

Cystic Fibrosis in Adults

Diagnostic, epidemiologic and quality-of-life aspects

AKADEMISK AVHANDLING

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av

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1. Gilljam M, Ellis L, Corey M, Zielenski J, Durie P, Tullis DE: Clinical manifestations of cystic fibrosis among patients diagnosed in adulthood. Chest 2004; 126: 1215-1224
2. Gilljam M, Molyaner Y, Downey G, Devlin R, Durie P, Cantin A, Zielenski J, Tullis E: Airway inflammation and infection in congenital bilateral absence of the vas deferens. Am J Respir and Crit Care Med. 2004; 169: 174-179
3. Gilljam M, Antoniou M, Shin J, Dupuis A, Corey M., Tullis E: Pregnancy in cystic fibrosis; Fetal and maternal outcome. Chest 2000; 118:85-91
4. *Tullis E, *Gilljam M, Corey M, Eriksson L, Bergman B: Development of the Cystic Fibrosis Quality of life Evaluative Self-administered Test (CF-QUEST), a new disease specific quality-of-life instrument for adults with cystic fibrosis
Submitted
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Abstract

Cystic Fibrosis in Adults

Diagnostic, Epidemiologic and Quality of Life Aspects

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Background: Cystic fibrosis (CF) is a severe hereditary disease. The type of mutation in the Cystic Fibrosis Transmembrane conductance Regulator (*CFTR*) gene will determine the degree of *CFTR* chloride channel malfunction. Disturbed salt transport leads to production of sticky mucus, blocking exocrine gland ducts and persistent airway infection, starting early in life. Most patients are pancreatic insufficient, and almost all males are infertile due to obstruction of the vas deferens. Diagnostic criteria of CF are identification of two CF causing mutations and/or laboratory evidence of disturbed chloride transport in a patient with symptoms compatible with CF. Survival has increased due to improved care and today most patients are adult.

CFTR mutations and elevated sweat chlorides are common in infertile men with congenital bilateral absence of the vas deferens (CBAVD).

Aim: To address issues of importance for adults with CF; 1) review diagnosis of CF in adult age, 2) to find out if men with CBAVD, *CFTR* mutations and intermediate or elevated sweat chloride concentrations have evidence of early airway disease, 3) to analyze outcome of pregnancy and 4) to construct a health-related quality of life questionnaire.

Methods: CF patients in Toronto (*Paper I-IV*), Göteborg and Lund (*Paper IV*) were included. Demographic, diagnostic and pregnancy data was extracted from the patient database and completed with chart review and patient interviews. Bronchoscopy with bronchoalveolar lavage (BAL) was performed in men with CBAVD, *CFTR* mutations and intermediate or elevated sweat chloride concentration. CF-related health issues were collected, a provisional questionnaire constructed and translated to Swedish, interviews with 135 patients performed in order to rank the items of importance to quality of life by frequency of occurrence and mean importance. The specific questionnaire was constructed based on the interview result.

Results: In patients diagnosed as adults, pancreatic sufficiency, lung disease, inconclusive sweat test results and a high prevalence of uncommon mutations were common. Nasal potential difference measurement was a diagnostic aid. There was light growth of opportunistic gram-negative bacteria in BAL in 6/8 men with CBAVD. IL-8 and TNF alpha levels were higher in men with CBAVD. Absence of *Burkholderia cenocepacia*, pancreatic sufficiency and pre-pregnancy $FEV_1 > 50\%$ of predicted was associated with better maternal survival. Pregnancy did not affect overall survival or decline in FEV_1 when compared to the whole adult female CF population. The Cystic Fibrosis Quality of life Evaluative Self-administered Test (CF-QUEST) was constructed; CF-related health issues were collected. A provisional 114-item questionnaire was constructed and semi-structured interviews with adult CF patients in Toronto and Sweden were conducted. Items were ranked according to frequency of occurrence and mean rated importance. The final questionnaire was constructed based on the results.

Conclusion: Diagnosis of CF in adults often requires extensive diagnostic methods. Some men presenting with CBAVD in adult age have a mild form of CF. Outcome is good for most pregnant women with CF. CF-QUEST is a new patient-derived HRQL instrument for adults with CF. Field studies to assess repeatability and responsiveness will follow.

Keywords: Cystic fibrosis, cystic fibrosis transmembrane conductance regulator, pregnancy, male infertility, bronchoalveolar lavage, quality of life, questionnaire

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