Published in final edited form as:

Pediatr Pulmonol. 2012 June ; 47(6): 567–573. doi:10.1002/ppul.21621.

The Sensitivity of Lung Disease Surrogates in Detecting Chest CT Abnormalities in Children with Cystic Fibrosis

Don B. Sanders¹, Zhanhai Li², Michael J. Rock¹, Alan S. Brody³, and Philip M. Farrell¹

¹Department of Pediatrics, University of Wisconsin School of Medicine and Public Health, Madison, WI

²Department of Biostatistics and Medical Informatics, University of Wisconsin, Madison, WI

³Department of Radiology, Cincinnati Children's Hospital Medical Center, Cincinnati, OH

Abstract

Rationale—Chest CT scans detect structural abnormalities in children with cystic fibrosis (CF), even when pulmonary function tests (PFTs) are normal. The use of chest CT is limited in clinical practice, because of concerns over expense, increased resource utilization, and radiation exposure. Quantitative chest radiography scores are useful in detecting mild lung disease, but whether they are sensitive to the presence of CT scan abnormalities has not been evaluated.

Objective—To determine in a cross-sectional study if quantitative chest radiography is a more sensitive marker of chest CT abnormalities than other lung disease surrogates.

Methods—Brody chest CT scores were calculated for 81 children enrolled in the Wisconsin CF Neonatal Screening Project. We determined the sensitivity for Wisconsin (WCXR) and Brasfield (BCXR) chest radiography scores, PFTs, positive cultures for *P. aeruginosa* (PA), and parental report of symptoms to detect a Brody score worse than the median score for study participants.

Measurements and Main Results—The mean FEV₁ for the study population was 91% predicted. Abnormal WCXR and BCXR scores had the highest sensitivity to detect a chest CT score worse than the median; abnormal PFTs, parental report of symptoms, and the presence of PA had much lower sensitivity ($p < 0.001$).

Conclusions—In this cross sectional study, quantitative chest radiography has excellent sensitivity to detect an abnormal chest CT and may have a role in monitoring lung disease progression in children with CF.

Keywords

Chest x-ray; quantitative radiography; pulmonary function

INTRODUCTION

Lung disease progression inevitably occurs for all patients with cystic fibrosis (CF) and traditionally has been monitored clinically and evaluated in clinical trials by forced expiratory volume in one second (FEV₁). Recent data in the CF Foundation Patient Registry, however, suggest that median FEV₁ values may remain normal well into adolescence for the most recent birth cohorts.¹ Similarly, reports from the Wisconsin

Corresponding Author/Requests for Reprints: Don B. Sanders, MD, MS, American Family Children's Hospital, 600 Highland Avenue, K4/920, Madison, WI 53792-9988, dbsanders@pediatrics.wisc.edu, Phone: 608-265-3425, Fax: 608-263-0510.

Data was presented at the European Cystic Fibrosis Society Conference in June, 2010

Randomized Control Trial of CF Neonatal Screening (WI RCT) when the oldest patients were adolescents indicated that the mean FEV₁ tended to be normal.² Others have recently reported that the slow rate of change of FEV₁ makes detecting lung disease progression difficult, both in clinical practice and in research.^{3,4}

In contrast, high-resolution computed tomography (CT) of the chest has become the gold standard for the detection and assessment of structural abnormalities of the lung⁵, demonstrating all aspects of morphologic lung disease in CF. CT scans have been shown to detect early structural abnormalities in young children with CF, even when FEV₁ is normal.^{6,7} Moreover, chest CT scans have been used to detect bronchiectasis in the first year of life in children diagnosed early via newborn screening.⁸ While chest CT is widely used in clinical practice,⁹ the use of chest CT scans is often limited over concerns regarding increased monetary expenses, increased utilization of resources, and significantly increased radiation exposure as compared to routine chest radiography.¹⁰ Recognizing the potential value of chest CT scanning, we added a chest CT scan to the protocol of the WI RCT in 2000.¹¹

