



# Cystic Fibrosis Research News

## Title:

Markers of bone turnover are reduced in patients with CF related diabetes; the role of glucose.

#### **Authors:**

Inger Hee Mathiesen<sup>a</sup>, Mette Friberg Hitz<sup>b</sup>, Terese Lea Katzenstein<sup>a</sup>, Peter Oturai<sup>c</sup>, Marianne Skov<sup>d</sup>, Niklas Rye Jørgensen<sup>e</sup>, Peter Oestrup Jensen<sup>f,g</sup>, Christine Raaberg Mikkelsen<sup>a</sup>, Rikke Krogh-Madsen<sup>h</sup>, Tacjana Pressler<sup>a,d</sup>, Daniel Faurholt-Jepsen<sup>a</sup>.

#### **Affiliations:**

<sup>a</sup>Copenhagen Cystic Fibrosis Center, Department of Infectious Diseases, Rigshospitalet, Copenhagen University Hospital, Blegdamsvej 9, DK2100 Copenhagen, Denmark;

<sup>b</sup>Dept. Of Medicine, Endocrine Division, Zealand University Hospital, Lykkebaekvej 1, DK4600 Koege, Denmark;

<sup>c</sup>Dept. of Clinical Physiology, Nuclear Medicine and PET, Rigshospitalet, Blegdamsvej 9, DK2100 Copenhagen University Hospital, Copenhagen, Denmark;

<sup>d</sup>Copenhagen Cystic Fibrosis Center, Danish Pediatric Pulmonary Service, Copenhagen University Hospital, Juliane Maries Vej 6, DK2100 Copenhagen, Denmark;

<sup>e</sup>Dept of Clinical Biochemistry, Rigshospitalet, Copenhagen University Hospital, Valdemar Hansens Vej 13, 2600 Glostrup Copenhagen, Denmark;

<sup>f</sup>Dept. of Clinical Microbiology, Rigshospitalet, Copenhagen University Hospital, Ole Maaløes Vej 26, DK2200 Copenhagen, Denmark;

<sup>g</sup>Institute for Inflammation Research, Center for Rheumatology and Spine Diseases, Copenhagen University Hospital, Rigshospitalet, Blegdamsvej 9, DK2100 Copenhagen, Denmark,

<sup>h</sup>The Centre of Inflammation and Metabolism (CIM) and the Centre for Physical Activity Research (CFAS), Rigshospitalet, Copenhagen University Hospital, Blegdamsvej 9, DK2100 Copenhagen, Denmark.

## What was your research question?

Because many people with cystic fibrosis (CF) develop CF-related diabetes (CFRD) and because people with diabetes without CF have higher risk of osteoporosis (a condition with weakened bones) and osteoporotic fractures, we wondered if the presence of CFRD and poor blood glucose control was important for bone quality in CF?

## Why is this important?





# Cystic Fibrosis Research News

People with CF and those with diabetes are in increased risk of osteoporotic bone fractures. Throughout life bone is broken down (resorption) and rebuilt (formation). The process of resorption and formation is called bone turnover. If bone turnover is unbalanced or low e.g. as seen in diabetes, the bone can become brittle and more susceptible to fractures. Osteoporotic fractures in people with CF most often occur in the spine and ribs and anatomic changes can complicate breathing, ability to cough and lung transplantation. Numerous conditions in CF have been associated with increased risk of osteoporosis such as pancreas insufficiency, inflammation and decreased physical activity.

## What did you do?

From January to October 2017 we invited 102 adults with CF from the Copenhagen CF Centre for additional blood tests with markers related to diabetes, calcium metabolism and inflammation (cytokines). We tested if these blood markers were related to bone resorption and formation. Dual-x-ray absorptiometry scan (DXA) and oral glucose tolerance test were also performed to determine bone mineral density (BMD) and their current diabetes status. Those with CF who were lung-transplanted or already in anti-osteoporotic treatment were excluded from analyses. Individuals were included during stable disease.

## What did you find?

In total, 21 out of 102 had diabetes. People with CFRD had lower levels of bone formation and bone resorption markers compared to those without CFRD. Irrespective of diabetes, high levels of blood glucose were associated with lower levels of bone turnover markers and increasing levels of glycated haemoglobin, an indicator of blood glucose control, were related to reduced bone resorption marker levels.

Although BMD was not different between people with CF with and without diabetes, blood glucose was associated with lower BMD at the hip and femoral neck. Inflammation did not affect bone turnover. Finally, older age was associated with low bone turnover marker levels.

### What does this mean and reasons for caution?

The results suggest that CFRD and in particular high blood glucose could have a negative effect on both bone quality and strength (BMD). The results are in line with what is observed in people with diabetes but without CF. But to verify if the low bone turnover also affect bone structure and thereby fracture risk, it is necessary to obtain bone samples for microscopic analysis. Because of our cross sectional design no causal relationship can be determined from the results.

Potentially certain glucose lowering medications could also positively affect bone status in CF.





## Cystic Fibrosis Research News

## What's next?

Bone samples together with bone turnover markers should be examined.

It should be considered, if oral antidiabetic medications (GLP1-RA, metformin) which have shown to have a positive effect in bone density could have a potential therapeutic value on both glucose control but also bone health in CF.

## Original manuscript citation in PubMed

https://www.ncbi.nlm.nih.gov/pubmed/?term=Markers+of+bone+turnover+are+reduced+in+patients+with+CF+related+diabetes%3B+the+role+of+glucose.