European Cystic Fibrosis Society

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Cystic Fibrosis Research News

Title:
CFTR-function and ventilation inhomogeneity in individuals with Cystic Fibrosis

Lay Title:
The association between the function of the cellular salt channel *cystic fibrosis transmembrane conductance regulator* and lung function in people with cystic fibrosis

Authors:
Nadine Bernasconi[1], Elisabeth Kieninger[2], Michelle Shaw[3], Johanna Kurz[2], Alexander Moeller[1], Felix Ratjen[3], Isabelle Rochat[4], Sanja Stanojevic[3], Florian Singer[2]

Affiliations:
[1]Division of Respiratory Medicine, University Children's Hospital of Zurich, Zurich, Switzerland.
[2]Pediatric Respiratory Medicine, Department of Pediatrics, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland.
[3]Division of Respiratory Medicine, Department of Pediatrics, The Hospital for Sick Children, University of Toronto, Toronto, Canada.
[4]Pediatric Pulmonology Unit, Department of Pediatrics, CHUV Lausanne, University Hospital of Lausanne, Switzerland.

Corresponding Author
Florian Singer, MD, PhD
Pediatric Respiratory Medicine, Department of Pediatrics,
Inselspital, Bern University Hospital, University of Bern,
Freiburgstrasse 15, Bern, Switzerland.
Tel.: +41 31 632 2111. E-mail: florian.singer@insel.ch

What was your research question?
Cystic Fibrosis Transmembrane Regulator (CFTR) gene variants producing poorly functioning CFTR cellular salt channel protein can cause CF. More than 2000 CFTR variants have been described in people with CF. The function of the corresponding CFTR protein differs between

the variants. We assessed the relation between CFTR protein function and a sensitive lung function marker, the Lung Clearance Index (LCI).

Why is this important?

The LCI measures how well gas transport (ventilation inhomogeneity) works in the central and peripheral airways. Efficient ventilation is key to normal working lungs, but this can be affected early in the course of CF lung disease. Classical lung function tests such as spirometry may miss impaired ventilation. LCI could become a "treatable trait", a specified treatable problem, for novel CFTR-variant specific small molecule therapies in people with CF and normal spirometry.

What did you do?

This was an international, multicentre study which followed participants between January 2012 and December 2016 in Zurich, Bern (Switzerland) and Toronto (Canada). We enrolled 176 people with CF aged from 3 to 25 years old who were clinically stable. Participants performed lung function tests, i.e. nitrogen multiple-breath washout (MBW) to measure LCI, spirometry, and other standard assessments. We grouped by CFTR genotype according to whether at least one of the two individual variants linked to some CFTR function. There were 35 participants with residual CFTR function and 141 participants with minimal CFTR function.

What did you find?

We found a clear relationship between LCI and CFTR function even if spirometry was normal in the majority of participants. We found abnormal LCI (more than 1.96 z-score(a measure showing how far from the average value the result is)) in 101 (72%) individuals with minimal CFTR function and in 14 (40%) with residual CFTR function. We measured LCI in units and z score; the average LCI was 9.8 units and 6.2 z-score in participants with minimal CFTR function and 8.2 units and 2.5 z-score in participants with residual CFTR function. This difference in LCI was confirmed after statistical adjustment for potentially influencing factors.

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What does this mean and reasons for caution?

Despite normal spirometry, LCI detects lung function abnormalities in both individuals with minimal and those with residual CFTR function. Abnormal LCI is more severe and occurs more often in people with minimal CFTR function compared to those with residual CFTR function. While LCI can detect disease early on, measuring LCI may not change which treatment physicians prescribe.

What's next?

Longer studies observing the same participants should assess if LCI measurement can guide personalized health care decisions including starting treatment with CFTR modulators and a measurement of treatment response.

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