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## Generation of new carotid plaque is influenced by ongoing disease activity of rheumatoid arthritis

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**Background/Purpose:** Rheumatoid arthritis (RA) is associated with an increased susceptibility to cardiovascular (CV) disease which has a causal relationship with carotid atherosclerosis. In the present study, we investigated the risk factors for progression of carotid atherosclerosis in RA patients in the Kyungpook National University Hospital Atherosclerosis Risk in Rheumatoid Arthritis (KARRA) cohort study. **Methods:** After a baseline evaluation for KARRA enrollment, all RA patients and healthy controls were prospectively followed up for 5 years or until deaths. We analyzed the demographic findings, conventional risk factors and RA disease activity. Carotid ultrasound at baseline and year 5 was performed to evaluation of the intima-medial thickness (IMT) and presence and progression of carotid plaque. **Results:** A total of 417 RA patients and 221 age- and sex- matched healthy controls were included at baseline, and 325 RA patients and 160 healthy controls were followed for the 5 year period. Mean age and female frequency of RA patients were not different compared with those of healthy controls. At year 5, the mean carotid IMT of RA patients was higher than that of controls [0.85 mm (S.D. 0.15) vs. 0.88 (S.D. 0.18),  $p=0.04$ ]. New development of carotid plaques at year 5 in RA patients ( $n=93$ ) was predicted by IMT and total and LDL cholesterol at baseline, while it was associated with IMT and DAS28-CRP at year 5. Multivariate logistic regression analysis revealed that baseline IMT (OR 72.14 [95% CI 5.15-101.12;  $p=0.001$ ]) and DAS28-CRP at year 5 (OR 1.69 [95% CI 1.15-2.48;  $p=0.008$ ]) were independent risk factors for new plaque formation in 5 year followed period. **Conclusions:** This study shows that generation of new carotid plaque after long-term follow-up depends on the preexisting carotid atherosclerosis that is aggravated by suboptimal disease control.

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## Impacts of disease activity and neurotrophic factors on depression in rheumatoid arthritis

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**Background:** Rheumatoid arthritis (RA) and depression is closely associated with each other. The neurotrophic factors are related with major depressive disorder (MDD). However, the impacts of disease activity, pro-inflammatory cytokines and neurotrophic factors on depression in RA patients have not well studied. **Objectives:** To determine the risk factors for depression and to examine the effect of disease activity, pro-inflammatory cytokines and neurotrophic factors on depression in patients with RA. **Methods:** This cross sectional study was conducted from Jan, 2014 to Jan, 2015 from 3 university hospitals. Demographic and laboratory data were examined and routine assessment of patient index data 3 (RAPID 3) questionnaire and 28 joints disease activity score (DAS28-CRP) were assessed for disease activity. Depression was measured by Korean version of the Beck Depression Inventory second edition (K-BDI II). Serum level of pro-inflammatory cytokines and neurotrophic factors such as BDNF, VEGF, GDNF, and IGF-1 were assessed by ELISA. **Results:** A total of 507 RA patients were recruited. The prevalence of depression was 33.1% ( $n=168$ ). RAPID 3 score (OR 1.2, 95% CI 1.1-1.4,  $p=0.006$ ) and severity of fatigue (OR 1.19, 95%CI 1.07-1.32,  $p=0.001$ ) showed significant associations with depression in multivariate analysis. The RA patients with DAS 28-CRP  $\geq 3.2$  ( $n=126$ ) had more risk for depression than those with DAS 28-CRP  $< 3.2$  ( $n=279$ ) in multivariate analysis (OR 2.02 95% CI 1.34-3.06,  $p=0.006$ ). When patients was followed up for a year after strict treatment, as DAS28-CRP decreased, BDI score also decreased ( $\Delta$ DAS28-CRP:  $-1.4 \pm 1.6$ , and  $\Delta$ K-BDI II:  $-5.4 \pm 10.1$ ,  $p < 0.001$ ). There were no relationships between pro-inflammatory cytokines and depression (IL-1 $\beta$ :  $r=0.057$ , IL-6:  $r=0.169$ , TNF- $\alpha$ :  $r=-0.078$ ). In the case of neurotrophic factors, the level of BDNF showed weakly correlation with K-BDI II score ( $r=-0.233$ ,  $p < 0.001$ ). **Conclusions:** This study suggests strict control of fatigue and disease activity is important in regulating depressive symptoms in patients with RA. To evaluate psychologic manifestation of RA patients, using both RAPID 3 score and DAS28 might be helpful.