During the WI RCT, we designed the Wisconsin chest radiograph scoring system (WCXR), a reproducible method of analyzing chest radiography with the ability to detect mild lung disease.¹² We² and others¹³ have demonstrated the utility of the WCXR in detecting mild structural lung abnormalities, and we have recently shown that quantitative chest radiography scores are as strongly associated with future measures of lung disease as chest CT scores.¹⁴ Whether WCXR is sensitive to concurrent CT abnormalities has not been evaluated. We hypothesized that WCXR would be a more sensitive marker of abnormal chest CT scans than traditional pulmonary function tests. If this were the case, then chest radiograph scoring systems could be evaluated as a means to monitor lung disease progression and reduce the number of chest CT scans in patients with CF. The results of this study were previously reported in abstract form.¹⁵

MATERIALS AND METHODS

Design of the Wisconsin Randomized Control Trial of CF Neonatal Screening

The design of the WI RCT is described in detail elsewhere.¹⁶ In summary, we conducted a randomized control trial (RCT) to assess the potential benefits and risks of early diagnosis through neonatal screening. Blood specimens of newborns born in Wisconsin between 1985 and 1994 were assigned either to an early CF diagnosis (screened) group or to a standard diagnosis (control) group.¹⁶ Control patients were unblinded at 4 years of age to avoid selection bias.¹¹ A sweat chloride level of ≥ 60 mEq/L at one of Wisconsin's two CF Centers (the University of Wisconsin and the Children's Hospital of Wisconsin) was required to establish the diagnosis. This investigation was approved by the institutional review boards at the University of Wisconsin and the Children's Hospital of Wisconsin.

Patients were seen every 3 months and assessed by an Evaluation and Treatment Protocol¹⁶ developed in 1984 and reviewed regularly. After diagnosis, each patient was placed on similar treatments and had the same systematic evaluations performed. Patients were prospectively followed in the study through age 21. Serial cultures of respiratory secretions were obtained quarterly as expectorated sputum or as oropharyngeal swabs.¹⁷ Parents reported frequency of cough and sputum production at each clinic visit. Pulmonary function tests (PFTs) were obtained when children were old enough to perform spirometry and/or body plethysmography, as described elsewhere.¹⁸ PFTs were generally begun when children reached 4 years of age, and obtained at least every 6 months with strict quality control measures.¹⁸ Chest radiographs were obtained at the time of diagnosis, age 2 years, age 4 years, and annually and were scored using the Brasfield (BCXR) and Wisconsin

(WCXR) scoring systems.^{19,20} These films were labeled with codes and scored randomly by a pediatric pulmonologist and thoracic radiologist who were unaware of patient identity or age, using the Wisconsin system^{12,19} with six components including bronchiectasis and air trapping and the Brasfield system²⁰ with five components including nodular/cystic lesions and air trapping. As a quality control procedure, in addition to scoring the study patients' chest radiographs, both raters were given 32 reference CF chest films repeatedly to assess their reproducibility and inter-rater agreement. Comparisons revealed more than satisfactory correlations.^{18,19} The scores from both the pulmonologist and radiologist were averaged using the Wisconsin additive method's formula¹⁹ or the Brasfield deduction method²⁰ to produce the final summary scores. The range of chest radiograph scores in the Wisconsin system is from 0–100, with 0 being the best and 100 being the worst, and the corresponding range is 1–25 in the Brasfield system, with 25 being the best.

A chest CT was added in 2000 for patients who continued to receive care in the protocol at the two CF centers. Enrollees who were ≥ 6 years of age and who gave additional informed consent underwent CT scanning performed as described previously.²¹ Briefly, one chest CT scan (Lightspeed; GE Medical Systems, Milwaukee) was obtained in each of the patients at their baseline health status using a thin-section technique (1.25-mm section thickness) with inspiratory images at 10 mm intervals and expiratory images at 20 mm intervals. Hard-copy images were scored independently by three radiologists (ASB and two others) blinded to patient identities using the Brody scoring system.²² Reference images were used for quality control purposes. The agreement of the three raters was excellent as reported elsewhere.²²

