Lung Diffusing Capacity in Adult Bronchiectasis: A Longitudinal Study

Paul T King MD PhD, Stephen R Holdsworth MD PhD, Nicholas J Freezer MD, Elmer Villanueva MD, Michael W Farmer MD, Paul Guy, and Peter W Holmes MD

BACKGROUND: Recent studies described a progressive decline in lung volumes in adult bronchiectasis. Interstitial lung disease is also a feature of bronchiectasis, but whether this is associated with a decline in lung diffusing capacity (measured as the diffusing capacity of the lung for carbon monoxide [D_{LCO}]) is not well known. OBJECTIVE: To assess longitudinal decline in diffusing capacity of the lung for carbon monoxide (D_{LCO}) in adult bronchiectasis. METHODS: Sixty-one subjects had a detailed baseline clinical and laboratory assessment, then were followed regularly with clinical and lung-function assessment for a median 7 years. RESULTS: Baseline spirometry demonstrated mild obstructive lung disease, with a mean FEV_1 of 72% of predicted, mean forced vital capacity 87% of predicted, and normal D_{LCO} (mean D_{LCO} 88% of predicted, and mean D_{LCO} adjusted for alveolar volume [D_{LCO}/V_A] 100% of predicted). There was an accelerated decline in D_{LCO} and D_{LCO}/V_A over the 7-year period. The median D_{LCO} decline was 2.9% of predicted per year (95% CI 2.3–4.1% of predicted per year). The median D_{LCO}/V_A decline was 2.4% of predicted per year (95% CI 2.1–4.0% of predicted per year). There was a significant relationship between D_{LCO} decline and age and decline in FEV_1. CONCLUSIONS: In our cohort of patients with bronchiectasis there was a progressive D_{LCO} decline. *Key words: bronchiectasis; diffusing capacity of the lung for carbon monoxide; D_{LCO}; interstitial lung disease; FEV_1; forced vital capacity; pulmonary function test.* [Respir Care 2010;55(12):1686–1692. © 2010 Daedalus Enterprises]

Introduction

Bronchiectasis is an inflammatory airway disease defined by permanent and abnormal bronchial dilatation.[1,2] Inflammation appears to arise predominantly from chronic bacterial infection. Recent studies emphasized that bronchiectasis patients tend to gradually become worse, with increased symptoms[3,4] and decline in lung volumes, principally FEV_1.[4-6]

Bronchiectasis is heterogeneous, with many potential causes, and its pathogenesis is generally not well understood. In contrast, its anatomical pathology was clearly defined in a number of studies, most done more than 50 years ago. The most definitive study was by Whitwell, who assessed 200 surgical lung specimens.[7] The most common pattern was inflammation of the bronchial walls, predominantly arising in association with lymphoid follicles and interstitial pneumonia. Interstitial pneumonia was present in all patients with that form of bronchiectasis, and progressed with increasing severity of disease to destroy the adjacent parenchymal tissue, with associated scar tissue/fibrosis and reduced alveolar volume. Changes of interstitial lung disease have not generally been reported in recent studies of bronchiectasis, although Loubeyre et al reported a high incidence of emphysema localized to bronchiectatic lobes.[8]

Studies of lung diffusing capacity for carbon monoxide (D_{LCO}) in patients with bronchiectasis and cystic fibrosis

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This research was partly supported by a grant (to Dr King) from the National Health and Medical Research Council of Australia.

The authors have disclosed no conflicts of interest.

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(CF) reported normal values except in the most severe disease.[5,9,10] Recent literature demonstrates that these patients tend to get worse, and the studies by Whitwell and Loubeyre showed inflammation spreading from the airways to the lung parenchyma, so there may also be a decline in D_{LCO}.[7,8]

Methods

This study was approved by the Southern Health Ethics Committee, Monash Medical Centre, Melbourne, Victoria, Australia.

