs decreased by 13%, 16%, 16% to 2,750 (95%UI 2,427-3,108), 6,974 (95%UI 6,192-7,862), 778 (95%UI 548-1,043). In 5 SDI regions, low SDI region has the highest percentage increases in number of incidence, prevalence and DALYs, the highest percentage decrease in age standardized rate of incidence, prevalence and DALYs were observed in High-middle SDI. In 21 GBD regions, the highest percentage increase in number of incidence, prevalence and DALYs