

# Longitudinal follow-up of exocrine pancreatic function in pancreatic sufficient cystic fibrosis patients

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## Background

Exocrine pancreatic insufficiency is one of the major clinical features of cystic fibrosis (CF). The endogenous production of pancreatic enzymes varies from normal to residual secretion of less than 1-2% of the secretion of control subjects. In 10-15% of adolescent and adult CF patients, pancreatic secretion allows for normal digestion and absorption (pancreatic sufficiency - PS). Steatorrhea in CF patients (pancreatic insufficiency - PI) is influenced by many factors such as fat intake, abnormalities in gastrointestinal motility, diminished pancreatic bicarbonate secretion and gastric hypersecretion with subsequent duodenal acidity, with inactivation of pancreatic enzymes by low pH and by the loss of bile salts. Thus, fecal fat excretion, although very useful from a practical point of view, presents with low sensitivity and is usually positive in CF subjects when the diagnosis of severe exocrine pancreatic insufficiency is rather obvious. In addition, the procedure is time-consuming, cumbersome and unpleasant for patients. The secretin-cholecystokinin test, which allows for early detection of the deterioration of pancreatic function, is invasive and not acceptable as a repeatable procedure in children, especially in those with pulmonary involvement. Therefore, there is a need for a new test which could allow for early detection of PS/PI conversion.

## The aim of the study

has been to evaluate the usefulness of the non-invasive fecal elastase 1 test in the longitudinal assessment of exocrine pancreatic function in individual pancreatic sufficient CF patients.

## Material & methods

### Patients

184 CF patients (94 males and 90 females) aged 4 months to 30 years. In all subjects, fecal elastase 1 (E1) concentrations and fecal fat excretion was measured at the same time. According to fecal fat excretion, CF patients having no steatorrhea were defined as pancreatic sufficient (PS) as opposed to those having steatorrhea who were defined as pancreatic insufficient (PI). PS CF patients were followed for five years with E1 concentration and fecal fat excretion measurements yearly or more often when needed.

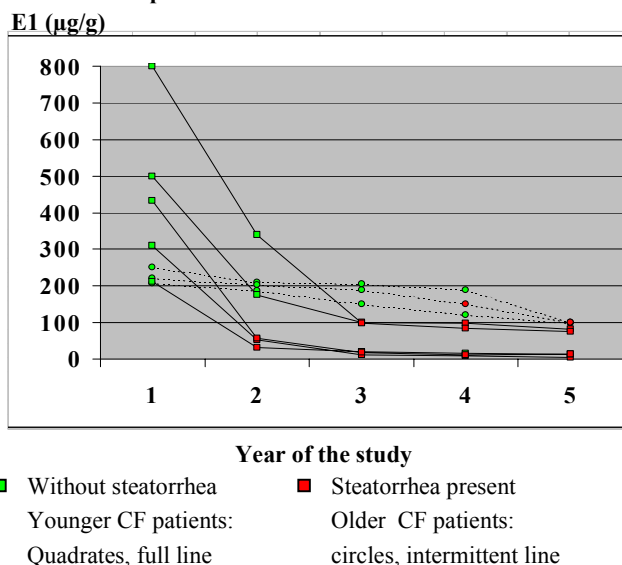
### Methods

Fecal elastase 1 - ELISA (ScheBo® • Biotoech AG, Giessen, Germany). Fecal fat was analyzed according to van de Kamer et al. The diet regimens were standardized for age, weight and sex, before and during the 3-day stool collection. Daily fecal fat excretion was defined as mean of a 72-hour collection period. The most common mutations in the populations studied were analyzed (Poland - 29 mutations, Greece - 20 mutations)

## Results

At the beginning of the study, 149 (81%) CF patients were PI and 35 (19%) were PS. None of the CF patients carrying two severe CFTR mutations ( $\Delta F508$  or other) was pancreatic sufficient. All PS patients had at least one mild or unknown CFTR mutation. Longitudinal measurements of E1 concentrations in 35 PS CF patients demonstrated stable enzyme output in 27 and essential decrease in 8 of them (Figure). Among PS patients with stable enzyme output, the following genotypes were found:  $\Delta F508/3849+10kbC-T$  (n=2),  $3849+10kbC-T/3849+10kbC-T$  (n=2),  $\Delta 508/1525-1G-A$  (n=1),  $\Delta F508/M$  (n=6),  $E822X/M$  (n=1),  $2789+5G-A$  (n=1),  $M/M$  (n=14). The genotypes of patients with declining exocrine pancreatic function were as follows:  $\Delta F508/M$  (n=5),  $CFTRdele2,3$  (21kb)/M (n=1),  $M/M$  (n=2). The decrease was fast and mutual in 5 younger patients (squares, full line) and gradual in 3 older patients (circles, intermittent line) (Figure). The decrease of E1 concentrations preceded the presence of steatorrhea (red shadow) in all 8 subjects. The decline of exocrine pancreatic function in CF appeared more frequently in the first months/years of life. Late PS/PI conversion, however, has been also observed.

**Figure: Decline of exocrine pancreatic function in pancreatic sufficient CF patients**



**In conclusion**, decrease of elastase 1 concentrations precedes the appearance of maldigestion. Thus, fecal elastase test is a helpful screening tool in the longitudinal assessment of declining exocrine pancreatic function in individual pancreatic sufficient CF patients to demonstrate the pancreatic deterioration.