Predictors of Cystic Fibrosis-Related Diabetes (CFRD) in Patients with CF and Pancreatic Insufficiency

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Financial Disclosure: The authors have no financial relationships relevant to this poster.

• Background:
  - Cystic fibrosis (CF) is the most common severe genetic disease in Caucasian populations, caused by a mutation in the CFTR gene and resulting in multi-organ damage.
  - Cystic Fibrosis Related Diabetes (CFRD) is a common complication of CF, associated with increased morbidity and mortality.
  - Early identification of CF patients at risk for developing CFRD would allow close supervision and early treatment, which is known to have a beneficial effect on the patients.
  - At the Graub CF center, Schneider Children’s, prospective comprehensive follow up of CF patients with pancreatic insufficiency above the age of 10 years has been part of routine care for more than 2 decades.

• Objective:
To identify potential demographic, clinical, and laboratory predictors of CFRD development in patients with CF.

• Methods:
  - The study group included patients over 10 years of age with CF and pancreatic insufficiency who attended the CF clinic between the years 1999-2013.
  - The following data were collected: demographics, anthropometric, clinical and laboratory data including FEV1 and annual oral glucose tolerance test (OGTT) values.
  - Findings were compared between patients with CFRD and those with normal glucose tolerance (NGT) or impaired glucose tolerance (IGT).

• Conclusions:
  - Glucose levels at 60 and 90 minutes after OGTT, AUC of glucose, and HbA1c values predict an increased risk of CFRD.
  - Insulin resistance appears to be the major cause of CFRD. CFRD is apparently not preceded by a significant decrease in insulin secretion.

• Results:
  - Forty-four patients met the study criteria.
  - The patients with CFRD (N=16) had significantly higher: glucose levels at 60 and 90 minutes after OGTT, area under the curve (AUC) of glucose, and HbA1c concentrations one and two years before CFRD was diagnosed as compared with the patients in whom CFRD did not develop (N=28).
  - On multiple regression analysis, the best predictor of CFRD was the AUC of glucose.
  - Analysis of HOMA-IR at diagnosis in patients without CFRD as compared to those in whom CFRD developed, yielded a significant between-group difference (0.95 and 1.78, respectively, P=0.02). No significant differences were found in levels of insulin, C-peptide, and C-reactive peptide.
  - The rate of liver disease was higher in the patients who acquired CFRD (62.5%) than in the patients with NGT or IGT (28.6%, P=0.028).
  - There were no difference between the two groups in BMI SDS, FEV1, or history of diabetes in the family.

Study group enrollment

- CF patients N = 243
- Patients without pancreatic insufficiency N = 45
- CF patients age > 10 y N = 44
- Study group N = 44
- Diagnosis of CFRDM at admission N = 2
- Lung transplantation N = 2
- OGTT not available N = 9
- Data = 1 year before diagnosis of CFRDM N = 4
- Data = 2 year before diagnosis of CFRDM N = 24