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Cystic Fibrosis Research News

Title:

Biomarkers for Cystic Fibrosis Drug Development

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What was your research question?

The goal of this paper was to summarize what is known and what we need to learn about measures that allow us to track disease in people with cystic fibrosis (CF), especially as many new therapies are being developed. Such measures are called "biomarkers".

Why is this important?

Biomarkers are necessary for clinical trials to assure that all outcomes are measured the same way. Biomarkers are also important for registration of new medications through regulatory agencies. In order to be informative, these biomarkers need to be easy to obtain and show measurable, clinically relevant changes within a reasonable time frame during a

study. Importantly biomarkers need to reflect what is relevant to patients, i.e. feeling and being healthier.

What did you do?

In this paper we discussed how biomarkers are defined and evaluated by agencies that monitor drug development (FDA in the U.S. and EMA in European Countries). We also discussed specific areas of biomarkers related to CF 1) how to track the underlying abnormalities of CF by measuring "ion-flow" (i.e. molecules in our body that carry an electric charge flow across cell membranes), 2) how to measure infection 3) how biomarkers of inflammation may be used, and 4) how new technologies (often called –omics) can help to discover new biomarkers.

What did you find?

Changes in sweat-chloride concentration, which is used for diagnosis of CF, is the most widely used biomarker to measure ion-flow and has been used in clinical trials of CF specific therapies (called ivacaftor and lumicaftor). Other measures of ion-flow are performed in the nose or in small biopsies obtained from the intestines, which can be obtained non-invasively. As biomarkers of infection, bacterial load in the airways and lungs using culture methods remain most used despite the fact that details of microbial communities have been defined by novel techniques. Either of these methods are difficult to interpret in patients with chronic infection who do not clear the bacteria. Many biomarkers have been used to measure inflammation in blood and in airway/lung secretions e.g. sputum. Young children often cannot produce sputum and an endoscopic procedure called bronchoscopy with bronchoalveolar lavage is needed to obtain secretions from the lungs. The –omics technologies, where many markers of proteins or metabolic activities can be measured in a very small sample, may discover new biomarkers. These –omics technologies have allowed discovery of biomarkers in diseases such as diabetes.

What does this mean and reasons for caution?

This summary paper shows the strengths of existing biomarkers but also the areas that need more development. It remains important to keep an ongoing dialog with the regulatory agencies to find the balance between the appropriate choice / use of biomarkers and allowing progress in the development of new medications.

While this review was extensive, it did not review measures related to lung function in different ages or details about imaging options that are discussed in other publications of this journal.

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What's next?

Existing biomarkers need to be further tested for their use in younger and healthier people with CF. Biomarkers, discovered by new technologies that are only available in the research setting, need to be further evaluated using standard equipment available in clinics and hospitals. Following these evaluations they can be developed for use in clinical trials.

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