Subjects

We saw a series of 92 adult patients with radiologically confirmed bronchiectasis at Monash Medical Centre, between 1984 and 2006. All the subjects were initially assessed and followed by a respiratory physician (PTK or PWH), and over 800 clinical reviews were performed. Twelve subjects were current smokers, incomplete follow-up occurred in 12 patients, 5 subjects were unable to perform aspects of spirometry, and 2 patients had or developed pulmonary fibrosis, and those subjects were excluded, which left a cohort of 61 subjects assessed for this project (no subjects were current smokers).

Study Design

This study was designed to assess longitudinal changes in D_{LCO} in adult bronchiectasis. Patients were followed for a median period of 7 years, with repeat testing, and the results were compared with other patient variables.

All 61 subjects had a detailed initial clinical assessment (by PTK or PWH) at Monash Medical Centre. Each subject was assessed at his or her baseline state (ie, no exacerbation for at least one month, and living independently in the community). Exacerbation was defined as at least one of: increased cough; increased sputum; or increased shortness of breath for at least 24 hours. The subjects were asked about the presence of productive cough, sputum volume, presence of rhinosinusitis, hemoptysis in the past year, frequency of exacerbations, and symptoms of dyspnea, using the Medical Research Council dyspnea scale. We obtained details about past medical problems, history of smoking, and current smoking status. Physical examination findings were also recorded.

To assess for predisposing factors for bronchiectasis, we recorded clinical details on family history, unexplained infertility, comorbidities, and examination findings. All subjects had blood taken for full blood examination, immunoglobulin levels, alpha-1 antitrypsin level, allergic bronchopulmonary aspergillosis (precipitins and immunoglobulin E), CF mutation analysis, and lymphocyte subsets. The patients were also asked to produce a sputum sample, which was analyzed via microscopy and culture. Bronchiectasis was diagnosed by a consultant radiologist, using standard criteria,[11] and scans were scored by a previously described method.[4] Details of interstitial changes were also recorded.

Subjects had spirometry performed for FEV_1, forced vital capacity (FVC), bronchodilator response to inhaled β-agonist, single-breath D_{LCO}, and D_{LCO} adjusted for alveolar volume (D_{LCO}/V_A). The American Thoracic Society criteria were met in each pulmonary function test.[12,13] For spirometry we recorded the best of 3 technically acceptable post-bronchodilator results, using the sum of FEV_1 and FVC for test selection. For D_{LCO} we used the average of 2 technically acceptable test results that were within 10% and had an inspired volume $>$ 90% of the subject's FVC. We used the largest volume for the analysis. Beginning in 1990 we used a different spirometer (Masterscreen, Erich Jaeger, Hoechberg, Germany) that was calibrated daily with a 2-L or 3-L syringe. Before 1990 we used a rolling seal spirometer (Rolling Seal, PK Morgan, Haverhill, Massachusetts). The D_{LCO} test gas consisted of 0.3% carbon monoxide, 10% helium, 21% oxygen, and 68.7% nitrogen.

We selected patients who had non-CF bronchiectasis and who could undergo/perform all the required assessments and tests and who were willing to be followed for the study period. We saw the patients every 3–6 months (with clinical assessment by PTH or PWK). Each patient had a lung-function test every 2 years. The patients were referred to a physiotherapist to learn sputum-clearance techniques; they received narrow-spectrum antibiotics (10–14-day course) for exacerbations; and they were prescribed bronchodilators and received influenzae and pneumococcal vaccinations. For bronchospasm in association with an exacerbation we prescribed a short course of systemic corticosteroids. The patients were hospitalized when appropriate and treated with narrow-spectrum antibiotics unless they had previously grown *Pseudomonas aeruginosa* or other resistant pathogens. We treated coexistent asthma or substantial airway reversibility with inhaled corticosteroids. All subjects were followed for at least 2 years, with a minimum of 3 clinical assessments and at least 2 lung-function assessments performed only when the patient was clinically stable.

