Treatment burden in patients with CF and at least one class 4 or 5 mutation

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According to their disease-causing mechanism, many of the CF mutations can be grouped in one of five mutation classes. These partially explain the heterogeneous presentation of CF. Several studies have demonstrated that patients having at least one mutation of class 4 or 5, usually present with a milder phenotype. We wanted to compare disease severity and, especially, treatment burden between these patients and subjects with two class 1, 2 or 3 mutations. Therefore, we included all CF patients enrolled in the 2010 database of the Belgian CF Registry who could be assigned to one of these two cohorts.

271 children and 335 adults with 2 known class 1/2/3 mutations were included, plus 42 children and 49 adults with at least one class 4/5 mutation. In both age categories mean sweat chloride was significantly lower and age at diagnosis was higher in class 4/5 patients. Pancreatic insufficiency, chronic Pseudomonas aeruginosa infection and CF related diabetes were less common. Mean FEV1 was lower in adults with class 4/5 mutations. Independent of age, class 4/5 patients had a lower mean number of clinic visits, days in hospital, days with intravenous antibiotics; a lower proportion used rhDNase, mucolytics, oral or inhaled antibiotics, azithromycin, and inhaled corticosteroids.

This study confirms the milder phenotype seen in patients with CF and at least one class 4 or 5 mutation. In addition, we demonstrate their significantly lower treatment burden compared to patients who have two class 1/2/3 mutations. These findings contribute to providing better individual counseling at time of diagnosis for patients with CF.

Oral Presentations

WS4.3 Modeling airway infections in cystic fibrosis

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Objective: Cystic fibrosis (CF) patients appear to demonstrate a temporal progression of airway infections. The study goal was to understand this pattern by distinguishing the effects of age, clinical status and infections.

Methods: We used data from the CF Foundation Patient Registry (CFFPR) for 2003–2011. We initially evaluated confounding effects of age, year of database entry and number of samples per patient. We applied general linear modeling to determine if the eight most common infections, namely methicillin sensitive Staphylococcus aureus (MSSA), methicillin resistant S aureus (MRSA), Burkholderia cepacia, Pseudomonas aeruginosa, Alcaligenes xylosoxidans, Candida species, Aspergillus species and Stenotrophomonas maltophilia. We modeled future from current status of infection, attempting to distinguish direct effects of infections from indirect effects mediated through clinical covariates.

Results: We used 1,045,241 cultures from 28,426 patients. Strong interactions appear to exist between specific infections. MSSA has a negative while MRSA has a positive association on development of future infection with P aeruginosa. P aeruginosa is negatively associated with future B cepacia and S maltophilia infections. Candida and Aspergillus vary both positive, negative and null associations with other infections.

Conclusions: Infections in CF do not follow a simple or stereotyped temporal progression. However, the direct effects of current on future infections can be accurately demonstrated. Understanding these effects may facilitate prediction of future health outcomes and identify transitions between infections as potential targets of intervention.

WS4.2 How different is the cohort of young CF children included in national registries of countries with and without newborn screening?

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More and more countries are implementing newborn screening (NBS) for CF. Early diagnosis via NBS may influence the genotype distribution and clinical characteristics of patients diagnosed with CF.

Objectives and Methods: To compare the demography and clinical characteristics of children with CF younger than 8 years included in national registries of countries with (France, Australia) and without (Belgium, the Netherlands, Sweden) a national NBS program. To avoid influence of regional screening pilot projects, only patients not diagnosed by NBS were included in the latter countries.

Results: See the table.

WS4.4 Multicenter prevalence study of nontuberculous mycobacteria in patients with cystic fibrosis in Scandinavia

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Background: The prevalence of nontuberculous mycobacteria (NTM) among CF patients, while frequently described as rising, also exhibits considerable regional differences. The prevalence in Scandinavia has not previously been reported.

Methods: All CF patients in Denmark, Sweden and Norway were included in the study. Microbiological data were collected from each of the 8 CF centres for the period 2000–2012. While variable over time and between centres, all microbiological procedures were performed according to standardised protocols, including pre-treatment, use of solid and liquid media and molecular diagnostics. Clinical data were extracted from patient files and national registries.

Results: In 2009–2012, Scandinavia had an average CF population of 1,294. NTM was cultured 1,187 times from 162 CF patients (12%). M. tuberculosis complex (MABC) was the most common NTM (56% of patients), followed by M. avium complex (MAC) (48% of patients). 38% had between 2–4 positive cultures and 40% had >5 positive cultures. The median age was 19 and the male/female ratio was 1:2. In 118/162 patients from whom clinical data was available from the time of first NTM, median FEV1 of predicted was 75%; 45% had a concurrent chronic infection with other bacteria, most frequently with P aeruginosa (34%) and 19/27% received azithromycin treatment. The annual NTM incidence increased from an average of 8.1/100 in 2000–2006 to 13.1/100 in 2006–2012. Only 2 CF centres reported changes in screening policy.

Conclusion: The annual incidence of NTM has increased in Scandinavia between 2000–2002 and presently 1 in 9 CF patients have been NTM culture positive at least once. The study is ongoing.