Impact of bronchiectasis and trapped air on quality of life and exacerbations in cystic fibrosis

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ABSTRACT Cystic fibrosis (CF) is primarily characterised by bronchiectasis and trapped air on chest computed tomography (CT). The revised Cystic Fibrosis Questionnaire respiratory symptoms scale (CFQ-R RSS) measures health-related quality of life.

To validate bronchiectasis, trapped air and CFQ-R RSS as outcome measures, we investigated correlations and predictive values for pulmonary exacerbations. CF patients (aged 6–20 years) underwent CT, CFQ-R RSS and 1-year follow-up. Bronchiectasis and trapped air were scored using the CF-CT scoring system. Correlation coefficients and backward multivariate modelling were used to identify predictors of pulmonary exacerbations.

40 children and 32 adolescents were included. CF-CT bronchiectasis ($r = -0.38$, $p<0.001$) and CF-CT trapped air ($r = -0.35$, $p=0.003$) correlated with CFQ-R RSS. Pulmonary exacerbations were associated with: bronchiectasis (rate ratio 1.10, 95% CI 1.02–1.19; $p=0.009$), trapped air (rate ratio 1.02, 95% CI 1.00–1.05; $p=0.034$) and CFQ-R RSS (rate ratio 0.95, 95% CI 0.91–0.98; $p=0.002$). The CFQ-R RSS was an independent predictor of pulmonary exacerbations (rate ratio 0.96, 95% CI 0.94–0.97; $p<0.001$).

Bronchiectasis, trapped air and CFQ-R RSS were associated with pulmonary exacerbations. The CFQ-R RSS was an independent predictor. This study further validated bronchiectasis, trapped air and CFQ-R RSS as outcome measures in CF.

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Introduction

Cystic fibrosis (CF) is a severe, life-shortening genetic disease affecting 70 000 patients in the European Union and USA. The most prominent components of CF lung disease are bronchiectasis and trapped air. Bronchiectasis reflects irreversible widening of the airways and trapped air indicates small airway disease. Both bronchiectasis and trapped air typically begin in early childhood and progress slowly throughout life, eventually leading to end-stage lung disease [1, 2].

Bronchiectasis and trapped air are important indicators of prognosis [3–5]. Therefore, accurate and sensitive monitoring of these indicators is needed for optimal clinical management and as potential outcome measures in clinical trials. To date, forced expiratory volume in 1 s (FEV_1), derived from pulmonary function tests (PFT), has been the central outcome measure for disease management and clinical trials. However, FEV_1 is a relatively insensitive measure for detecting and monitoring disease progression [6]. Bronchiectasis, assessed with chest computed tomography (CF-CT bronchiectasis score), is more sensitive and accurate than chest radiography [6]. The literature suggests that the CF-CT bronchiectasis score is a valuable outcome measure since it is associated with pulmonary exacerbations [7, 8], is an important component of end-stage lung disease [9] and is associated with mortality [9]. It is not known whether the presence of bronchiectasis correlates with standardised, patient-reported outcome measures [10]. In adults with chronic obstructive pulmonary disease, bronchiectasis is associated with reduced health-related quality of life, as measured by the symptoms scale of the St George's Quality of Life Questionnaire [11]. We hypothesised that a similar association may exist for bronchiectasis in CF.

The importance of trapped air as an outcome measure is less well established than bronchiectasis. The volume and distribution of trapped air can be visualised well on end-expiratory chest CT [12]. Trapped air is observed in approximately two-thirds of newly diagnosed infants and it is also an important component of end-stage lung disease [1, 4, 9]. Hence, trapped air is considered a potential marker of early CF lung disease [2–4, 9]. To date, as an outcome measure for clinical management and trials, trapped air has not yet been validated against other clinical markers of disease severity, such as pulmonary exacerbations and patient-reported respiratory symptoms on a health-related quality-of-life measure.

