ORIGINAL RESEARCH LETTER

Occupational exposures and asthma–COPD overlap in a clinical cohort of adult-onset asthma

To the Editor:

Asthma–COPD overlap (ACO) has recently been recognised as a separate phenotype of obstructive airway diseases and is included in several guidelines of asthma and COPD [1–5]. ACO patients have previously been shown to have lower diffusing capacity of the lung, higher blood neutrophil counts and higher interleukin-6 levels compared with asthma patients [6]. In COPD, fixed airway obstruction is considered to develop in response to chronic exposure to noxious inhaled particles [7]. In western countries, the most common cause of COPD is tobacco smoking, but occupational exposure to dusts and fumes has also been shown to increase the risk for developing COPD [7, 8]. However, the role of occupational exposures in the development of ACO is not known.

We studied the association between ACO and occupational exposures to vapours, gases, dusts or fumes (VGDF) in the cohort of the Seinäjoki Adult Asthma Study (SAAS). In the SAAS, 257 patients were diagnosed with new-onset asthma at adult age and followed for 12 years. Diagnosis was made by a respiratory physician and based on objective lung function measurements and medical history [6, 9–12]. Ex- and current smokers were included, and the smoking history of every patient was carefully assessed. After 12 years (years 2012–2013), patients had a control visit, and the occupational data were retrospectively collected. To evaluate the duration of the patients' occupation, the occupation at the time of asthma diagnosis was confirmed from patient records. Patients with detailed smoking history available (n=194) at the follow-up visit were included in the current study. Patients were considered as ACO patients if they had a ⩾10-pack-year history of smoking and post-bronchodilation forced expiratory volume in 1 s (FEV_1)/forced vital capacity (FVC) ratio <0.7 at the follow-up visit. The subjects were divided into two groups based on whether they had occupational exposure history to VGDF (*i.e.* welders, foundry workers, sheet metal workers, smiths, machine workshop workers, mechanics and farmers).

The prevalence of ACO was higher in the group with occupational VGDF exposure, compared to patients with no exposure. Patients with occupational VGDF exposure were older and more often males. A tendency towards higher body mass index (BMI) in patients with occupational VGDF exposure was seen. No differences in the prevalence of allergic conditions or in the use of daily inhaled corticosteroids were seen between the groups (table 1). No statistically significant differences in the rate of airway obstruction at the time of diagnosis were seen between the groups, although a tendency towards more severe obstruction among patients with occupational VGDF exposure was observed: post-bronchodilation FEV_1/FVC (95% CI) was 0.77 (0.72–0.81) among patients with occupational VGDF exposure, and 0.79 (0.75–0.84) in patients with no VGDF exposure (p=0.060).

The mean±SD smoking history of the ACO patients did not differ between the groups: 27.4±13.0 pack-years in ACO patients with no occupational VGDF exposure, and 27.4±17.4 pack-years in ACO patients with VGDF exposure (p=0.992). The prevalence of obstructive asthma was similar between the groups, *i.e.* asthma patients with low smoking history (<10 pack-years) but fixed airway obstruction (post-bronchodilation FEV_1/FVC <0.7) (table 1).

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Occupational exposure to vapours, gases, dusts or fumes (VGDF) increases the prevalence of asthma–COPD overlap (ACO) in adult-onset asthma. VGDF exposure is independently associated with ACO and an additive effect with smoking is proposed. http://bit.ly/2LiMiXW

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TABLE 1 Clinical characteristics and prevalence of asthma–COPD overlap in groups of different occupational exposure to vapours, gases, dusts or fumes (VGDF)

	No occupational exposure to VGDF	Occupational exposure to VGDF	p-value
Patients n	150	44	
Asthma–COPD overlap	21 (14)	13 (30)	0.024¶
Age years	57.3±13.3	62.3±13.9	0.030¶
BMI kg·m^{-2}	27.7 (24.2–30.8)	29.6 (25.4–32.0)	0.057
Males	50 (33)	31 (71)	<0.001¶
Allergic rhinitis or conjunctivitis	90 (62)	28 (65)	0.723
ICS in daily use	120 (80)	33 (75)	0.530
Smoking history ⩾10 pack-years	47 (31.3)	19 (43.2)	0.152
Obstructive asthma#	15 (10)	5 (11)	0.782

Data are presented as n (%), mean±SD or median (interquartile range), unless otherwise stated. BMI: body mass index; ICS: inhaled corticosteroids. #: <10 pack-years and forced expiratory volume in 1 s/forced vital capacity ratio <0.7; ¶: p<0.05.

