

Cystic Fibrosis Research News

Title:

Nasal Potential Difference in suspected Cystic Fibrosis patients with 5T: A step towards better characterization of a CFTR variant with varying clinical consequences

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on behalf of the Diagnostic Network Working Group of the ECFS

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What was your research question?

Our aim was to describe the variability in the group of patients with the 5T variant and assess if NPD (Nasal Potential Difference) measurement could help in estimating the risk of deterioration of their symptoms (if the measurement is used complementary to general workup with genotyping and sweat test).

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Why is this important?

5T is a CFTR gene variant that causes part of the CFTR protein to be left out of the chain and in some, but not all occasions, leaving a non-functional protein. Lab research suggests that the consequence of the 5T variant depends on additional genetic factors around 5T.

There is enormous variation in clinical consequences of 5T, stretching all the way from no symptoms to CF with pancreatic insufficiency. Because of this variability it brings insecurity to both patients and caregivers, stressing the need for more information about the clinical effects of 5T.

What did you do?

We collected anonymized data from patients with 5T who were referred to a CF centre because of possible CF to undergo diagnostic testing with at least genetic analysis, sweat test, and NPD (this is a measurement of the electrical charge difference across the nasal wall, to assess CFTR function). Data about these diagnostic tests, symptoms at presentation, and evolution of symptoms over time was recorded. Patients were divided into groups according to their mutations, NPD result, and sweat test result, and these groups were compared.

What did you find?

We found that the variation between patients with 5T that was described in lab research is even larger in the clinic: variability of symptoms between 5T patients is enormous. The additional genetic factors do not fully predict if a patient will get more symptoms over time. There is not one single test that will predict deterioration of symptoms. NPD can help in estimating the risk, when added to the other tests in symptomatic patients.

What does this mean and reasons for caution?

This means that, there is no easy way to predict if a 5T patient will develop (more) symptoms in the future. A combination of genetic factors, NPD, and sweat test will provide the best available guidance when it comes to strictness of follow up and treatment in these patients. This approach will have to be tailored to each individual patient.

Reasons to be cautious in interpreting these results are that in a substantial part of the group, information about the genetic factors next to 5T was missing. Also, the length of follow up was quite variable between patients.

What's next?



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Hopefully a large series of 5T patients in whom more genetic details are known and follow up is longer will shed more light on the importance of additional genetic factors and NPD in predicting risk of deteriorating symptoms. Ideally, a risk calculation model could then be set up and validated.

Original manuscript citation in PubMed

<https://www.ncbi.nlm.nih.gov/pubmed/?term=Aalbers+nasal+potential>

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