Standardised, well-validated measures of health-related quality of life in CF, such as the disease-specific Cystic Fibrosis Questionnaire-revised (CFQ-R) have been developed [13]. The CFQ-R consists of several domains (*e.g.* physical functioning, vitality, health perceptions and respiratory symptoms). The CFQ-R physical functioning scale, CFQ-R vitality scale, CFQ-R health perceptions and CFQ-R respiratory symptoms scale (CFQ-R RSS) have been shown to correlate with FEV_1 [14]. The CFQ-R RSS has been utilised successfully both in controlled trials and in longitudinal studies [15–20]. The CFQ-R RSS was used as an outcome measure in several clinical trials showing responsivity to inhaled tobramycin [18], dornase alfa [19], hypertonic saline [20] and ivacaftor [16]. CFQ-R RSS was used as primary outcome in a phase III study for US Food and Drug administration (FDA) approval of aztreonam lysine for inhalation. A significant improvement in CFQ-R RSS was found in the treated *versus* placebo group, with continued efficacy documented in an 18-month open-label follow-up study [15, 21].

Although a minimal important difference has been established for the CFQ-R RSS, it is not clear what change in respiratory symptoms reflects the extent of bronchiectasis and trapped air [22].

The objectives of this study were to further validate bronchiectasis and trapped air as outcome measures by correlating them with CFQ-R RSS and pulmonary exacerbations. Furthermore, we aimed to validate bronchiectasis, trapped air and CFQ-R RSS by investigating their predictive value for pulmonary exacerbations in the following year.

Methods

Study population

Patients (aged 6–20 years) were diagnosed as having CF by a positive sweat test and/or genotyping for known CF mutations. We included clinically stable children and adolescents with CF, monitored at the Erasmus MC-CF Center (Rotterdam, the Netherlands), who had a CFQ-R and CT performed on the same day, at the annual check-up and at 1-year follow-up. If CT and the CFQ-R were not completed on the same day, a maximal time difference of 3 months was considered acceptable (n=1). Patients in need of *i.v.* antibiotics for respiratory signs or symptoms at the time of the annual examination were considered unstable and excluded. This retrospective cohort study was approved by the institutional review board of the Erasmus MC-CF Center Rotterdam (MEC-2011-250).

Chest CT evaluation of bronchiectasis and trapped air

All volumetric CTs were acquired using a six-slice multi-detector CT scanner (Siemens Medical Solutions, Erlangen, Germany). Each CT consisted of a volumetric inspiratory and expiratory acquisition.

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Instructions for voluntary breath holds were given before scanning. Tube voltages of 80 kV (patients weighing <35 kg) or 110 kV (patients weighing >35 kg) were used with a 0.6-s rotation time. Scanning was performed from apex to base at 1.5 pitch and 6×2 mm collimation. Images were reconstructed with a 3.0-mm slice thickness, 1.2-mm increment and kernel B60s. For the inspiratory protocol a modulating current was used (Siemens) with a reference tube current-time product of 20 mA, for optimal image quality. For expiratory CTs a tube current fixed at 25 mA with an effective tube current-time product of 10 mA (the typical value for a 5-year-old child) was used. This produced a lower radiation dose than the inspiratory protocol with sufficient image quality. Total radiation dose was in the order of 1 mSv.

All CTs were scored using the CF-CT scoring system, a modified version of Brody II scoring, evaluating the five lung lobes and the lingula as a sixth lobe for severity, extent of central and peripheral bronchiectasis, airway wall thickening, central and peripheral mucus plugging, opacities (atelectasis, consolidation and ground-glass pattern) and cysts and bullae on inspiratory CTs and the pattern and extent of trapped air on expiratory CTs [7, 23]. The maximum possible composite CT score is 207 points. For statistical analysis, composite and component CT scores were expressed as a percentage of the maximum possible score (0–100). All scans were de-identified, using Myrian (Intrasense, Montpellier, France), and scored in random order by an observer blinded to clinical background [7]. To test intraobserver agreement, observer one rescored 25 random scans after 1 month. A second observer scored 25 random scans to assure a good interobserver agreement. Both observers were trained in CF-CT scoring and began scoring the study CTs after establishing good intra- and interobserver agreement.

