Liver disease in cystic fibrosis

Rate of decline in serum trypsinogen as a validation for the prevalence of cystic fibrosis related diabetes unaffected by steadily improving clinical condition. A Danish retrospective birth cohort

Evidence suggests that cystic fibrosis liver disease (CFLD) does not impact on mortality or morbidity in patients with Cystic Fibrosis (CF). However, the selection of an appropriate comparison group is central to the interpretation of any differences in mortality and morbidity in CFLD. The aim of this study was to examine differences in mortality and morbidity 10 years after the baseline data was collected on 42 children with CFLD and their 42 age and sex matched controls described elsewhere [1].

Participants were interviewed at a routine hospital visit or by telephone to determine hospital admissions, medication use and current well-being. Clinical data was collected from medical records. No clinical assessment was performed. Medical records of the deceased (n = 20) were reviewed to determine cause of death. Ethical approval was obtained, and participants provided informed consent.

Eighty-five percent (72/84) or the original cohort were available for follow-up; 36 participants with CFLD and 36 CF controls. At follow-up 15/36 (41.7%) participants with CFLD had died compared to 5/36 (13.9%) CF controls (Relative Risk = 3.0, 95%CI = 1.2−7.4). Females with CFLD had a much higher mortality risk than males. In a logistic regression model lung function defined as FEV1 <70% predicted (adjusted odds ratio 4.3 95%CI 1.1−17.3), female gender (adjusted odds ratio 6.5 95%CI 1.5−27.4) and liver disease (adjusted odds ratio 4.3 (1.1−17.3) were all independent risk factors for mortality in CF.

Participants with CFLD have a increased mortality risk compared to CF controls without liver disease, and females with CFLD have a poorer outcome than males with CFLD.

Reference(s)

WS1.2 Rate of decline in serum trypsinogen as a validation for the PIP score

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Background: Despite >1800 identified CFTR mutations and increasing availability of genetic sequencing, the clinical consequences of most mutations remain uncertain. Since exocrine pancreatic function is the best phenotypic barometer of CFTR function, we developed and validated an alternative surrogate marker of CFTR severity using phenotype data, known as the pancreatic insufficiency prevalence (PIP) score. We evaluated this rating system in 2 cohorts by calculating the decline in longitudinal serum trypsinogen measurements as a marker of the rate of pancreatic acinar cell destruction.

Methods: The first cohort consisted of Toronto patients who were evaluated longitudinally since 1980 and the second consisted of newborn screen (NBS) positive patients with either a confirmed or uncertain diagnosis of CF enrolled from the Toronto and Verona CF clinics. Patients were excluded if their first trypsinogen measurement was below the lower limit of the reference range or if their first and last measurements were less than one year apart. The rate of decline was calculated as Atrypsinogen/Δage. CFTR mutations were classified by mild (<0.25) or severe (>0.25) PIP scores.

Results: 292 patients were included from the older Toronto cohort and 39 from the NBS study. In both cohorts those with higher PIP scores (>0.25) had a significantly more rapid decline in their trypsinogen values as compared to the mild group (P < 0.001).

Conclusion: PIP scores can be used as a tool for predicting the rate of pancreatic acinar cell destruction and for determining the severity of CFTR mutations.

WS1.3 Prevalence of cystic fibrosis related diabetes unaffected by steadily improving clinical condition. A Danish retrospective birth cohort

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Objectives: Several studies have shown that cystic fibrosis related diabetes (CFRD) is associated with an increase in morbidity and mortality. Improvements in the quality and implementation of medical care for individuals with cystic fibrosis (CF) have resulted in a reduction of chronic infections and in an improvement in survival. The aim of this study was to investigate the incidence of CFRD over the last 20 years, to identify factors that can predict the development of CFRD and examine whether CFRD affects lung function and survival rate.

Methods: A retrospective chart review of a birth cohort, including 161 CF patients born in the period 1975−1994. Patients are followed until 2011. Prospectively recorded data of BMI, pulmonary function, chronic infection and oral glucose tolerance test (OGGT) are used. Diabetes is defined as an abnormal OGGT (WHO criteria’s), consecutive augmented home glucose monitoring and insulin treatment.

Results: In the study period the proportion of children with chronic pulmonary infection at 10 years declined from 36% to 5% (p = 0.001), whereas the incidence of CFRD among 11−16 year old patients remained unchanged at 13%. All patients with CFRD carried CF mutations class I or II. Occurrence of CFRD did not influence BMI, pulmonary function nor survival.

Conclusion: Cystic fibrosis related diabetes remained unchanged despite concurrent decline in proportion of children with chronic pulmonary infection. CFRD was only related to CF mutations class I or II and did not impair survival in this CF population.

WS1.4 The glucose metabolism in CFRD: comparing the different methods for screening CFRD

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Cystic fibrosis-related diabetes (CFRD) is a late manifestation of the disease but its prevalence is increasing sharply. The oral glucose tolerance test (OGTT), the standard test for diagnosis of CFRD, is neither sensitive nor specific. The aims of this study were to compare different methods of testing for CFRD diagnosis in children and adolescents with exocrine pancreatic insufficiency.

Methods: We prospectively compared for each patient the data from the OGTT, HOMA-%B (homeostasis model assessment of insulin resistance) and HOMA-IR (%B (homeostasis model assessment index of beta-cell function) with a standard the continuous glucose monitoring system (CGMS) data. HOMA-IR = fasting plasma glucose (FPG) x fasting plasma insulin (FPI)/22.5; HOMA-%B = (20×FPI)/(FPG − 3.5). Patients were classified into three groups according to the 2-h glycemia for OGTT and the glycemia over 48h for CGMS: normal glucose tolerance (NGT), impaired glucose tolerance (IGT) and diabetes mellitus (DM).

Results: 21 patients from 10 to 17 years of age (median: 12.9) were included. According to the CGMS, 7 had DM, 9 IGT and 5 NGT whereas only 1 patient had DM and 3 IGT according to the OGTT. All data confirmed that abnormalities of glucose metabolism were frequent, even in younger children, and associated both insulin deficiency and insulin resistance. The HOMA-IR was the most sensitive method for screening CFRD (sensitivity 100%, specificity 50%, negative predictive value 100%).

Conclusion: CGMS revealed pathological glucose excursions were frequent and occurred early in life. OGTT should no longer be considered the gold standard for CFRD diagnosis. HOMA-%B could be used for screening CFRD.