Statistical Analysis

Statistical analysis was performed with statistics software (Stata SE 10.1, StataCorp, College Station, Texas, or Prism 5, GraphPad Software, La Jolla, California). We calculated the mean and standard deviation or median and interquartile range (IQR), as appropriate, for continuous

variables, and constructed cross-tabulations for categorical variables. Comparisons between categorical variables used the Pearson's chi-square statistic, or Fisher's exact test for small samples. When comparing continuous outcome variables by categorical predictors, we used Student's *t* test, or its non-parametrical equivalent, the Wilcoxon rank-sum test. We performed comparisons between initial and final outcomes with the paired-samples *t* test.

We used a linear mixed model to estimate the average decline in percent-of-predicted values for FEV_1, FVC, D_{LCO}, and D_{LCO}/V_A, similar to previous studies.[10,14,15] We express the results as the average percent decline per year, with 95% confidence intervals. Because of the complexity of the structure of the data (ie, multiple measurements on a single participant over time), we applied general estimating equations[16] with an exchangeable correlation matrix and robust standard errors, to account for the dependencies of the collection of measurements for each individual over time. We used this technique to quantify the relationship between average decline in D_{LCO} and D_{LCO}/V_A and age, sex, smoking history, lobes with bronchiectasis, volume of sputum, frequency of exacerbations, isolation of *P. aeruginosa* in sputum, and average decline in FEV_1 and FVC. We present the results as β coefficients, which can be interpreted as the "average" change in percent-of-predicted lung function over time per unit increase in a continuous covariate, or against a reference category for categorical variables.

Similar to the approach used in conventional regression procedures, we started by examining unadjusted relationships in each of the outcomes (FEV_1, FVC, D_{LCO}, and D_{LCO}/V_A) and a set of independent variables (age, sex, smoking history, lobes with bronchiectasis, volume of sputum, frequency of exacerbations, isolation of *P. aeruginosa* in sputum). For the analysis of D_{LCO} and D_{LCO}/V_A we also explored the unadjusted relationship of the average declines in FEV_1 and FVC.

Finally, we proceeded to adjusted analyses of D_{LCO} and D_{LCO}/V_A, initially by regressing each of the outcomes against the full set of independent variables. Through the sequential application of likelihood ratio tests, we derived parsimonious sets of predictors. We used model estimates to produce predictive plots of D_{LCO} and D_{LCO}/V_A changes in "typical" patients 30, 50, and 70 years old.

We did not explore interactions between variables. We did conduct sensitivity analyses to explore the effect of including or excluding participants who had only 2 visits (ie, an initial and a final visit) on the effect estimates, and the results were within 10% of each other, so we present the results from the full cohort.

In all the analyses we considered differences statistical significant when the 2-tailed *P* value was $< .05$.

Table 1. Subject Characteristics ($n = 61$)

Years of follow-up per subject—median (IQR)	7 (4–9)
Years between lung-function tests*—median (IQR)	2 (1–2)
Total number of lung-function tests	291
Age—mean ± SD	57 ± 14
Male—no. (%)	25 (41)
Female—no. (%)	36 (59)
Smoking history—no. (%)	14 (23)
Patients with idiopathic bronchiectasis—no. (%)	43 (70)
Sputum volume—median (IQR) mL	50 (30–50)
MRC dyspnea score—mean ± SD	2.3 ± 0.9
Exacerbations per year—median (IQR)	3 (3–4)
Auscultation findings—no. (%)	
Crackles	47 (77)
Wheeze	17 (28)
HRCT findings	
Lobes involved—median (IQR)	2 (2–3)
Score—mean ± SD	33 ± 17
Interstitial changes—no. (%)	39 (64)
Microbiology findings—no. (%)	
Haemophilus influenzae	28 (46)
Pseudomonas aeruginosa	11 (18)

* Lung volumes and diffusing capacity of the lung for carbon monoxide.
HRCT = high-resolution computed tomography
MRC = Medical Research Council