We further analysed the factors associated with airway obstruction and ACO with two multivariable logistic regression analyses: 1) with a regression model among all patients (n=194), we analysed the factors associated with airway obstruction (*i.e.* FEV_1/FVC <0.7); and 2) with a regression model among patients with ⩾10 pack-years of smoking history (n=65), we analysed the factors associated with ACO. Among all patients, the number of pack-years (OR 1.05, 95% CI 1.02–1.08; p<0.001) and age (OR 1.04, 95% CI 1.01–1.07; p=0.008) were significantly associated with airway obstruction, whereas BMI ⩾30 kg·m^{-2} was associated with lower risk of obstruction (OR 0.37, 95% CI 0.16–0.85; p=0.019). Sex or occupational VGDF exposure were not associated with obstruction. Among patients with ⩾10 pack-years of smoking, a significant factor associated with ACO was occupational VGDF exposure (OR 4.2, 95% CI 1.1–15.3; p=0.030), whereas BMI ⩾30 kg·m^{-2} was associated with lower risk of ACO (OR 0.18, 95% CI 0.06–0.59; p=0.004). The number of pack-years was not associated with ACO among patients with smoking history ⩾10 pack-years (OR 1.02, 95% CI 0.98–1.07; p=0.281). Sex, age or smoking status (never-/ex-/current smoker) were not significantly associated with ACO as analysed by backward, forward or enter methods and, thus, were not included in the final model.

Our results suggest that adult-onset asthma patients with occupational exposure to VGDF more often develop ACO, compared with patients with no such exposure. The smoking history of ACO patients was similar, regardless of their exposure to VGDF, suggesting that heavier smoking is not the reason for increased ACO prevalence in the group with occupational VGDF exposure in our study. In addition, the proportion of patients with smoking history ⩾10 pack-years did not differ between the groups. The patients with occupational VGDF exposure were older than patients without. However, the rate of airway obstruction at the time of asthma diagnosis was not significantly different between the groups. Thus, the increased ACO rate in the group of occupational VGDF exposure is not merely explained by inferior lung function at the diagnosis. Furthermore, when we evaluated the prevalence of non- or low-smoking patients (<10 pack-years) with fixed airway obstruction (*i.e.* obstructive asthma), we found no differences between the groups. This finding suggests that, in adult-onset asthma, occupational exposure alone is not driving the risk of ACO but rather the combination of occupational exposure and smoking. This is in keeping with the previous suggestions of the additive effect of smoking and other environmental exposures in the development of COPD [13]. Furthermore, the multivariable regression analyses showed that occupational VGDF exposure was independently associated with ACO among patients with ⩾10 pack-years of smoking history. In contrast, obesity seemed to lower the risk of ACO. This finding might be explained by reduction of FVC in obese patients, leading to decreased sensitivity of FEV_1/FVC ratio in detecting obstruction [14]. Although patients in the group with occupational exposures were older and more often males, age and sex were not associated with ACO.

In the current study, 17% (n=33) reported farming as their main profession, and when metal workers were also assessed, up to 23% (n=44) were considered as working in a profession linked to increased risk of developing COPD. This gives us a good view of work-related ACO in real-life asthma patients. Furthermore, the diagnosis of asthma was based on objective lung function measurements, and diagnostic guidelines were carefully followed. The quantity of exposure to occupational particles was not measured, which could be considered as a limitation of the current study. However, the reported occupational

information was confirmed from patient records, showing stability of profession during the 12 years of follow-up on nearly all patients. We also recognise the possibility of occupational exposures in other professions (*e.g.* cleaners, waiters). However, considering the current knowledge of occupational exposures, we assessed the professions that are presumed to have the highest exposure related to development of fixed airway obstruction.

Taken together, our results show increased prevalence of ACO in the group of adult-onset asthma patients with occupational VGDF exposure. This is a new finding and in line with what is known on the additive effect of smoking and occupational exposure in the development of fixed airways obstruction and COPD. We thus support active intervention in primary and occupational healthcare, aiming towards smoking cessation and protection against occupational noxious particles in the air.

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