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Current and emerging comorbidities in cystic fibrosis

Nicola J. Ronan [1], Joseph Stuart Elborn [2], Barry J. Plant [1]

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1. Cork university hospital, university college Cork, Cork adult cystic fibrosis centre, HRB clinical research facility, Wilton,T12 DFK4 Cork, Ireland
2. London and Queen's university Belfast, National heart and lung institute, Imperial College, Royal Brompton hospital, London, United Kingdom

Correspondence:
Barry J. Plant, Cork university hospital, university college Cork, Cork adult cystic fibrosis centre, HRB clinical research facility, Wilton, Cork, Ireland.
b.plant@ucc.ie

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Summary

Cystic fibrosis transmembrane conductance regulator (CFTR) is expressed ubiquitously throughout the body. Thus, while respiratory manifestations dominate much of cystic fibrosis (CF) care, there are prominent multi-organ manifestations and comorbidities. In the general population, the number of comorbidities increases with aging. Few illnesses have experienced such a dramatic improvement in survival as CF, which has been transformed from an illness of childhood death to one of adult survival. Hence, as longevity increases in CF, it is paralleled by an increasing number of patients with multicomplex comorbidities availing of care from adult CF multi-disciplinary teams. This review gives an overview of the traditional CF associated comorbidities and those emerging in an aging adult cohort. While historically the treatment of CF focused on the consequences of CFTR dysfunction, the recent advent of CFTR modulators with the potential to enhance CFTR function represents an opportunity to potentially reverse or delay the development of some of the comorbidities associated with CF. Where evidence is available for the impact of CFTR modulatory therapy, namely ivacaftor on comorbidities in CF, this is highlighted.

Introduction

The global burden of disease study 2013 demonstrated an increase in the number of people living with multiple comorbidities, with the aging of the global population [1]. Thirty-two percent of adults aged 20–64 have 5 or more comorbidities and the number of comorbidities in an individual increased with age [1]. Life expectancy is increasing with CF. A recent European CF Registry study highlighted that by the year 2025, there would be a 75% increase in adults with CF [2]. These calculations were based on a cohort of patients who were CFTR modulatory therapy naive. CFTR modulation treatment offers a new personalised approach to CF care and given its systemic mode of action there is potential for modification of both pulmonary and non-pulmonary CFTR disease and outcome [3]. Given the improved CF survival with traditional approaches, the potential of augmenting this by new CFTR modulation, whilst working in a clinical arena where morbidities in aging populations (independent of CF) are a greater issue, this review attempts to integrate these concepts for the CF clinician [1–3]. *Table I* summarises comorbidities in CF.

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TABLE I
Comorbidities in cystic fibrosis

Pulmonary
Pneumothorax
Annual incidence 0.64%
Risk factors include FEV1 < 30%, pancreatic insufficiency, massive haemoptysis, ABPA, sputum colonisation with *Pseudomonas aeruginosa*, *Burkholderia cepacia complex* or *aspergillus*
Haemoptysis
Annual incidence 0.87%
Risk factors include sputum colonisation with *Staphylococcus aureus* and CFRD
Sinus disease
Rhinosinusitis prevalence 32–65%
Nasal polyps prevalence 25%
Sinuses may serve are reservoir for pathogens
Ivacaftor appears to improve CT sinus appearances
VTE and pulmonary hypertension
VTE relatively is uncommon, may be associated with central venous catheters
Pulmonary HTN is correlated with hypoxaemia and lung function
Pancreatic disease
Pancreatic insufficiency
Prevalence 85–90% and increases with age
Ivacaftor may result in an improvement in exocrine pancreatic function in younger patients
Pancreatitis
Occurs in 10–15% of pancreatic sufficient patients
Cystic fibrosis related diabetes (CFRD)
Prevalence 20% in adolescents and up to 40–50% in adults
Associated with accelerated decline in FEV_1 and increased pulmonary exacerbation frequency
Ivacaftor appears to be associated with an improved insulin secretion profile and possibly a reversal of CFRD
Hepatobiliary disease
CF related liver disease (CFLD)
Prevalence of severe CFLD with portal hypertension occurs in 3–5% of patients
Hepatic cirrhosis is the most common non-respiratory cause of death in people with CF
Typically de novo CFLD does not develop after 18 years of age
Case report suggests ivacaftor may result in an improvement in hepatic steatosis in CF
Gallbladder abnormalities occur in 24–50%, hepatic steatosis 23–75%
Gastrointestinal tract
Meconium ileus (MI)
Presents at birth
Prevalence 10–15%