Heart, Lung and Circulation (2015) **24,** 1002–1010
1443-9506/04/$36.00
http://dx.doi.org/10.1016/j.hlc.2015.03.006

ORIGINAL ARTICLE

Heart Involvement in Children and Adults with Cystic Fibrosis: Correlation with Pulmonary Indexes and Inflammation Markers

Valentina Giacchi *, **Novella Rotolo, Barbara Amato, Giovanna Di Dio, Pasqua Betta, Mario La Rosa, Salvatore Leonardi, Pietro Sciacca**

Department of Medical and Paediatric Science, University of Catania, Catania, Italy

Received 24 February 2015; received in revised form 8 March 2015; accepted 12 March 2015; online published-ahead-of-print 24 March 2015

Background Cardiovascular involvement in Cystic Fibrosis (CF) is a not rare condition, although the prevalence of subclinical pulmonary hypertension (PH) and cardiac dysfunction is not known in the early stages of CF progression. The aim of our study was to assess cardiac involvement in children and adults affected by cystic fibrosis compared with healthy subjects of same age using echocardiography.

Methods Fifty-five patients, 25 adults and 30 children completed the study. We assessed FEV1 (Forced Expiratory Volume in one second), and carried out colour Doppler-echocardiography evaluating ejection fraction (EF) measurement of left ventricle, tricuspid annular plane systolic excursion (TAPSE) of right ventricle and pulmonary artery pressure (PAP). We compared the auxological, respiratory and cardiologic data with those of 16 adults and 34 children of the same age.

Results We discovered significantly different values of PAP between patients and controls in both children ($p = 0.0001$, $r = -0.62$) and adults ($p = 0.0001$, $r = -0.63$), whereas the EF and TAPSE showed significantly different values in only adults ($p = 0.0023$ and $p = 0.0194$ respectively).
We found in both children and adults with CF an inverse correlation between PAP and FEV1 ($p = 0.000$, $p = 0.001$), Erythrocyte Sedimentation Rate (ESR) and FEV 1 ($p = 0.015$, $r = -0.43$; $p = 0.009$, $r = -0.51$), and highly sensitive C-reactive protein (hs-CRP) and FEV 1 ($p = 0.007$, $r = -0.48$; $p = 0.001$, $r = -0.60$). In adults we also detected direct correlation between PAP and hs-CRP ($p = 0.008$, $r = 0.51$) and PAP and ESR ($p = 0.009$, $r = 0.51$).

Conclusions In paediatric-aged CF patients there are already early signs of potential heart impairment, represented by an increase of pulmonary blood pressure, and in adult age the systolic function of right ventricle may be impaired. We hypothesise that such cardiac impairments may gradually arise due to preceding chronic inflammation related to prior degeneration of lung function and thus it is very important to keep patients clinically stable and address chronic inflammation as early as possible in the progression of CF.

Keywords Cystic Fibrosis • Lung function • Cardiac impairment • Flogosis • Pulmonary hypertension.

Abbreviations: CF, Cystic Fibrosis; PH, pulmonary hypertension; FEV1, Forced Expiratory Volume in one second; EF, ejection fraction; TAPSE, tricuspid annular plane systolic excursion; PAP, pulmonary artery pressure; hs-CRP, highly sensitive C-reactive protein; ESR, Erythrocyte Sedimentation Rate.

*Corresponding author. Valentina Giacchi. Department of Pediatrics – University of Catania - ''Policlinico Hospital'' - Via Santa Sofia 78, 95123 - Catania, Italy. Tel.: +00393334126158; fax: +00390953782417, Email: valentina.giacchi@yahoo.it

Background

Cystic fibrosis (CF) is the most common life-threatening autosomal recessive disease seen in the Caucasian population [1]. The pathophysiology of CF lung disease is known to involve self-perpetuating cycles of airway obstruction, infection, and inflammation [2].

Cardiovascular impairment in CF is well-known, with cor pulmonale being the most serious cardiovascular complication [3]. The development of alveolar hypoxia (in hypoventilated areas) leads to hypoxic pulmonary vasoconstriction. When the hypoxic state is prolonged, the pulmonary circulation suffers structural alterations collectively known as remodelling, characterised by hypertrophy and hyperplasia of the arterial media, as well as by muscle fibres in the peripheral vessels [4]. These events have a strong impact on pulmonary arterial pressure (PAP) and right ventricle function [6–8], bearing a strongly negative prognostic value [5]. So, the evaluation of right ventricular (RV) function in this patient population is thus extremely important [3]. Although clinically apparent cor pulmonale is a preterminal event in many patients, the prevalence of subclinical PH and cardiac dysfunction in patients is not known [6]. Echocardiography allows us to identify and quantify PH, as well as to determine its variability and the repercussions for right heart chambers [4].

Aim of Study

The aim of our observational, cross-sectional, case-control study was to assess cardiac involvement in children and adults affected by cystic fibrosis compared with healthy subjects of the same age using echocardiography. In addition, we measured hs-CRP and ESR as markers of inflammation that may be associated with severity of CF and abnormal echocardiographic parameters.

Patients and Methods

This is an observational case-control study conducted in paediatric and adult subjects affected by cystic fibrosis regardless of the severity of the pulmonary disease, followed in our Cardiology and Cystic Fibrosis Clinic of Pediatric Department in University of Catania in Italy between September 2013 and May 2014. A total of 105 patients were enrolled, and 55, 25 adults (13 male and 12 female) and 30 children (23 male and seven female) completed the study. The main features of the paediatric and adult patients are reported in Table 1 and Table 2 respectively.

The patients, if of age, or at least one parent or legal guardian of the child if underage, gave their written, informed consent before the patient's inclusion in the study. The study was conducted in accordance with the Helsinki

Table 1 Demographic, clinical and echocardiographic features of pediatric patients.

P	Age (ys)	Gender	Weight (Kg)	Height (cm)	FEV1 (%)	SpO2 (%)	ESR (mm/h)	CRP (mg/dl)	EF (%)	TAPSE (mm)	Z-SCORE	PAP (mmHg)	Antibiotics History
1	6	M	18.4	114.0	88.0	98	6	0.10	70.8	16.0	-2.00	25	Ciprofloxacin Tobramycin
2	14	M	31.5	143.5	54.0	97	17	0.58	75.0	22.0	0	14	Meropenem Amikacin
3	5	F	17.7	108.0	38.0	100	14	3.30	69.8	20.0	+1.38	48	Ceftazidime Amikacin
4	9	F	23.7	124.0	76.3	99	5	1.50	62.7	23.0	+2.20	35	Ceftazidime Amikacin Cotrimoxazole
5	14	M	41.2	147.5	50.5	96	50	2.27	59.3	22.4	+0.23	52	Meropenem Amikacin
6	11	M	36.0	136.0	100.7	98	33	3.20	75.0	24.0	+2.69	14	Aztreonam Colistin
7	18	F	53.6	148.0	32.9	96	49	3.80	70.0	19.0	-2.68	49	Meropenem Colistin
8	9	M	25.5	123.7	86.5	98	57	3.60	71.0	28.0	+5.53	28	Ceftazidime Amikacin Cotrimoxazole
9	6	M	15.0	101.0	65.0	96	15	0.21	63.0	17.0	-1.26	35	Ciprofloxacin Tobramycin
10	7	M	18.5	112.5	33.9	97	29	2.90	62.0	17.0	-1.43	42	Meropenem Amikacin Cotrimoxazole
11	13	M	52.8	161.0	139.5	97	8	0.11	62.0	24.0	+1.73	25	Ciprofloxacin Tobramycin