Cystic Fibrosis Research News

Title:
ECFS standards of care on CFTR-related disorders: updated diagnostic criteria

Lay Title:
New guidelines on non CF disorders related to the *CFTR* gene

Authors:
Castellani C1, De Boeck K2, De Wachter E3, Sermet-Gaudelus I4, Simmonds NJ5, Southern KW6, on behalf of the ECFS Diagnostic Network Working Group.

Affiliations:
1 IRCCS Istituto Giannina Gaslini, Cystic Fibrosis Center, Genoa, Italy
2 Department of Pediatrics, University of Leuven, Leuven, Belgium
3 Cystic Fibrosis Center, Pediatric Pulmonology department, Universitair Ziekenhuis Brussel, Vrije Universiteit Brussel, Brussels, Belgium.
4 INSERM U1151, Institut Necker Enfants Malades, Paris, France; Université de Paris, Paris, France; Centre de référence Maladies Rares, Mucoviscidose et maladies apparentées. Hôpital Necker Enfants malades, Paris, France
5 Adult Cystic Fibrosis Centre, Royal Brompton Hospital and Imperial College, London, UK

6 Department of Women's and Children's Health, University of Liverpool, University of Liverpool, Alder Hey Children's Hospital, Liverpool, UK

What was your research question?
Providing updated guidance on the definition, evaluation and management of people with a Cystic Fibrosis Transmembrane conductance Regulator (CFTR)-Related Disorder (CFTR-RD)

Why is this important?
It is crucial that people with CFTR-RD are recognized early, accurately diagnosed and appropriately managed. This is the aim underpinning these new guidelines. The previous recommendations were a major step forward, and augmented awareness of CFTR-RD in the medical community, including not only CF specialists, but also general pulmonologists, fertility experts, gastroenterologists and clinical geneticists. However, since then, diagnosis rates have steadily increased and there have been significant advances in knowledge of the clinical, functional and molecular aspects of CFTR-RD, necessitating updated recommendations.

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What did you do?

A six-member committee designed the workplan. The committee established workgroups of 46 international experts from 13 countries. Participants were recruited according to their clinical knowledge of specific disorders, experience in CFTR function studies and familiarity with interpretation of clinical liability of CFTR variants. Patients with CFTR-RD were also involved, where appropriate. The plan provides for four documents, of which the present one is the first: 1) diagnosis; 2) biomarkers of CFTR function; 3) specific disorders; 4) objectives for the future. The draft was shared among the members of the ECFS Diagnostic Network Working Group for comments and final assessment.

What did you find?

We suggested to maintain the previously recommended three components of the definition of CFTR-related disorders: 1) presence of specific clinical features; 2) exclusion of a diagnosis of CF; 3) evidence of partially functioning CFTR protein. These three components contained some elements of ambiguity which we contributed to define better, in order to be used in clinical practice. The ideal follow-up of a person with CFTR-RD should be by a clinician with expertise in CFTR-RD and in CF. The follow-up frequency may be adapted according to the clinical impact of the disease, the patient's convenience and the medical facility availability.

What does this mean and reasons for caution?

CFTR-RD treatment is largely dependent on the specific disorder, e.g. assisted reproduction techniques in the patients with infertility, preventing exacerbations and improving pain in the patients with recurrent pancreatitis, preventing loss of lung function and pulmonary exacerbations in those with bronchiectasis. It seems reasonable to hypothesize that people with CFTR-RD may benefit from the symptomatic therapies used in CF, but specific clinical trial evidence is missing. In CFTR-RD there is a decrease in CFTR function, and CFTR modulators might benefit some of these patients. At present, the evidence for this does not exist, but it should be developed.

What's next?

This paper is the first in a series providing updated guidance on the definition, evaluation and management of people with CFTR-RD. The second document in this series gives an in-depth review on how biomarkers of CFTR function can be utilized to diagnose CFTR-RD.

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