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Title: Indications of small airways disease in healthy smokers

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Body: It has been well established that small airways disease is a risk factor for COPD development. Cigarette smoking is the main risk factor for COPD development. We investigated whether smokers, without COPD and an FEV₁ >80 %pred, have indications of small airways involvement. Healthy smokers and non-smokers (asymptomatic, FEV₁ >80 %pred, FEV₁/FVC >70%) were included. We performed spirometry, body plethysmography, and impulse oscillometry (IOS) in all subjects. Smokers were compared to non-smokers using Student's t- or Mann Whitney U test. 56 non-smokers (28 ≤40 years and 28 >40 years old) and 54 smokers (26 ≤40 years and 28 >40 years old) were included. Large airways parameters were comparable between smokers and non-smokers. In contrast, small airways parameters differed between smokers and non-smokers. Smokers had a lower FEF₂₅₋₇₅ %pred than non-smokers. Furthermore, smokers had a higher R5-20 (difference between the resistance at 5Hz and 20Hz), a higher reactance area (AX) and a higher resonance frequency (Rf) than non-smokers. In addition, smokers ≤40 years had a higher R5-20, AX and Rf than non-smokers. No differences in RV or RV/TLC were found between smokers and non-smokers. We demonstrate changes in small airways parameters in smokers with normal lung function. These changes are already present in smokers ≤40 years old. Whether this small airways disease in young smokers is a first step in COPD development, remains to be elucidated in further studies.