Results

Patient Characteristics

Table 1 describes the 61 subjects. The total follow-up period for the group was 472 calendar years, with a median follow-up period of 7 years (IQR 4–9 y). Fourteen subjects were ex-smokers, with a mean pack-year history of 28 ± 16 years. Forty-three subjects (70% of the cohort) had idiopathic bronchiectasis. The bronchiectasis etiologies in the other 18 subjects were: sequelae of infectious disease (9), low immunoglobulin subclasses (4), allergic bronchopulmonary aspergillosis (2), rheumatoid arthritis (1), Young's syndrome (1), and Kartegener's syndrome (1). The subjects were generally healthy apart from the bronchiectasis, with a low incidence of comorbidities, and all continued to live independently throughout the follow-up period. Ten subjects had asthma, 4 had COPD, 7 had hypertension, and 5 had ischemic heart disease. Twenty-one patients (34% of the group) were treated with inhaled corticosteroids, and the 2 patients with allergic bronchopulmonary aspergillosis were treated with long-term systemic corticosteroids. The subject with rheumatoid arthritis was treated with methotrexate. No other subjects received any immunosuppressive therapy.

The subjects generally had prominent sputum production and mild dyspnea on exertion. The median number of

Table 2. Initial and Final Lung-Function Test Results

Lung-Function Test	Initial Assessment		Final Assessment		*P*
	Mean ± SD	Mean ± SD % Predicted	Mean ± SD	Mean ± SD % Predicted	
FEV_1 (L)	1.74 ± 0.59	72 ± 23	1.46 ± 0.55	62 ± 22	< .001
FVC (L)	2.74 ± 0.84	87 ± 21	2.46 ± 0.86	81 ± 20	< .001
FEV_1/FVC (%)	65 ± 14	—	60 ± 15	—	< .001
D_{LCO} (mL/min/mm Hg)	21.1 ± 6.03	88 ± 21	15.7 ± 5.9	68 ± 22	< .001
D_{LCO}/V_A (mL/min/mm Hg/L)	4.87 ± 1.30	100 ± 24	4.04 ± 1.29	82 ± 24	< .001

FVC = forced vital capacity
D_{LCO} = diffusing capacity of the lung for carbon monoxide
D_{LCO}/V_A = D_{LCO}, adjusted for alveolar lung volume

exacerbations was 3 per year (IQR 3–4 per year). Crackles were the most common finding on examination. Ninety-two percent of the group had multi-lobar bronchiectasis on high-resolution computed tomography (CT). There were interstitial changes on initial CT in 39 subjects (64%), with scarring in the area of the bronchiectasis in 16 patients (26%), pleural thickening in 4 patients (7%), emphysema in 15 patients (25%), collapse/atelectasis in 9 patients (15%), and cystic bronchiectasis in 4 patients (7%) (10 patients had more than one interstitial change). Apart from emphysema, the subjects had no evidence of primary interstitial lung disease such as hypersensitivity pneumonitis, or pulmonary fibrosis. There was emphysema in both ex-smokers (5 subjects) and in non-smokers (10 subjects). Scarring was minor and occurred in association with the areas of bronchiectasis. None of the subjects had traction bronchiectasis. The most common pathogen in sputum was *Haemophilus influenzae*. Fifteen patients (25%) had no bacteria growth in sputum.

Lung Function

In this cohort of 61 subjects there were 291 lung-function tests (lung volumes and D_{LCO}), with a median interval of 2 years between each test. The median number of lung-function tests per subject was 4. Eleven subjects had 2 lung-function tests, and fifty had at least 3 lung-function tests. The initial lung-function tests demonstrated mild airway obstruction: mean ± SD percent of predicted FEV_1 72 ± 23%, and forced expiratory ratio (FEV_1/FVC) 65 ± 14%. The mean D_{LCO} and volume-adjusted D_{LCO} were both in the normal range: 88 ± 21% predicted, and 100 ± 24% predicted, respectively. We followed the subjects for a median of 7 years. On their last visit there had been significant declines in the percent-of-predicted FEV_1, FVC, FEV_1/FVC, D_{LCO}, and D_{LCO}/V_A (all $P < .001$, Table 2).

