Cystic Fibrosis Research News

Title:
Pulmonary Exacerbation Inflammatory Phenotypes in Adults with Cystic Fibrosis

Lay Title:
Pulmonary exacerbation groupings based on blood inflammation in Cystic Fibrosis

Authors:
Kang Dong[1,2], Sung Moon Huh[1,3], Grace Y Lam[1,4], Jiah Jang[1], Alessandro N. Franciosi[1], Pearce G Wilcox[1], Bradley S Quon[1,5]

Affiliations:
1. Centre for Heart Lung Innovation, University of British Columbia, Vancouver, BC, Canada
2. Prevention of Organ Failure (PROOF) Centre of Excellence, Vancouver, BC, Canada
3. University of Victoria, Victoria, BC, Canada
4. Division of Pulmonary Medicine, University of Alberta, Edmonton, AB, Canada
5. Division of Respiratory Medicine, Department of Medicine, University of British Columbia, Vancouver, BC, Canada

What was your research question?
Can we identify clusters of pulmonary exacerbations (PEx) based on patients blood inflammatory profiles?

Why is this important?
Cystic fibrosis (CF) PEx are important clinical events. Both infectious (i.e., viruses, bacteria) and non-infectious (i.e., poor medication adherence, air pollution) causes can trigger PEx; however, antibiotics are typically used to treat these events regardless of the suspected cause. Given the growing concern about overuse of antibiotics, we are interested in whether PEx can be clustered into types based on patients blood inflammation profiles and whether there are meaningful clinical differences between clusters either at the time of PEx or after antibiotic treatment. Understanding the PEx clusters may help clinicians tailor treatment strategies for each exacerbation type.

What did you do?
We conducted a pilot study and measured six blood inflammatory proteins from 37 PEx events. Clusters based on the results were identified using advanced statistical methods. We compared the levels of blood inflammatory proteins at PEx presentation, and clinical

outcomes (i.e., lung function, respiratory symptom score) at both PEx presentation and after intravenous antibiotic treatments between clusters.

What did you find?

We identified three clusters of PEx by analysing blood inflammatory proteins, including neutrophil-predominant (i.e. lots of blood neutrophils), pro-inflammatory (i.e. lots of blood inflammation), and pauci-inflammatory (i.e. no or limited blood inflammation) phenotypes. These inflammatory phenotypes were associated with differences in symptom duration and lung function decline at presentation, as well as varied responses to treatment with IV antibiotics. Subjects in the pauci-inflammatory group had the smallest improvement in lung function and the highest proportion of individuals who failed to recover to baseline lung function. Subjects in the neutrophil-predominant phenotype had a much larger lung function drop but also the most improvement following treatment.

What does this mean and reasons for caution?

PEx in CF are commonly thought to be caused by neutrophilic airway inflammation; however, nearly half of the PEx events in our study were classified as pauci-inflammatory. Given that this cluster was associated with chronic respiratory symptoms before admission and poor recovery to baseline lung function, it is possible that the inflammatory phase had resolved and the optimal treatment window was missed. Future research should focus on whether IV antibiotics can be avoided or treatment protocols modified for the treatment of this cluster to improve outcomes.

What's next?

The small sample size and retrospective design of this pilot study limit its scope. Therefore, we have initiated a prospective multi-center study by recruiting CF patients during PEx clinical visits, which will address these limitations and allow us to comprehensively cluster CF pulmonary exacerbations using parameters beyond blood inflammation.

Original manuscript citation in PubMed

https://pubmed.ncbi.nlm.nih.gov/36572614/