CFQ-R

Three age-appropriate versions of the Dutch CFQ-R were administered, using a multi-informant approach (table 1): 1) the CFQ-R Child version (ages 6–13 years; 35 items covering eight domains); 2) CFQ-R Parent version (caregivers of children aged 6–13 years; 43 items covering 11 domains); and 3) CFQ-R Teen/Adult version (ages ⩾14 years; 47 items covering 12 domains) [13]. In addition to analysing the CFQ-R RSS, we analysed three health-related secondary domains: CFQ-R physical functioning, CFQ-R vitality and CFQ-R health perceptions scales. Unfortunately, the CFQ-R vitality and CFQ-R health perceptions do not exist for younger children (CFQ-R Child version).

All scale scores were standardised on a 0–100 scale, with higher scores indicating better health-related quality of life [13].

PFT and pulmonary exacerbations

PFT results (diagnostic system: Jaeger AG, Würzburg, Germany) were expressed as percentages of predictive values, according to Stanojevic *et al.* [24] for forced vital capacity (FVC) and FEV_1 and Zapletal *et al.* [25] for forced expiratory flow at 75% of FVC.

Because there is no consensus on the definition of pulmonary exacerbations, they were conservatively defined as episodes of treatment with *i.v.* antibiotics for pulmonary indications in the year following administration of CT and CFQ-R [7, 8]. *Pseudomonas aeruginosa* positivity was defined as the presence of at least one and less than three positive respiratory cultures in the year previous to the CT scan. Chronic colonisation with *Pseudomonas aeruginosa* was defined as three or more consecutive positive respiratory cultures.

TABLE 1 Selected Cystic Fibrosis Questionnaire-revised (CFQ-R) scores for children, their parents and adolescents

	Children (6–13 years)		Adolescents (⩾14 years)
	CFQ-R Child version	CFQ-R Parent version	CFQ-R Teen/Adult version
Subjects	40	37	32
Respiratory symptoms	83 (50–100)	89 (50–100)	77 (11–100)
Physical functioning	83 (39–100)	93 (52–100)	90 (38–100)
Vitality		73 (47–93)	67 (25–100)
Health perceptions		78 (22–100)	67 (22–100)

Data are presented as n or median (range). CFQ-R scale scores are shown for the different versions of the CFQ-R. The CFQ-R respiratory symptoms scale was the primary target. Physical functioning, vitality and health perceptions were secondary domains correlating with forced expiratory volume in 1 s. For each domain, a score of 0–100 is calculated. Higher scores indicate better health-related quality of life.

Statistical analysis

Inter- and intraobserver agreement of CF-CT scores were calculated using intra-class correlation coefficients (ICC) (0.40–0.60 moderate; 0.60–0.80 good; and ⩾0.80 very good agreement). In case of low or moderate agreement between the observers, Bland–Altman plots were calculated and used to visualise whether one over- or underestimated the CT scores on the different indices [26]. Spearman's correlation coefficients were used to correlate CF-CT bronchiectasis and CF-CT trapped air scores with CFQ-R RSS, CFQ-R physical functioning, CFQ-R vitality and CFQ-R health perceptions scale scores. Negative binomial regression models were used to investigate the association between CF-CT bronchiectasis, CF-CT trapped air and CFQ-R RSS and the number of pulmonary exacerbations in the subsequent year. A multivariate model was evaluated (backward, stepwise approach) to identify independent predictors of pulmonary exacerbations in the subsequent year. In order to reach sufficient power the univariate and multivariate regression analyses were performed on the complete study population (n=72). Analyses were repeated using the CFQ-R Child version and CFQ-R Parent version in children aged 6–13 years. In our final model, the CFQ-R Child version was used, because it is better to use the patient's own report on his/her symptoms as recommended by the FDA [27] and the European Medicines Agency. To interpret our results in clinical terms, we used a logistic model.

Statistical analyses were performed using SAS version 9.2 (SAS Institute Inc., Cary, NC, USA). Results are displayed as median (range) unless otherwise defined. Two-tailed testing was performed. p-values <0.05 were considered to be significant.

