Lung function and cardiovascular disease: a two-sample Mendelian randomisation study

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Shareable abstract (@ERSpublications)
This two-sample multivariable Mendelian randomisation study provides strong evidence that FVC (but not FEV_1 or FEV_1/FVC <0.7) is causally associated with coronary artery disease https://bit.ly/3t05kWJ

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Abstract

Background Observational studies suggest an association between reduced lung function and risk of coronary artery disease and ischaemic stroke, independent of shared cardiovascular risk factors such as cigarette smoking. We use the latest genetic epidemiological methods to determine whether impaired lung function is causally associated with an increased risk of cardiovascular disease.

Methods and findings Mendelian randomisation uses genetic variants as instrumental variables to investigate causation. Preliminary analysis used two-sample Mendelian randomisation with lung function single nucleotide polymorphisms. To avoid collider bias, the main analysis used single nucleotide polymorphisms for lung function identified from UKBiobank in a multivariable Mendelian randomisation model conditioning for height, body mass index and smoking.

Multivariable Mendelian randomisation shows strong evidence that reduced forced vital capacity (FVC) causes increased risk of coronary artery disease (OR 1.32, 95% CI 1.19–1.46 per standard deviation). Reduced forced expiratory volume in 1 s (FEV_1) is unlikely to cause increased risk of coronary artery disease, as evidence of its effect becomes weak after conditioning for height (OR 1.08, 95% CI 0.89–1.30). There is weak evidence that reduced lung function increases risk of ischaemic stroke.

Conclusion There is strong evidence that reduced FVC is independently and causally associated with coronary artery disease. Although the mechanism remains unclear, FVC could be taken into consideration when assessing cardiovascular risk and considered a potential target for reducing cardiovascular events. FEV_1 and airflow obstruction do not appear to cause increased cardiovascular events; confounding and collider bias may explain previous findings of a causal association.