Cystic Fibrosis Research News

Title:

Abnormal Alveolar Microstructure in Cystic Fibrosis Lung Disease via Hyperpolarized ^{129}Xe Diffusion MRI

Lay Title:

Measuring Abnormal Lung Microstructure in People with Cystic Fibrosis Using Xenon Magnetic Resonance Imaging

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What was your research question?

Alveoli are microscopic air sacs that perform pulmonary gas exchange (i.e., the uptake of oxygen and elimination of carbon dioxide by the pulmonary blood). When alveoli are abnormally small, they can collapse and reduce gas exchange. When alveoli are destroyed or enlarged by diseases like emphysema, gas-exchange surface area decreases, which also reduces gas exchange. Do people with cystic fibrosis have abnormally sized alveoli?

Why is this important?

Because people with CF now experience decades of increased lifespan, new structural and functional abnormalities may emerge over time. Sub-clinical pathology (disease-related abnormalities that can be identified in a laboratory testing or imaging, etc. but cause no

current signs or symptoms to the individual)—in particular lung pathology—must be identified, so it can be treated before becoming irreversible. Lung disease begins in the small airways and worsens through progressive damage to the pulmonary tissues. Studies using x-ray computed tomography (CT) suggest structural pathology extends down to the alveolar level in people with CF. Unfortunately, it is difficult to measure these microstructural changes over time, because current clinical tools are invasive (biopsy) or require ionizing radiation (CT). Therefore, non-invasive imaging techniques are needed to measure alveolar damage across the lifespan.

What did you do?

Diffusion-weighted, xenon MRI is a safe, radiation-free method to measure the motion (diffusivity) of inhaled xenon atoms, and this diffusivity is restricted by alveolar walls. Xenon MRI can therefore assess alveolar size noninvasively. Xenon MRI was performed in 38 healthy people and 39 people with CF (ages 6-40 years). Because alveolar size increases with normal growth and aging, diffusion MRI data from healthy participants were used to create an age-dependent model of normal alveolar size. Based on the results from the healthy people, the alveolar sizes in people with CF were divided into three levels: abnormally small, normal, and abnormally large.

What did you find?

As expected, xenon MRI showed alveolar size increases significantly with age in both healthy participants and people with CF. However, the lungs of people with CF contained a high percentage of both abnormally small and large alveoli, and these abnormalities were prevalent across all ages.

What does this mean and reasons for caution?

Alveolar size—and therefore—also regional gas exchange is abnormal in people with CF. As people with CF age into adult and ultimately geriatric care, these abnormalities may become important contributors to lung disease. However, these studies were conducted at one time-point and data were collected before participants started highly effective modulator therapy (drugs that correct the malfunctioning protein responsible for causing CF). Therefore, the rate of alveolar remodelling and the degree to which it will remain widespread remains uncertain.

What's next?

Establishing the prevalence, progression rate, and clinical significance of alveolar abnormalities in CF will require multi-centre, longitudinal studies with diffusion-weighted

xenon MRI. Xenon MRI is increasingly available and is approved for clinical use in multiple countries. Therefore, multi-centre studies are feasible and may enable improved monitoring of CF lung disease.

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