Results

Study population

72 patients (40 children and 32 adolescents) had 72 CTs and PFTs completed. Baseline characteristics are shown in table 2. A total of 109 CFQ-Rs were collected: 40 CFQ-R Child version; 37 CFQ-R Parent version; and 32 CFQ-R Teen/Adult version. Three parents did not return the CFQ-R (see table 1). ICCs for intraobserver agreement ranged from 0.68 (CF-CT trapped air score) to 0.98 (CF-CT bronchiectasis score), whereas interobserver agreement ranged from 0.50 (CF-CT trapped air score) to 0.91 (CF-CT total score).

Correlations between CT and CFQ-R

In children the CF-CT airway wall thickening ($p<0.001$), mucus plugging ($p<0.001$) and opacities ($p=0.007$) were significantly correlated with the CFQ-R RSS (table 3). Similarly, CF-CT airway wall thickening ($p=0.01$) and mucus plugging ($p=0.008$) were significantly correlated with the CFQ-R RSS scores in the parent questionnaires, but, in addition, so was the CF-CT bronchiectasis score ($p=0.033$). Similar associations were found among adolescents: CF-CT bronchiectasis score ($p=0.007$), airway wall thickening ($p=0.005$), mucus plugging ($p=0.004$) and opacities ($p=0.004$) all significantly correlated with the CFQ-R RSS scores.

TABLE 2 Baseline characteristics of the study cohort

	Total	Children	Adolescents
Subjects	72	40	32
Male	35 (48.6)	20 (50)	15 (46.9)
Age years	13.4 (6–20)	11.5 (6–14)	16.5 (14–20)
FEV1 % predicted	83.4 (22–110)	85.7 (31–110)	75.9 (22–110)
FVC % predicted	91.9 (32–119)	97.9 (53–119)	85.9 (32–112)
FEF75 % predicted	48.5 (6–95)	48 (7–95)	49.2 (6–92)
Positive *Pseudomonas aeruginosa* culture[#]	26 (36)	10 (25)	16 (50)
Chronic infection with *Pseudomonas aeruginosa*[¶]	19 (26)	5 (13)	14 (44)
CF-CT total score %	7.8 (0–33)	5.2 (0–20)	11.8 (0–33)
Bronchiectasis score %	0.0 (0–26)	0 (0–19)	2.6 (0–26)
Airway wall thickening score %	8.3 (0–37)	4.9 (0–33)	14.8 (0–37)
Mucus plugging score %	8.3 (0–50)	5.6 (0–50)	16.7 (0–42)
Opacities %	5.6 (0–19)	4.6 (0–13)	7.4 (0–19)
Trapped air %	36.7 (0–97)	33.3 (0–70)	43.3 (7–97)

Data are presented as n, n (%) or median (range). FEV1: forced expiratory volume in 1 s; FVC: forced vital capacity; FEF75: forced expiratory flow at 75% of FVC; CF-CT: cystic fibrosis computed tomography scoring system. [#]: includes all positive *Pseudomonas aeruginosa* cultures positive in the year prior to computed tomography and Cystic Fibrosis Questionnaire-revised; [¶]: chronic infection with *P. aeruginosa* defined as three or more consecutive positive respiratory cultures for *P. aeruginosa*.

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TABLE 3 Correlations between cystic fibrosis computed tomography (CF-CT) scores and selected revised Cystic Fibrosis Questionnaire (CFQ-R) scaled scores across versions

	Children (6–13 years)						Adolescents (⩾14 years)				Children and adolescents	
	CFQ-R Child version (n=40)		CFQ-R Parent version (n=37)				CFQ-R Teen/Adult version (n=32)				Total (n=72)	
	Respiratory symptoms	Physical functioning	Respiratory symptoms	Physical functioning	Vitality	Health perceptions	Respiratory symptoms	Physical functioning	Vitality	Health perceptions	Respiratory symptoms	Physical functioning
CF-CT bronchiectasis score	-0.22	0.09	-0.35*	-0.26	0.01	-0.02	-0.46**	-0.50**	-0.23	-0.28	-0.38**	-0.09
CF-CT airway wall thickening score	-0.51**	-0.13	-0.42*	-0.41*	-0.19	-0.18	-0.49**	-0.53**	-0.22	-0.37*	-0.51**	-0.17
CF-CT mucus plugging score	-0.63**	-0.15	-0.43**	-0.14	-0.09	-0.03	-0.49**	-0.49**	-0.25	-0.36*	-0.56**	-0.25*
CF-CT opacities scores	-0.42**	0.17	-0.31	0.14	0.07	0.20	-0.50**	-0.42*	-0.28	-0.30	-0.47**	-0.04
CF-CT trapped air scores	-0.26	0.08	-0.14	0.03	0.03	0.09	-0.40*	-0.37*	-0.26	-0.18	-0.35**	-0.09