Statistical Analysis

The mean Brody chest CT score was determined from the three radiologists' individual scores. We determined the correlation between the Brody chest CT score and the most recent (i.e., within the one year prior to the chest CT) measurements for WCXR, BCXR, PFTs, PA, and parental report of cough and sputum for each patient. We compared the sensitivity for an abnormal value for each surrogate to detect a Brody score worse than the median Brody score for the study participants. Abnormal values were defined as: WCXR > 5,¹⁸ BCXR < 21,¹⁸ FEV₁ < 82.4% predicted,²³ FEV₁/FVC < 80%, FEF_{25–75} < 67.9% predicted,²³ RV/TLC > 30%, culture positive for PA, daily cough, and daily sputum. We determined the sensitivity of abnormal values for each surrogate to detect a Brody bronchiectasis and air trapping subscore worse than the median Brody subscore for the study participants. We also determined the sensitivity of a WCXR bronchiectasis subscore and BCXR nodular cystic subscore > 0, and WCXR and BCXR air trapping score > 0, to detect a Brody bronchiectasis and air trapping subscore worse than the median Brody subscore for the study participants, respectively. We performed sensitivity analyses to compare the sensitivities for detecting a Brody score worse than the 10th and 25th percentile score, as well as using only the data available within 6 months prior to the chest CT.

RESULTS

There were 132 children with CF originally enrolled in the Wisconsin CF Neonatal Screening Project (Figure 1). When the chest CT was added to the protocol in 2000, there were 98 patients who continued to receive care at the two CF centers. Of these, 89 patients gave consent to undergo CT scanning, however, five patients never came for their scheduled appointment and three scans could not be used due to protocol deviations. Thus, 81 patients participated in the CT study. All CT scans scored were of good quality as indicated by the lack of patient motion or any other factor that would interfere with recognition of bronchiectasis, with no patients excluded due to inadequate image quality. There were no significant differences in demographics or population description between these patients and the original Wisconsin CF Neonatal Screening Project cohort (Table 1).

The median (range) Brody score was 2.0 (0–12.8), out of a total possible score of 34.5. The mean Brody score was similar between patients in the control group (3.6) and the screened group (2.7), $p = 0.2$. The mean WCXR (15.4) and BCXR (18.8) scores indicated the presence of irreversible abnormalities (Table 2), based on criteria of scores greater than 5 for WCXR and less than 21 for BCXR.¹⁸ Scores were indicative of irreversible changes for 83% of WCXR scores and 73% of BCXR scores.

Although all of the correlations between chest CT and the lung disease surrogates were statistically significant ($p < 0.04$ for all), the correlations between WCXR and BCXR and chest CT score were much higher (Table 3 and Figures 2–3 and Online Supplement Figures E1–E4). Similarly, abnormal WCXR and BCXR scores had perfect sensitivity to detect a chest CT score worse than the median, whereas abnormal PFTs, parental report of daily cough or sputum, and the presence of PA in respiratory secretions had much lower sensitivity (Table 4). RV/TLC was the most sensitive PFT; other PFT measures were not as sensitive as parental report of symptoms or PA. WCXR was significantly more sensitive than other lung disease measures tested ($p < 0.001$ for each, McNemar's test), with the exception of BCXR. Using the subscores of the CT and CXR scoring systems, we found that WCXR and BCXR scores had excellent sensitivity to detect chest CT bronchiectasis and air trapping subscores worse than the median (Figures 4–5, Table 5, and Online Supplement Figures E5–E6). Abnormal WCXR (Figures 6–7) and BCXR subscores (Online Supplement Figures E7–E8) had similarly high sensitivities although the correlation was much weaker for the air trapping scores, whereas abnormal PFTs and parental report of daily cough or sputum had much lower sensitivities (Online Supplement Figures E9–E18).

The results were not different when we determined the sensitivity to detect a chest CT score worse than the 10th or 25th percentile, or restricted data to the 6 months prior to the chest CT (Table 6).

DISCUSSION

Using data gathered prospectively as part of the Wisconsin CF Neonatal Screening Project, we have demonstrated that the Wisconsin and Brasfield chest radiography scoring systems are highly sensitive in detecting chest CT abnormalities. Our findings confirm previous research that has demonstrated the lack of sensitivity of FEV₁ in detecting changes in chest CT images, especially in young patients.^{6,7,24,25} Additionally, the Wisconsin and Brasfield chest radiography scoring systems are more sensitive than PFTs or the other markers of lung disease progression available in the WIRCT and are sensitive to bronchiectasis and air trapping, two specific CT findings that are prominent in early CF lung disease.⁸

