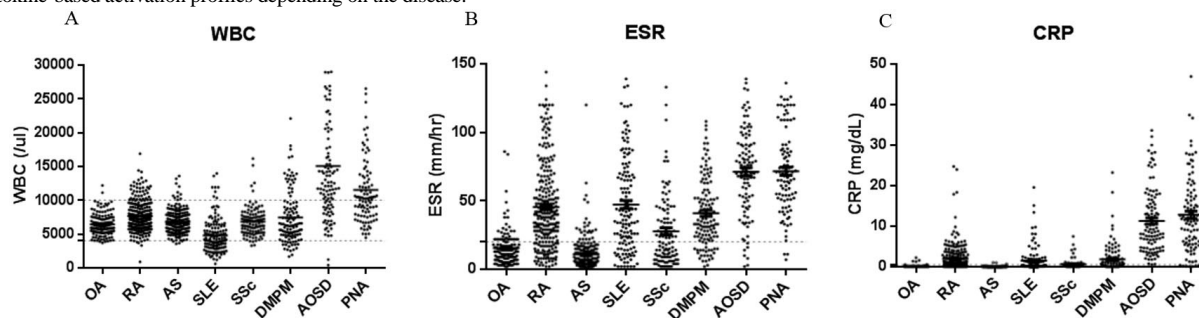


Association of inflammatory markers in treatment-naïve patients with systemic rheumatic diseases

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Background/Aims: Routine inflammatory markers are not always elevated in systematic rheumatic diseases (SRD). Here, we aimed to evaluate and compare inflammatory markers in SRD systematically. **Methods:** A total of 1191 treatment-naïve patients with SRD which include rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), systemic sclerosis (SSc), dermatomyositis/polymyositis (DM/PM), ankylosing spondylitis (AS) and adult onset Still's disease (AOSD) patients, and patients with osteoarthritis (OA) and pneumonia, who were treated at Seoul National University Hospital during 2004-2016 was included in this retrospective study. Association between erythrocyte sedimentation rate (ESR), C reactive protein (CRP) and white blood cell (WBC) count in SRD assessed by correlation and regression analysis. **Results:** Leukocytosis was present less than 15% in all SRD. Compared with pneumonia, the mean WBC count was lower and normal in patients with SRD. Both ESR and CRP were elevated in RA patients, while only ESR was elevated in patients with SLE and DM/PM. Patients with SSc and AS showed normal range of both ESR and CRP, similar with OA. The WBC count showed no significant correlation with ESR in all SRD. Patients with all SRD showed significant correlation between ESR and CRP, but weakest correlation in SLE patients ($r=0.20$, $p=0.03$). **Conclusions:** Unlike acute infection, leukocytosis was rare and consequently there was discrepancy between WBC count and acute phase proteins in rheumatic diseases. In addition, magnitude of correlation between ESR and CRP in each rheumatic diseases was different and it indicates distinct cytokine-based activation profiles depending on the disease.



The effect of peripheral arthritis on TNF inhibitor treatment duration in patient with AS

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Background/Aims: Tumor necrosis factor α inhibitor (TNFi) therapy has been shown to be remarkably effective for treating ankylosing spondylitis (AS); however, nearly 30% of AS patients every year either stop TNFi therapy or switch to a different TNFi due to inefficacy or adverse effects. The goal of this study was to identify predictors of TNFi treatment duration, including extra-articular manifestations, using a nationwide registry in Korea. **Methods:** Data were obtained from the Korean College of Rheumatology Biologics (KOBIO) registry, a nationwide, multi-center database representing 58 tertiary-care hospitals in Korea. Demographics, clinical features, laboratory findings, disease activity indices (BASDAI, ASDAS-ESR, ASDAS-CRP), peripheral arthritis, and extra-articular manifestations (uveitis, enthesitis, dactylitis, psoriasis, and inflammatory bowel disease) were studied in patients with AS during TNFi therapy. We also analyzed treatment duration outcomes for 5 TNFi agents (etanercept, infliximab, infliximab biosimilar, adalimumab, and golimumab), as well as factors associated with treatment duration, particularly in terms of extra-articular manifestations. Univariable and multivariable cox regression analyses were performed to verify preliminary results. **Results:** A total of 1,482 AS patients starting TNFi drug therapy between Dec 2012 and Jan 2017 were included. No differences in demographics, disease activity, or extra-articular manifestations were evident between continued and discontinued TNFi groups at baseline, though baseline differences were detected for gender distribution, CRP, platelet counts, and HLA-B27 positivity. The presence of peripheral arthritis was significantly associated with TNFi treatment duration (unadjusted HR: 2.21, 95% CI: 1.66 to 2.95; adjusted HR: 1.38, 95% CI: 1.01 to 1.88). Among disease activity indices, higher ASDAS-ESR levels were significantly associated with TNFi treatment duration (unadjusted HR: 1.87, 95% CI: 1.73 to 2.03; adjusted HR: 2.23, 95% CI: 2.00 to 2.63). **Conclusions:** The development of peripheral arthritis during TNFi therapy was associated with a higher risk of TNFi treatment discontinuance in AS patients.