*: Correlation is significant at the 0.05 level (two-tailed); **: correlation is significant at the 0.01 level (two-tailed).

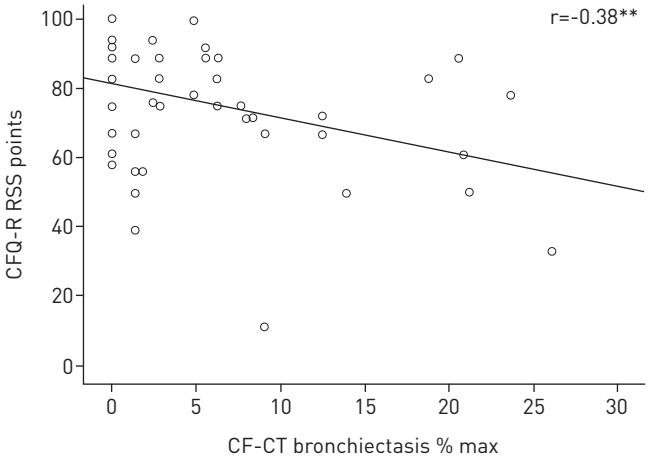

FIGURE 1 Correlation between Cystic Fibrosis Questionnaire-revised respiratory symptoms scale (CFQ-R RSS) and cystic fibrosis computed tomography (CF-CT) bronchiectasis score across ages. n=72. **: $p<0.01$.

No significant correlations were found between the CF-CT scores and the physical functioning scale in children, whereas in adolescents all of the CF-CT scores correlated.

In the other health-related secondary domains (vitality and health perceptions), only CFQ-R health perceptions in adolescents was significantly associated with CF-CT airway wall thickening ($p=0.038$) and CF-CT mucus plugging ($p=0.041$).

Across ages (n=72), CF-CT bronchiectasis scores were significantly correlated with CFQ-R RSS ($r= -0.38$, $p<0.001$), with more structural changes being associated with worse respiratory symptoms (fig. 1). This relationship was also present between CF-CT trapped air scores and CFQ-R RSS ($r= -0.35$, $p=0.003$) (fig. 2).

Associations between CT, CFQ-R RSS and pulmonary exacerbations in the following year

Associations between CT, CFQ-R RSS and pulmonary exacerbations in the year following CT and CFQ-R RSS are shown in table 4.

CF-CT bronchiectasis scores were significantly associated with the number of pulmonary exacerbations in the following year (rate ratio 1.10, 95% CI 1.02–1.19; $p=0.009$). This indicates that the expected number of pulmonary exacerbations increased by 10% in the following year (95% CI 2.4–19%) for each point increase in a patient's CF-CT bronchiectasis score. The rate ratio for CF-CT trapped air on pulmonary exacerbations in the following year was smaller, but also significant (rate ratio 1.02, 95% CI 1.00–1.05; $p=0.034$). CFQ-R RSS were associated with pulmonary exacerbations in the following year (rate ratio 0.95, 95% CI 0.91–0.98; $p=0.002$). Thus, the expected number of pulmonary exacerbations decreased 5% for each one-point increase in CFQ-R RSS scores.

