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Cystic Fibrosis Research News

Title:

Disease Burden in People With Cystic Fibrosis Heterozygous for *F508del* and a Minimal Function Mutation

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What was your research question?

We looked at the burden (impact) of CF on people with CF who have a particular combination of mutations in the *CFTR* gene: one mutation called *F508del-CFTR* and another called a minimal function mutation. This combination of mutations is referred to as the *F*/MF genotype.

Why is this important?

We know a lot about the burden of illness in people with CF who have two copies of the *F508del-CFTR* mutation. However, the burden of CF in people with *F*/MF genotypes has not been thoroughly studied.

What did you do?

We used data from the US CF Foundation Patient Registry (which collects information on the health of people in the US with CF) from the year 2017 to look at health information for people with *F*/MF genotypes who were at least 2 years old, prior to these patients starting any CFTR modulator treatment. We looked at how well the lungs work (measured by the amount of air blown out in 1 second), nutrition, and rates of bacterial lung infections, hospitalizations, episodes of worsening lung disease symptoms (pulmonary exacerbations), and other health complications related to CF.

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What did you find?

People with CF with *F*/MF genotypes have a high burden of disease that worsens with age. We found that older people with *F*/MF genotypes had more bacterial lung infections, hospitalizations, and pulmonary exacerbations than younger people. The use of medications to treat CF symptoms was higher and lung function was lower in older people than in younger people. Compared with younger people, more adolescents and adults had CF-related health complications, including liver disease bone conditions that result in weak, easily broken bones (osteoporosis and osteopenia), and sinus disease. People with worse lung function tended to have a particular bacterial infection, called *Pseudomonas aeruginosa,* more frequently. They also were prescribed medications for CF more often. Additionally, in people of all ages, lung function was slightly better in non-Hispanic people with CF than in Hispanic people with CF.

What does this mean and reasons for caution?

This finding is consistent with what is known about the progressive nature of CF, and it highlights the need for additional treatment options in this group. One factor that limits our interpretation of this study is that we did not include a second group of people with CF with well-known disease burden for comparison (such as a group with two copies of the *F508del-CFTR* mutation).

What's next?

The combination drug elexacaftor/tezacaftor/ivacaftor is now approved by the US Food and Drug Administration (FDA) to treat CF in people 6 years and older and by the European Commission to treat CF in people 12 years and older. It was shown to be effective and safe in people with *F*/MF genotypes. Additional studies looking at the disease burden in this group may help future researchers to understand the impact of elexacaftor/tezacaftor/ivacaftor and similar treatments in this group of people with CF.

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