Postdoc Journal
Vol. 3, No. 12, December 2015

Journal of Postdoctoral Research
www.postdocjournal.com

FFC Proceedings 2015

13th Convention of Investigators in Cystic Fibrosis – Italian Cystic Fibrosis Research Foundation (FFC)

Clinical implications of the natural history of insulin secretory and sensitivity defects in cystic fibrosis

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Background. Cystic Fibrosis Related Diabetes, the most prevalent comorbidity in older patients, is often anticipated by pulmonary and nutritional decay. Insulin secretory (IS) and resistance (IR) defects are involved but their progression rates, determinants and implications for nutritional, respiratory and clinical outcomes are unclear. We reported that IS and IR are related to respiratory and nutritional status (Project FFC #16/2005)

Hypothesis and objectives. 1) To provide CF population-specific estimates of the time course of IS and IR defects quantified by a model previously developed; 2) To identify risk factors associated to their progression rates and patients negative outcomes

Methods. Three groups, led by Dr Battezzati (ICANS), Dr Colombo (CF Center, Milan) and Dr Mari (ISIB-CNR) cooperated to: repeat 287 OGTT, respiratory function, nutritional assessment in 201 patients in follow-up; OGTT modeling of IR and IS parameters in the 995 OGTTs set since 2003; validate the relationship of anthropometric and BIA measures to body composition reference Methods; modelling natural history of IS and IR

Results. The patients follow-up length increased by 4 yrs. In subsets, new respiratory tests (Lung Clearance Index) and state of the art body composition techniques were implemented. Main achievements:

1. In a cross-sectional analysis of the ongoing cohort, IS defects progressively worsen, but are not sex specific and do not explain the worse glucose tolerance in females. Insulin clearance increases with age, more in females, worsening glucose tolerance. We provided sex and age normograms of the main parameters for clinical use
2. Using DXA as reference method, the estimates of body composition obtained from skinfolds and BIA techniques cannot be part of the standard nutritional assessment of CF patients until reliable CF-specific equations will become available.
3. defective IS is a long term predictor of future diabetes. Simpler parameters (C-peptide and glucose concentrations at 30- 60?) may be useful surrogates.

Spin-offs for research and clinical purposes. We have described cross-sectionally the time course of IR and IS and we provided age and sex specific reference values. We estimated the reliability of field nutritional assessment techniques in clinical practice. We also showed that defects in the early IS to glucose are long term predictors of future diabetes and growth failure.

Acknowledgment. FFC #21/2013: funded by FFC, supported by Compass Gruppo Mediobanca, Donatori numero solidale 2014