

Smoking does not protect axial spondyloarthritis patients from attacks of uveitis

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Acute anterior uveitis (AAU) is the commonest extra-axial manifestation in axial spondyloarthritis (axSpA) and can lead to visual impairment if untreated. Cross-sectional axSpA studies have consistently reported lower odds of AAU in current smokers than ex- or never smokers [1,2], which is in contrast to higher AAU risk among smokers in the general population [3]. One explanation for this apparent paradox is behaviour change; those with AAU may be more likely to quit smoking. However, this does not explain the higher odds of AAU in never smokers. Another possibility is that smoking is protective for AAU as it is for ulcerative colitis, which shares patho-aetiology with axSpA and AAU [4]. If smoking is protective of AAU, it should also reduce the frequency of flares. We examined the impact of smoking status on the number of AAU episodes among patients with AAU.

The British Society for Rheumatology Biologics Register for Ankylosing Spondylitis is a prospective study of patients fulfilling the ASAS criteria for axSpA [5]. AAU diagnoses were physician confirmed. The number of documented episodes of, and treatment for, AAU between each study visit were extracted from patient records. The maximum number of episodes in each 12-month period was our outcome of interest. Participants who received AAU treatment were assumed to have had an episode. Study visits with ≤ 6 -month interval were discarded to reduce the likelihood of recording the same episode more than once. We used negative binomial mixed models to test whether smoking status (current, ex- or never) was associated with frequency of episodes, adjusting for age, gender, symptom duration, the Bath AS Disease Activity Index and use of TNF inhibitors. Since smoking has been suggested to influence response to biologic therapy, we also stratified the analysis for the biologic and non-biologic cohorts. As sensitivity analysis, we restricted the maximum number of episodes per year to 5 and 10 to test whether effect estimates were robust against potential outliers.

Among 2,420 axSpA participants, 632 (26%) were diagnosed with AAU through the study period, contributing 1,457 patient-years of follow-up. The mean age was 50.8 years ($SD \pm 13.3$) and 68% were males. The number of recorded AAU episodes per 12-month period ranged from 0 to 15. Compared to never smokers, both current (incidence rate ratio (IRR) 1.33; 95%CI 0.92, 1.92) and ex-smokers (IRR 1.19; 95%CI 0.88, 1.59) had higher incidence of AAU episodes, although not statistically significant. In the biologic cohort, current smokers had 76% per year higher incidence (IRR 1.76; 95%CI 1.02, 3.04) compared to never smokers, while ex-smokers had 29% higher incidence (IRR 1.29; 95%CI 0.77, 2.15) (figure 1). As covariates, age and symptom duration were not associated with IRR of uveitis attacks. Results from sensitivity analyses were similar (see online supplementary text).

In this longitudinal axSpA cohort, we showed general trends that smoking was associated with increased incidence rate of AAU episodes. The 'protective' effect of smoking seen in cross-sectional studies is likely not causal. This is consistent with increased risk of uveitis observed among smokers

in the general population [3]. Although nicotine may have anti-inflammatory properties, cigarette smoking is overall pro-inflammatory. When studies restrict to a disease population, spurious relationships can emerge between two common causes: Smoking, which is known to increase risk of psoriatic arthritis in the general population, was found to reduce this risk when restricted to patients with psoriasis [6]. Larger population studies are needed to further examine the role of collider bias for smoking and uveitis in axSpA. Smoking increases radiographic progression in AS and may reduce response to treatment; our study provides yet another line of evidence highlighting the importance of smoking cessation among patients with axSpA.

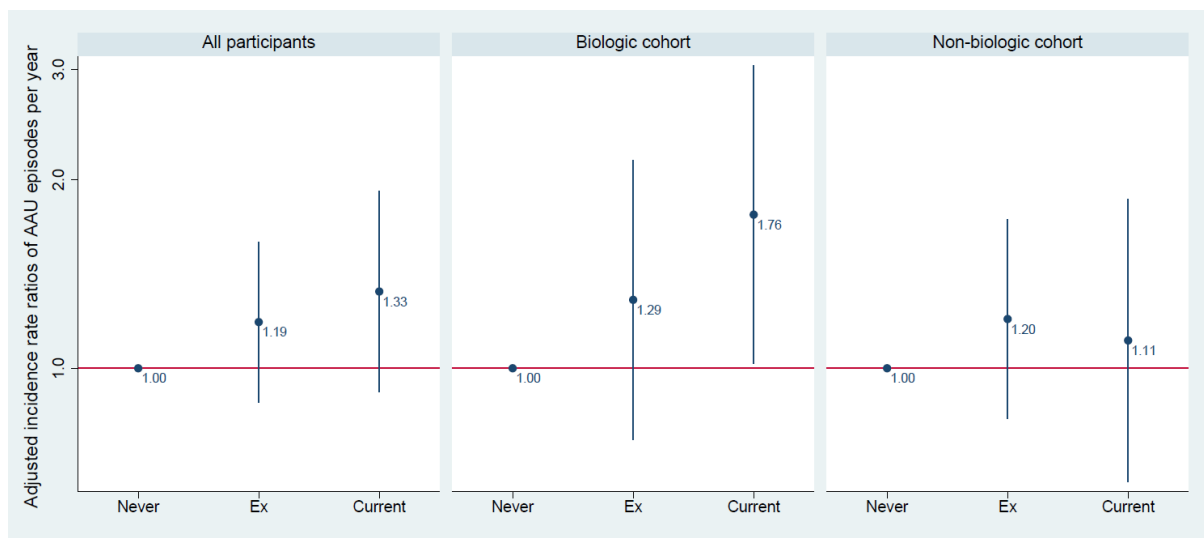


Figure 1. Smoking was associated with higher incidence rate of acute anterior uveitis episodes.

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