Göteborg, 2022

Monitoring cystic fibrosis lung disease in children

Clinical utility and associations between functional and structural methods

Akademisk avhandling

Som för avläggande av medicine doktorsexamen vid Sahlgrenska akademin, Göteborgs universitet kommer att offentligen försvaras i konferenssalen Tallen, Drottning Silvias barnsjukhus, Remissvägen 12, Göteborg, den 2:a september, klockan 09.00 av Marcus Svedberg.

Fakultetsopponent:

Mirjam Stahl, professor och överläkare i pediatrik

Charité Universitätsmedizin Berlin, Tyskland

Avhandlingen baseras på följande delarbeten

I. **Svedberg M**, Gustafsson PM, Robinson PD, Rosberg M, Lindblad A. Variability of lung clearance index in clinically stable cystic fibrosis lung disease in school age children. *Journal of cystic fibrosis. 2017:17:236-241.*

II. **Svedberg M**, Gustafsson PM, Tiddens H, Imberg H, Piovic A, Lindblad A. Risk factors for progression of structural lung disease in school-age children with cystic fibrosis. *Journal of cystic fibrosis. 2020;19:910-916.*

III. **Svedberg M**, Imberg H, Gustafsson PM, Tiddens H, Davies G, Lindblad A. Longitudinal lung clearance index and association with structural lung damage in children with cystic fibrosis. *Thorax. 2022 Mar 11;thoraxjnl-2021-218178.*

IV. **Svedberg M**, Imberg H, Gustafsson PM, Mela Brink, Håkan Caisander, Lindblad A. Chest x-rays are less sensitive than multiple breath washout examinations when it comes to detecting early cystic fibrosis lung disease. *Acta Paediatr. 2022;00:1–8.*

SAHLGRENSKA AKADEMIN
INSTITUTIONEN FÖR KLINISKA VETENSKAPER

GÖTEBORGS UNIVERSITET

Göteborg, 2022

Monitoring cystic fibrosis lung disease in children

Clinical utility and associations between functional and structural methods

Marcus Svedberg

Avdelningen för pediatrik, institutionen för kliniska vetenskaper, Sahlgrenska akademin, Göteborgs universitet, Sverige.

Abstract

Background: Cystic Fibrosis (CF) is an inherited progressive disease that causes severe damage to the airways and other organs of the body. Many methods are available to track CF lung disease but longitudinal data are needed to better understand the clinical utility and associations between different methods. The main aim of this doctoral thesis was to analyse and compare longitudinal data from lung function tests and image tests in children with CF.

Methods: In **study I** children aged 6–17 years attending Gothenburg's CF clinic underwent multiple breath washout examinations, spirometry tests and a clinical stability assessment every 3rd month over a period of 1 year. Variability of the outcome parameters were analysed. In **study II–IV** 75 children aged 0–17 years underwent multiple breath washout examinations, spirometry tests, chest computer tomography (CT) and chest x-ray examinations between 1996–2016 at Gothenburg CF centre. Longitudinal trends and associations between outcome measures were analysed together with the effect of respiratory infections and other confounding factors.

Results: A total of 25 children completed a total of 107 visits of which 104 visits had complete data available in **study I**. The relative change in lung clearance index and FEV_1% was +-17% (95th percentile) at clinical stable visits. In **study II–IV** a total of 75 participants with CF were included together with a healthy cohort of 140 children aged 0–17 years. Children with CF underwent lung functions tests and image tests and the healthy cohort only underwent multiple breath washout examinations. **Study II** demonstrated that intermittent and chronic infections were associated with an increased progression rate of structural lung disease measured with chest CT. **Study III** demonstrated associations between longitudinal LCI and the extent and progression rate of structural lung damage assessed with chest CT. The Lung clearance index was more sensitive than chest x-rays to detect early CF lung disease in **study IV.** The combined results of a normal chest x-ray and a normal lung clearance index were associated with a low extent of lung damage assessed with chest CT.

Conclusions: Multiple breath washout is a sensitive method to detect early CF lung disease. Lung function and imagine tests captured different dimensions of CF lung disease. The use of multiple methods in clinical practice provides a more robust assessment of CF lung disease than using either measure alone.

ISBN: 978-91-629-833-5 (TRYCK) http://hdl.handle.net/2077/71506
ISBN: 978-91-629-834-2 (PDF)