Prediction model for pulmonary exacerbations

72 patients had complete longitudinal data for the multivariate prediction model. Due to the relatively small sample size, a limited number of predictors were tested: sex, age, CF-CT bronchiectasis score, CF-CT trapped air score, CFQ-R RSS and positive culture for *P. aeruginosa* in the year before the CT. In the final

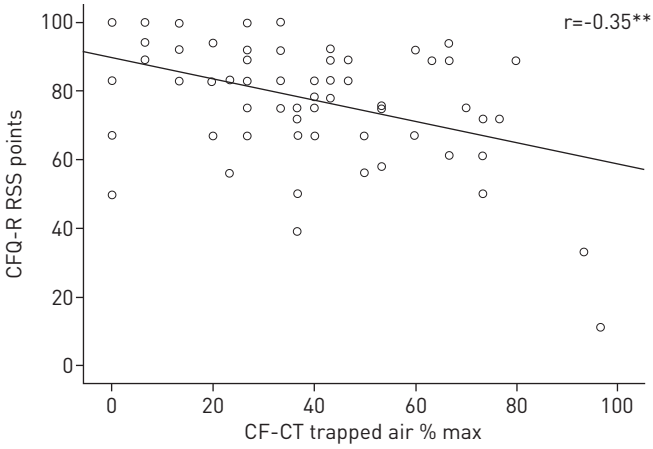

FIGURE 2 Correlation between Cystic Fibrosis Questionnaire-revised respiratory symptoms scale (CFQ-R RSS) and cystic fibrosis computed tomography (CF-CT) trapped air score across ages. n=72. **: $p<0.01$.

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TABLE 4 Univariate and multivariate associations with pulmonary exacerbations in the year following computed tomography and completion of the Cystic Fibrosis Questionnaire-revised (CFQ-R)

Predictor	Univariate associations		Multivariate prediction model#	
	Rate ratio¶ (95% CI)	p-value	Rate ratio¶ (95% CI)	p-value
CF-CT bronchiectasis score	1.10 (1.02–1.19)	0.009		NS
CF-CT trapped air score	1.02 (1.00–1.05)	0.034		NS
CFQ-R RSS	0.95 (0.91–0.98)	0.002	0.96 (0.94–0.97)	<0.001
Positive culture *Pseudomonas aeruginosa*+	1.98 (1.22–3.23)	0.006	1.72 (1.10–2.69)	0.008
Age	1.21 (1.02–1.44)	0.030	1.52 (1.00–2.30)	0.001
Sex	1.03 (0.38–2.80)	0.951		NS

Data are presented as rate ratio (95% CI), unless otherwise stated. n=72. In young children (6–13 years) the CFQ-R Child version was used. CF-CT: cystic fibrosis computed tomography; CFQ-R RSS: revised Cystic Fibrosis Questionnaire respiratory symptoms scale; NS: not significant. #: only variables significant at the p=0.05 level are included in the multivariable model; ¶: rate ratio for scores calculated per point increase in score; +: defined as at least one positive respiratory culture for *P. aeruginosa* in the year before computed tomography and completion of CFQ-R.

model, significant predictors of subsequent pulmonary exacerbations were: age (p=0.001), CFQ-R RSS (p<0.001), and positive cultures for *P. aeruginosa* (p=0.008) (table 4). A decrease of one point in CFQ-R RSS scores predicted a 4.7% (95% CI 3.0–6.3%) increase in pulmonary exacerbations in the following year. QUITTNER *et al.* [22] showed that a four-point reduction in CFQ-R RSS scores was clinically meaningful. According to the logistic model used in our study, this would equate to a 20% (4.7^4) increase in the number of pulmonary exacerbations in the following year. To determine whether CFQ-R scores were merely a reflection of the number of pulmonary exacerbations in the previous year, we performed a sensitivity analysis adding the number of pulmonary exacerbations in the previous year to the multivariate model. Interestingly, CFQ-R RSS scores continued to add predictive value for number of pulmonary exacerbations in the following year (2.6% decrease per point in CFQ-R, 95% CI 0.4–4.8%; p=0.014). CF-CT bronchiectasis and trapped air did not remain significant in the multivariate model. No meaningful differences were present when the analysis was performed using the CFQ-R Parent version in place of the CFQ-R Child version.

Discussion

This is the first study to investigate the relationship between bronchiectasis and trapped air, assessed by chest CT and CFQ-R RSS scores. The most important finding was that more severe bronchiectasis was significantly associated with worsening respiratory symptoms. Bronchiectasis, trapped air and CFQ-R RSS were all significantly associated with pulmonary exacerbations in the following year.

