



<b>Title</b>	<b>Age-dependent alterations of cigarette smoke-induced oxidative and inflammatory responses in rats</b>
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**Introduction:** Depression has previously been reported to be more common among patients with rheumatoid arthritis (RA). Whether active disease and decreased function are associated with depressive symptoms in Chinese patients with RA remains controversial. The study aimed to examine whether disease activity and functional status were associated with depressive symptoms in a cohort of Chinese RA patients and their effects on the health-related quality of life (QOL).

**Methods:** Consecutive RA patients were recruited from a local rheumatology clinic. Socio-demographics, depressive symptoms (depression subscale of the Hospital Anxiety and Depression Scale [HADS]), disease activity (Disease Activity Score using 28 joint counts [DAS28]), functional status (Health Assessment Questionnaire [HAQ], and functional class) and QOL (Short-Form 36 version 2 health survey [SF36v2]) of the patients were analysed.

**Results:** A total of 202 RA patients were recruited. Multivariate linear regression using HADS depression score as dependent variable showed that higher HAQ scores ( $\beta=0.33$ ,  $P<0.001$ ), higher functional class ( $\beta=0.41$ ,  $P<0.001$ ) and past history of depression ( $\beta=0.17$ ,  $P<0.001$ ) were significantly associated with depressive symptoms. DAS28 was not found to be a significant factor. The RA cohort was found to have worse QOL compared with the general population in Hong Kong. The HADS depression score, DAS28 and HAQ were all inversely correlated with SF36v2 physical and mental health with  $P<0.001$ .

**Conclusion:** Functional limitation and past history of depression were independently associated with depressive symptoms in RA patients. Both disease parameters including DAS28 and HAQ as well as depressive symptoms contributed to poor QOL of these patients.

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**Background:** Cigarette smoking (CS) is a leading cause of chronic obstructive pulmonary disease (COPD). The prevalence of COPD is much higher among the elderly. However, the impact of early-age CS exposure on CS-induced COPD is unknown. This study aimed to investigate whether CS-induced oxidative and inflammatory responses were age-dependent in an acute CS-exposed rat model.

**Methods:** Male Sprague-Dawley rats of 6-7 weeks of age (juvenile) and >8 months of age (adult) were randomly divided into two groups, respectively (n=5-6 in each group), one of which was exposed to 4% CS for 1 hour twice daily for 5 days in ventilated smoking chambers, while the other group was exposed to sham air (SA). Blood and lung tissues were collected 24 hours after last CS exposure. Oxidative stress markers such as 8-isoprostane and malondialdehyde (MDA) and pro-/anti-inflammatory markers such as transforming growth factor- $\beta_1$  (TGF- $\beta_1$ ) and adiponectin were measured.

**Results:** Cigarette smoking exposure significantly elevated serum 8-isoprostane and lung MDA levels in juvenile group (8-isoprostane:  $4.56 \pm 0.33$  ng/mL vs  $2.46 \pm 0.21$  ng/mL for CS- and SA-exposed rats respectively;  $P<0.01$ ) [MDA:  $12.06 \pm 0.94$  nmol/mg protein vs  $6.06 \pm 0.35$  nmol/mg protein for CS- and SA-exposed rats respectively;  $P<0.001$ ) but not in adult group. In contrast, serum adiponectin level was unaltered in juvenile group but significantly decreased in adult group after CS exposure ( $9.72 \pm 0.65$   $\mu$ g/mL vs  $14.00 \pm 0.9$   $\mu$ g/mL for CS- and SA-exposed rats respectively;  $P<0.01$ ). For plasma TGF- $\beta_1$  level, CS exposure caused significant elevation in adult group ( $15.70 \pm 3.20$  ng/mL vs  $8.24 \pm 1.33$  ng/mL for CS- and SA-exposed rats respectively;  $P<0.05$ ) but not in juvenile group.

**Conclusion:** The oxidative and inflammatory responses to CS vary depending on age. The early life is particularly at risk for the development of CS-induced oxidative stress, which may be one of the mechanisms leading to lung tissue damage following CS exposure over time.

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