Others have demonstrated the usefulness of quantitative chest imaging in monitoring lung disease progression in patients with CF. Slattery et al.²⁶ evaluated the effectiveness of aerosolized tobramycin by comparing the rates of change of Brasfield scores before and after initiating aerosolized tobramycin in 14 patients, ages 2 months to 22 years. They were able to demonstrate a statistically significant improvement in the decline of Brasfield scores. They did not detect a statistically significant improvement in FEV₁ decline. Terheggen-Lagro et al.¹³ showed that mean chest radiograph scores (including the Wisconsin and Brasfield scores) worsened for 21 preschool-aged children and 30 school-aged children over a 3-year study period. There was not a concurrent change in FEV₁, although they did find a statistically significant change in FEV₁/FVC.

Chest CT is the current gold standard for detection of bronchiectasis, the defining structural abnormality in CF.⁵ In the current study, we have shown that quantitative chest radiography has excellent sensitivity for chest CT abnormalities, including bronchiectasis and air

trapping. The WCXR and BCXR cut-offs ($WCXR > 5$ and $BCXR < 21$) were chosen because these values represent changes that have a high likelihood of being irreversible on serial evaluations.¹⁸ For patients with CF, irreversible changes on quantitative chest radiography correlate with the presence of bronchiectasis.¹⁸ Moreover, WCXR and BCXR have high sensitivity to detect elevated Brody bronchiectasis and air trapping subscores, both when the composite WCXR and BCXR and when the bronchiectasis (nodular cystic) and air trapping subscores are used. In practice, a WCXR and/or BCXR score could be calculated annually from a chest radiograph obtained during a period of clinical stability for patients with CF. Elevated scores, or specific subscores, may be used as an indication for further evaluations of CF lung disease. This may include a chest CT to confirm the presence of abnormalities, and to further characterize and evaluate the severity and extent of the abnormalities. If WCXR and/or BCXR scores are to be introduced into clinical care, it is important to have multiple scorers, with randomly mixed patients and quality control with standard or repeat films to maintain objectivity and avoid bias.¹²

Our study has several limitations. The first is that our study was cross-sectional and cannot address whether serial quantitative chest radiography can be used to monitor lung disease progression longitudinally. However, the results reported here, in combination with our previous findings that quantitative chest radiography is as strongly associated with future measures of lung disease as chest CT scores,¹⁴ indicates that this may be a possibility and should be evaluated. Second, not all lung disease surrogates were measured at the same time as the chest CT, creating the possibility that lung disease measures were not accurate reflections of lung disease severity at the time of the chest CT. When the study was restricted to measurements made less than 6 months prior to the chest CT, however, there was no difference in the results and our conclusions (Table 6). Additionally, only 8 of the 82 patients were hospitalized in the year prior to the chest CT, which would indicate that lung disease was generally stable for these patients. Third, there is no agreed-upon definition of Brody chest CT score severity. Given the lack of clinically-meaningful cut-points, we chose to determine the sensitivity to detect a chest CT score worse than the median of the chest CT scores for the 81 patients in this study. This cut-point is indicative of mild disease,⁶ suggesting that WCXR and BCXR are sensitive in detecting early changes of CF lung disease. Furthermore, if a cut-point of a Brody score of 1 were used, then the sensitivity of FEV_1 (36%) remains significantly worse than the sensitivity of WCXR (85%), $p < 0.001$. Finally, the CT protocol used in this study used an interval technique that samples only 10% of the lung parenchyma. Current volumetric techniques would likely be more sensitive to the presence of CF lung disease, including bronchiectasis and air trapping.

Despite these limitations, we have shown that quantitative chest radiography has excellent sensitivity to detect an abnormal chest CT. The CF community is not yet in agreement regarding the optimal role of chest CT in the routine care of children with CF. Additional considerations should be made to include quantitative chest radiography, as it may have a role in monitoring of lung disease progression, especially in children with normal PFTs.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Support: NIH R01 DK34108-23S1 Revised (Farrell)

We thank the patients and the families who participated in this project and remain grateful to the entire Wisconsin Neonatal CF Screening Project team in Madison and Milwaukee. The authors would like to thank Anita Laxova for assistance with manuscript preparation and with the database.