We assessed the changes in FEV_1, FVC, D_{LCO}, and D_{LCO}/V_A for each patient with a linear mixed model. We also combined the whole cohort's data to find the average decline in lung function from the time of initial assessment (when the group's mean age was 57 y) over the follow-up period (median of 7 years). FEV_1, FVC, D_{LCO}, and D_{LCO}/V_A all declined: FEV_1 by −1.1% predicted per annum ($P = .001$); FVC by −0.82% predicted per annum ($P < .001$); D_{LCO} by −2.9% predicted per annum ($P < .001$); and D_{LCO}/V_A −2.4% predicted per annum ($P < .001$, Table 3 and Figure 1).

Table 3. Change in Lung Function During the Follow-up Period

Lung-Function Test	Initial Assessment % predicted (95% CI)	Slope, % predicted per annum (95% CI)	*P*
FVC	87 (64 to 77)	−0.8 (−1.5 to 0.0)	< .001
FEV_1	72 (64 to 77)	−1.1 (−2.4 to –0.6)	< .001
D_{LCO}	88 (83 to 93)	−2.9 (−4.1 to −2.3)	< .001
D_{LCO}/V_A	100 (94 to 106)	−2.4 (−4.0 to −2.1)	< .001

FVC = forced vital capacity
D_{LCO} = diffusing capacity of the lung for carbon monoxide
D_{LCO}/V_A = D_{LCO} adjusted for alveolar lung volume

Predictors of D_{LCO}

Unadjusted analysis of the D_{LCO} decline (Table 4) and D_{LCO}/V_A decline (Table 5) compared to other factors demonstrated some significant associations. Greater age and a history of smoking were associated with faster D_{LCO} decline, whereas subjects with higher FEV_1 had slower D_{LCO} decline. The results for volume-adjusted D_{LCO} were very similar: greater age and a history of smoking were negatively associated with D_{LCO}/V_A, and FEV_1 was positively associated.

Following multivariable adjustment (see Tables 4 and 5), the relationships of D_{LCO} and D_{LCO}/V_A to age and FEV_1 remained statistically significant. In addition, D_{LCO}/V_A was significantly related to lobar involvement. Based on these models, Figure 2 shows the estimated average D_{LCO} change

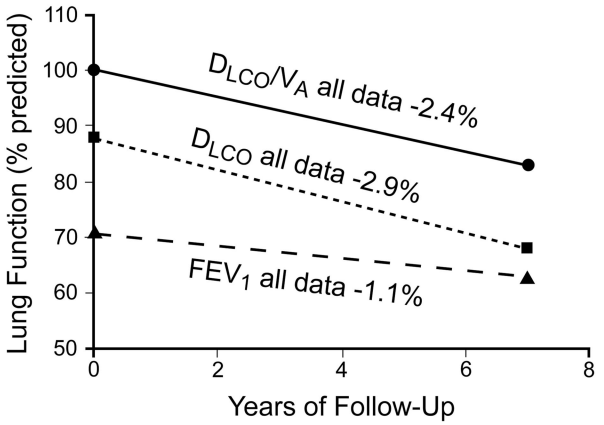

Fig. 1. Linear mixed model for lung function over 7 years of follow-up in 61 patients with bronchiectasis. The slopes represent the annual change in percent-of-predicted value. D_{LCO} = diffusing capacity of the lung for carbon monoxide. D_{LCO}/V_A = D_{LCO} corrected for alveolar volume.

in bronchiectasis patients (30, 50, and 70 y old) over 7 years of follow-up.

Discussion

To our knowledge, this is the first longitudinal study of D_{LCO} in adult bronchiectasis. Our results show a progressive decline in D_{LCO} and D_{LCO}/V_A. There was a significant relationship between D_{LCO} decline and FEV_1 decline. Other associated factors were age and smoking history. The results were similar for D_{LCO} and D_{LCO}/V_A.