Table 2. Cumulative comparison between discontinued and continued group with univariate and multivariate cox regression analysis of TNFi, peripheral arthritis, extra-articular manifestations and disease activity indices.

	Discontinued N=78 (cases)	Continued N=78 (cases)	Univariate HR(95% CI)	p-value	Multivariate HR(95% CI)	p-value
Tumor necrosis factor α inhibitor, n (%)						
Etanercept	58 (74.2)	110 (14.1)	Reference			
Infliximab	41 (52.6)	52 (6.7)	1.30 (0.87-1.94)	0.21	1.48 (0.97-2.28)	0.07
Infliximab biosimilar	62 (79.5)	121 (15.5)	0.94 (0.54-1.55)	0.74	0.84 (0.56-1.26)	0.40
Adalimumab	131 (168.8)	287 (36.7)	0.84 (0.41-1.15)	0.29	1.06 (0.75-1.51)	0.73
Golimumab	46 (59.0)	211 (27.0)	0.46 (0.31-0.68)	<0.001**	0.65 (0.43-0.99)	0.04*
Peripheral arthritis, n (%)	57 (73.1)	77 (9.9)	2.21 (1.66-2.95)	<0.001**	1.38 (1.01-1.88)	0.04*
Extra-articular manifestations, n (%)						
Enthesitis	19 (24.4)	31 (4.0)	1.94 (1.25-3.09)	0.005*		
Uveitis	18 (23.1)	55 (7.1)	0.92 (0.57-1.48)	0.74		
Dactylitis	3 (3.9)	2 (0.3)	2.05 (0.66-6.39)	0.22		
Psoriasis	19 (24.4)	22 (2.8)	2.22 (1.39-3.53)	0.003*		
Inflammatory bowel disease	2 (2.6)	9 (1.2)	0.55 (0.14-2.19)	0.392		
Disease activity indices, mean (s.d.)						
BASDAI (0-10)	4.2 (2.8)	2.3 (1.7)	1.36 (1.01-1.82)	<0.001**		
VAS for PGA (0-10)	4.6 (2.8)	2.7 (2.1)	1.30 (1.01-1.65)	<0.001**		
ESR (mm)	21.8 (25.1)	12.0 (13.7)	1.02 (1.02-1.03)	<0.001**	0.99 (0.98-1.00)	0.001**
CRP (mg/dL)	1.10 (2.35)	0.45 (0.77)	1.14 (1.10-1.19)	<0.001**		
ASDAS-ESR (0-10)	2.6 (1.3)	1.7 (0.8)	1.87 (1.57-2.03)	<0.001**	2.23 (2.00-2.63)	<0.001**
ASDAS-CRP (0-10)	2.4 (1.4)	1.5 (0.9)	1.74 (1.61-1.89)	<0.001**		

If the patient stopped or switched again after discontinuation of another TNFi, the case was again counted as part of the discontinued group. Therefore, the size of discontinued group is greater than the number of discontinued patients.
Cox regression analysis with: baseline values: HR, hazard ratio; CI, confidence interval; BASDAI, Bath ankylosing spondylitis disease activity index; VAS for PGA, Visual Analogue Scale for Patient Global Assessment; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein; ASDAS, Ankylosing Spondylitis Disease Activity Score. * $p < 0.05$, ** $p < 0.001$.

Figure 2. Kaplan-Meier treatment duration curves for peripheral arthritis and each extra-articular manifestation. Patients who do not have peripheral arthritis (A), enthesitis (B), and psoriasis (C) show longer treatment duration. Uveitis (D), dactylitis (E), and inflammatory bowel disease (F) do not affect treatment duration. * $p < 0.05$, ** $p < 0.001$.