References

1. CF Foundation. Cystic Fibrosis Foundation Patient Registry 2008 Annual Data Report. Bethesda, MD;
2. Farrell P, Li Z, Kosorok M, Laxova A, Green C, Collins J, Lai H, Rock M, Splaingard M. Bronchopulmonary disease in children with cystic fibrosis after early or delayed diagnosis. *Am J Respir Crit Care Med*. 2003; 168(9):1100–1108. [PubMed: 12917228]
3. Gustafsson P, De Jong P, Tiddens H, Lindblad A. Multiple-breath inert gas washout and spirometry versus structural lung disease in cystic fibrosis. *Thorax*. 2008; 63(2):129–134. [PubMed: 17675316]
4. Saiman L, Anstead M, Mayer-Hamblett N, Lands LC, Kloster M, Hocevar-Trnka J, Goss CH, Rose LM, Burns JL, Marshall BC, Ratjen F. AZ0004 Azithromycin Study Group. Effect of azithromycin on pulmonary function in patients with cystic fibrosis uninfected with *Pseudomonas aeruginosa*: a randomized controlled trial. *JAMA*. 2010; 303(17):1707–1715. [PubMed: 20442386]
5. Hansell DM. Bronchiectasis. *Radiol Clin North Am*. 1998; 36(1):107–128. [PubMed: 9465870]
6. Brody A, Klein J, Molina P, Quan J, Bean J, Wilmott R. High-resolution computed tomography in young patients with cystic fibrosis: distribution of abnormalities and correlation with pulmonary function tests. *J Pediatr*. 2004; 145(1):32–38. [PubMed: 15238903]
7. de Jong P, Nakano Y, Lequin M, Mayo J, Woods R, Paré P, Tiddens H. Progressive damage on high resolution computed tomography despite stable lung function in cystic fibrosis. *Eur Respir J*. 2004; 23(1):93–97. [PubMed: 14738238]
8. Stick S, Brennan S, Murray C, Douglas T, von Ungern-Sternberg B, Garratt L, Gangell C, De Klerk N, Linnane B, Ranganathan S, Robinson P, Robertson C, Sly P. Australian Respiratory Early Surveillance Team for Cystic Fibrosis (AREST CF). Bronchiectasis in infants and preschool children diagnosed with cystic fibrosis after newborn screening. *J Pediatr*. 2009; 155(5):623–628.e621. [PubMed: 19616787]
9. Tiddens HA. Chest computed tomography scans should be considered as a routine investigation in cystic fibrosis. *Paediatr Respir Rev*. 2006; 7(3):202–208. [PubMed: 16938643]
10. Cooper P, MacLean J. High-resolution computed tomography (HRCT) should not be considered as a routine assessment method in cystic fibrosis lung disease. *Paediatr Respir Rev*. 2006; 7(3):197–201. [PubMed: 16938642]
11. Farrell P, Kosorok M, Rock M, Laxova A, Zeng L, Lai H, Hoffman G, Laessig R, Splaingard M. Early diagnosis of cystic fibrosis through neonatal screening prevents severe malnutrition and improves long-term growth. Wisconsin Cystic Fibrosis Neonatal Screening Study Group. *Pediatrics*. 2001; 107(1):1–13. [PubMed: 11134427]
12. Weatherly M, Palmer C, Peters M, Green C, Fryback D, Langhough R, Farrell P. Wisconsin cystic fibrosis chest radiograph scoring system. *Pediatrics*. 1993; 91(2):488–495. [PubMed: 8424032]
13. Terheggen-Lagro SW, Arets HG, van der Laag J, van der Ent CK. Radiological and functional changes over 3 years in young children with cystic fibrosis. *Eur Respir J*. 2007; 30(2):279–285. [PubMed: 17459897]
14. Sanders DB, Li Z, Brody AS, Farrell PM. Chest CT Scores of Severity are Associated with Future Lung Disease Progression in Children with CF. *Am J Respir Crit Care Med*. 2011
15. Sanders D, Li Z, Rock M, Brody A, Collins J, Farrell P. The sensitivity of lung disease surrogates in children with CF: limited value of FEV1. *Journal of Cystic Fibrosis*. 2010; 9(S1):S110.
16. Farrell PM. Improving the health of patients with cystic fibrosis through newborn screening. Wisconsin Cystic Fibrosis Neonatal Screening Study Group. *Adv Pediatr*. 2000; 47:79–115. [PubMed: 10959441]
17. Kosorok M, Jalaluddin M, Farrell P, Shen G, Colby C, Laxova A, Rock M, Splaingard M. Comprehensive analysis of risk factors for acquisition of *Pseudomonas aeruginosa* in young children with cystic fibrosis. *Pediatr Pulmonol*. 1998; 26(2):81–88. [PubMed: 9727757]
18. Farrell P, Li Z, Kosorok M, Laxova A, Green C, Collins J, Lai H, Makhholm L, Rock M, Splaingard M. Longitudinal evaluation of bronchopulmonary disease in children with cystic fibrosis. *Pediatr Pulmonol*. 2003; 36(3):230–240. [PubMed: 12910585]
19. Kosciuk R, Kosorok M, Farrell P, Collins J, Peters M, Laxova A, Green C, Zeng L, Rusakow L, Hardie R, Campbell P, Gurney J. Wisconsin cystic fibrosis chest radiograph scoring system:

- validation and standardization for application to longitudinal studies. *Pediatr Pulmonol*. 2000; 29(6):457–467. [PubMed: 10821728]
20. Brasfield D, Hicks G, Soong S, Tiller R. The chest roentgenogram in cystic fibrosis: a new scoring system. *Pediatrics*. 1979; 63(1):24–29. [PubMed: 440798]
21. Farrell P, Collins J, Broderick L, Rock M, Li Z, Kosorok M, Laxova A, Gershan W, Brody A. Association between mucoid *Pseudomonas* infection and bronchiectasis in children with cystic fibrosis. *Radiology*. 2009; 252(2):534–543. [PubMed: 19703887]
22. Brody AS, Kosorok MR, Li Z, Broderick LS, Foster JL, Laxova A, Bandla H, Farrell PM. Reproducibility of a scoring system for computed tomography scanning in cystic fibrosis. *J Thorac Imaging*. 2006; 21(1):14–21. [PubMed: 16538150]
23. Wang X, Dockery D, Wypij D, Fay M, Ferris BJ. Pulmonary function between 6 and 18 years of age. *Pediatr Pulmonol*. 1993; 15(2):75–88. [PubMed: 8474788]
24. de Jong P, Lindblad A, Rubin L, Hop W, de Jongste J, Brink M, Tiddens H. Progression of lung disease on computed tomography and pulmonary function tests in children and adults with cystic fibrosis. *Thorax*. 2006; 61(1):80–85. [PubMed: 16244089]
25. Brody A, Sucharew H, Campbell J, Millard S, Molina P, Klein J, Quan J. Computed tomography correlates with pulmonary exacerbations in children with cystic fibrosis. *Am J Respir Crit Care Med*. 2005; 172(9):1128–1132. [PubMed: 16100015]
26. Slattery DM, Zurakowski D, Colin AA, Cleveland RH. CF: an X-ray database to assess effect of aerosolized tobramycin. *Pediatr Pulmonol*. 2004; 38(1):23–30. [PubMed: 15170870]

Figure 1.

Patients with CF in the Wisconsin RCT of newborn screening who were investigated with a chest CT scan. Because the Early Diagnosis and Control Groups were indistinguishable with regard to lung disease, they were combined for a total of 81 subjects for this analysis. ^aA sweat chloride level ≥ 60 mmol/L was required to make the diagnosis of CF. ^b98 patients were still followed at the time of the chest CT scan.

Figure 2. Scatter plot and correlation between chest CT score and WCXR obtained within 1 year prior to the chest CT

Figure 3.
Scatter plot and correlation between chest CT score and FEV₁ % predicted obtained within 1 year prior to the chest CT

Figure 4. Scatter plot and correlation between chest CT bronchiectasis subscore and WCXR obtained within 1 year prior to the chest CT

Figure 5. Scatter plot and correlation between chest CT air trapping subscore and WCXR obtained within 1 year prior to the chest CT

Figure 6. Scatter plot and correlation between chest CT bronchiectasis subscore and WCXR bronchiectasis subscore obtained within 1 year prior to the chest CT

Figure 7. Scatter plot and correlation between chest CT air trapping subscore and WCXR air trapping subscore obtained within 1 year prior to the chest CT