The importance of bronchiectasis in CF lung disease has been well established [1, 3–5, 7–9]; however, the impact of bronchiectasis on patient-reported outcome measures in CF had not previously been examined [10]. Our finding that bronchiectasis and CFQ-R RSS are negatively associated supports the validity of bronchiectasis as a clinically relevant outcome measure. Previous studies have shown that bronchiectasis was associated with pulmonary exacerbations in the following 2 years [7, 8], while our data showed a similar association over a 1-year time period. Unfortunately, in our multivariate model, CF-CT bronchiectasis did not remain a significant predictor for pulmonary exacerbations, probably because we have a patient population with very mild CF, reflected by a median bronchiectasis score of 0.0 (table 2).

Although trapped air has been less well validated as an outcome measure, we found a significant, independent correlation between trapped air and CFQ-R RSS. Although the associations between CF-CT trapped air scores and both CFQ-R RSS and pulmonary exacerbations were significant, they were not as strong as the associations with bronchiectasis. This may be because trapped air has less impact on patient functioning than bronchiectasis and can be reversible to some extent [1, 2]. A recent study showed that patients with severe advanced lung disease, such as bronchiectasis, had a higher mortality risk compared to patients who predominantly had trapped air [9]. Our results suggested that trapped air can also be considered as a valuable CT-related surrogate outcome measure in CF.

Interestingly, we also found significant associations in other CT indices: CF-CT airway wall thickening, mucus plugging and opacities were significantly associated with the CFQ-R RSS in children and adolescents. Airway wall thickening and mucus plugging are considered to be early indicators of developing disease, in contrast to bronchiectasis, which is considered to be advanced structural damage in the larger airways. Therefore, it is not surprising that these early indicators, and not bronchiectasis, were significantly

associated with the CFQ-R RSS in the younger age group. Note that this was a young population with very mild CF lung disease. This further validates the CFQ-R RSS as a sensitive measure of structural lung damage in the early stages of CF lung disease.

We found that the lower the CFQ-R RSS score, the higher the risk for pulmonary exacerbations, irrespective of other predictors. This innovative result is consistent with the research of BRITTO *et al.* [28]. They concluded that pulmonary exacerbations have a profound negative impact on health-related quality of life in CF children, using a generic instrument (Child Health Questionnaire). Furthermore, our data suggested that the CFQ-R RSS is sensitive to early minor respiratory symptoms preceding pulmonary exacerbations. Therefore the CFQ-R RSS may allow earlier detection of disease progression.

In our multivariate model, after including CFQ-R RSS, CT had no added value to predict the frequency of pulmonary exacerbations. It is important to realise that the CFQ-RSS and CT provide different information. The CFQ-R RSS focuses exclusively on the frequency and severity of respiratory symptoms, whereas CT provides critical information about structural lung changes such as the extent of bronchiectasis and trapped air. CT also provides information about airway wall thickening and mucus plugging, which can be considered early leading indicators of developing disease. Consequently, aggressive treatment to prevent structural lung damage should be considered if either indicator is present on CT. Therefore, both CT and CFQ-R RSS are considered important outcome measures.

Limitations

This was a retrospective study. Therefore, we selected a robust, conservative definition of pulmonary exacerbations that were unlikely to be missed [7, 8, 29, 30]. Data were collected from a single centre, which may reduce the generalisability of the results. Furthermore, we used an age-range of 6–20 years; whether similar correlations exist in infant or adult CF populations requires further study. Considering the progressive nature of CF, we would expect a higher rate of pulmonary exacerbations in adults and, thus, stronger associations.

In conclusion, we showed that in children with CF, more severe bronchiectasis and trapped air were associated with worse CFQ-R RSS scores. Bronchiectasis, trapped air and the CFQ-R RSS were significantly associated with pulmonary exacerbations in the following year. Our findings validate the importance of CT measures of bronchiectasis and trapped air and the CFQ-R RSS as clinically relevant outcome measures for CF.

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