

Cystic Fibrosis Research News

Title:

Lung Function Decline is Delayed But Not Decreased in Patients With Cystic Fibrosis and the *R117H* Gene Mutation

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What was your research question?

We wanted to see if lung function decline differs between patients with cystic fibrosis (CF) who have "mild" lung disease (e.g. patients with at least one R117H CF gene mutation) and those with "typical" lung disease (e.g. patients with two F508del CF gene mutations).

Why is this important?

Some patients with CF are considered to have "mild" lung disease based on their CF gene mutations; however, they still develop progressive breathing problems as they get older. We questioned if lung disease in this patient group begins in childhood and is slow to progress, or if lung disease is delayed into adulthood and then rapidly progresses. Answering this question will lead to better clinical care for these patients, as well as providing a better understanding of the basic lung disease in CF.

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What did you do?

We used the US CF Foundation Patient Registry to identify patients with either one/two R117H or two F508del CF gene mutations. We then used 5 years of data to determine the rate of lung function decline, as measured by the forced expiratory volume in one second (FEV1), in both group of patients. This rate of decline was calculated first for all patients and subsequently, for separate age groups (6-12 years, 13-17 years, 18-24 years, and 25 years or older).

What did you find?

We found that the overall rate of lung function decline was less in the patients with one/two R117H CF gene mutations (156 patients included) compared to those with two F508del CF gene mutations (6251 patients included). However, a large difference in lung function decline was observed when the patients were separated by age. For patients under 18 years old, lung function in the patients with one/two R117H CF gene mutations did not decline over time (in fact lung function improved slightly in the 6-12 years old group). However, in the patients with one/two R117H CF gene mutations, who were 18 years and over, the rate of lung function decline did not differ from that observed in the patients with two F508del CF gene mutations.

What does this mean and reasons for caution?

The results suggest that there is a delayed lung disease progression in those with one/two R117H CF gene mutations and this finding provides an opportunity for better understanding of the factors that contribute to CF related lung disease. Clinically the finding may lead to more effective interventions and monitoring of these patients. Although we were unable to evaluate how younger patients were being treated, the findings suggest that younger patients may not benefit from therapies designed to treat patients with deteriorating lung function. Additionally, the findings strongly indicate that adults with the R117H CF gene mutation need close monitoring to detect changes in lung function and potentially intervene early, before rapidly progressive lung disease occurs.

What's next?

Further study is needed to better understand the factors causing progressive lung disease in patients with "mild" CF. Risk factors need to be defined so that patients at risk of rapid lung function decline can be identified. Therapies for "typical" CF lung disease need to be evaluated in patients with "mild" CF lung disease. Finally, other "mild" CF gene mutations need to be studied.



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