Table 1

Characteristics of subjects

Characteristic	Category	Study cohort N (%) ^a (total N=81)	Overall WI cohort N (%) (total N=132)
Patient group	Control	42 (52)	63 (48)
	Screened	39 (48)	69 (52)
Center	Madison	44 (54)	70 (53)
	Milwaukee	37 (46)	62 (47)
Gender	Male	47 (58)	78 (59)
	Female	34 (42)	54 (41)
Genotype	F508del/F508del	46 (57)	70 (53)
	F508del /Other	31 (38)	49 (37)
	Other/Other	4 (5)	13 (10)
Pancreatic status	Pancreatic Sufficiency	13 (16)	21 (16) ^b
	Pancreatic Insufficiency	68 (84)	107 (84)
Meconium ileus	No	62 (77)	103 (78)
	Yes	19 (23)	29 (22)
Age in years of patients ^c		Mean (SD) 11.5 (3.0)	
		Median 11.3	
		Range 6.6–17.6	

^aData are expressed as N (%) unless otherwise noted

^bPancreatic status is unknown for 4 subjects

^cAt the time of the chest CT

Table 2

Lung disease surrogates obtained within 1 year prior to the chest CT. Number of subjects = 81 unless otherwise noted.

Measure (Number of observation)	Mean (standard deviation) or %
Brody chest CT score	3.1 (3.0)
FEV ₁ % predicted (n=76)	91.1 (16.7)
FEV ₁ /FVC (n=75)	81.0 (7.3)
FEF ₂₅₋₇₅ % predicted (n=72)	85.4 (29.3)
RV/TLC (n=70)	30.2 (7.9)
WCXR (n=71)	15.4 (13.0)
BCXR (N=71)	18.8 (2.9)
Daily cough	46%
Daily sputum production	41%
Culture positive for <i>P. aeruginosa</i>	48%
Chronic antibiotics	25%
Acute antibiotics	25%
Hospitalization	9%

Table 3

Correlations between lung disease surrogates and chest CT score

Measure	Pearson correlation coefficient	P-value
Wisconsin CXR score	0.83	<0.001
Brasfield CXR score	−0.81	<0.001
Culture positive for <i>P. aeruginosa</i>	0.23	0.04
Daily cough	0.31	0.004
Daily sputum production	0.41	<0.001
RV/TLC	0.53	<0.001
FEV ₁ /FVC	−0.47	<0.001
FEV ₁ % predicted	−0.59	<0.001
FEF _{25–75} % predicted	−0.52	<0.001

Table 4

The sensitivity of detecting a chest CT score worse than the median for surrogate measures of lung disease

Measure	Sensitivity
Wisconsin CXR score	100%
Brasfield CXR score	100%
Culture positive for <i>P. aeruginosa</i>	55%
Daily cough	55%
Daily sputum production	53%
RV/TLC	51%
FEV ₁ /FVC	46%
FEV ₁ % predicted	41%
FEF ₂₅₋₇₅ % predicted	38%

Table 5

The sensitivity of detecting a chest CT bronchiectasis or air trapping subscore worse than the median for surrogate measures of lung disease

Measure	Sensitivity	
	Chest CT bronchiectasis	Chest CT air trapping
WCXR	94%	86%
BCXR	91%	81%
WCXR bronchiectasis subscore	91%	
BCXR nodular cystic subscore	97%	
WCXR air trapping subscore		72%
BCXR air trapping subscore		72%
FEV ₁ % predicted	42%	38%
FEF ₂₅₋₇₅ % predicted	38%	35%
RV/TLC	55%	55%
Daily cough	59%	45%
Daily sputum production	54%	40%

Table 6

Sensitivity analysis

Measure	Sensitivity		
	CT score worse than 10 th percentile	CT score worse than 25 th percentile	CT score worse than median (Data within 6 months)
Wisconsin CXR score	83%	87%	100%
Brasfield CXR score	78%	81%	100%
Culture positive for <i>P. aeruginosa</i>	54%	57%	54%
Daily cough	50%	52%	55%
Daily sputum production	43%	45%	53%
RV/TLC	41%	40%	47%
FEV ₁ /FVC	39%	38%	43%
FEV ₁ % predicted	34%	36%	39%
FEF ₂₅₋₇₅ % predicted	30%	29%	39%