Several previous studies assessed D_{LCO} in CF[9,10,17] and bronchiectasis.[5,18] Cross-sectional data from subjects with CF[9] and bronchiectasis[5] showed that the subjects with the lowest FEV_1 had mild D_{LCO} impairment. A longitudinal study over 3.8 years in 53 children with CF found no D_{LCO} decline; those subjects had normal lung volumes (mean FEV_1 90% of predicted).[10] In the present study the D_{LCO} decrease appeared to occur later in the disease, and D_{LCO}/V_A had higher initial values but a similar rate of decline to D_{LCO}.

Bronchiectasis is characterized by substantial bronchial inflammation. The D_{LCO} decrease in the present study suggests that the inflammation extended from the airways into the interstitium and alveoli. Whitwell, in his pathology series, described this as the most common pattern, with interstitial pneumonia arising from the spread of bronchial inflammation.[7] He described reduction in alveolar volume, with scarring of adjacent tissue, and in more advanced cases destruction of parenchyma. This process may explain why D_{LCO} decrease only occurs in subjects with more severe disease. In COPD, small-airway inflammation is correlated with FEV_1 and D_{LCO} decreases.[19]

In over half of the subjects in our group, on initial evaluation with CT there were changes of interstitial lung disease, despite the fact that most of the subjects had normal D_{LCO} and D_{LCO}/V_A. A previous study of 90 patients with bronchiectasis found that nearly half of the subjects had CT evidence of emphysema, which was generally localized to the areas of bronchiectasis,[8] despite the fact that D_{LCO} was in the normal range. In patients with CF, de Jong et al found progressive damage on high-resolution CT, despite stable lung volumes.[20] Those studies suggest that lung-function testing may be relatively insensitive for detecting earlier stages of pulmonary damage in bronchiectasis.

Table 4. Associations Between D_{LCO} and Patient Characteristics

	Unadjusted			Adjusted*		
	β coefficient	95% CI	*P*	β coefficient	95% CI	*P*
Age	−0.46	−0.82 to −0.09	.01	−0.42	−0.73 to −0.11	.007
FEV_1, % predicted	0.68	0.55 to 0.81	< .001	0.67	0.54 to 0.80	< .001
Female (vs male)	5.72	−4.76 to 16.21	.29			
Smoker (vs non-smoker)	−17.75	−27.51 to −7.99	< .001			
Number of lobes	−3.50	−8.28 to 1.27	.15			
Sputum volume	−0.06	−0.20 to 0.08	.39			
MRC dyspnea score	−9.25	−14.36 to −4.14	< .001			
Sinusitis (yes vs no)	11.14	0.33 to 21.96	.04			
Exacerbations (yes vs no)	0.05	−2.99 to 3.09	.97			
Pseudomonas (yes vs no)	−4.43	−17.83 to 8.97	.52			
FVC, % predicted	0.03	−0.01 to 0.06	.17			

* Estimates were derived from a model that incorporated all variables with specified results. Variables eliminated in the model-selection process are shown without estimates.
D_{LCO} = diffusing capacity of the lung for carbon monoxide
MRC = Medical Research Council
FVC = forced vital capacity

Table 5. Associations Between D_{LCO}/V_A and Patient Characteristics

	Unadjusted			Adjusted*		
	β coefficient	95% CI	*P*	β coefficient	95% CI	*P*
Age (y)	−0.49	−0.84 to −0.14	.005	–0.41	−0.77 to −0.05	.02
FEV_1, % predicted	0.42	0.25 to 0.59	< .001	0.46	0.30 to 0.62	< .001
Number of lobes	3.13	−1.72 to 7.98	.21	5.41	0.41 to 10.41	.03
Female (vs male)	3.39	−6.82 to 13.60	.52			
Smoker (vs non-smoker)	−15.69	−25.75 to −5.63	.002			
Sputum volume	−0.02	−0.17 to 0.13	.79			
MRC dyspnea score	−8.15	−13.19 to −3.11	.002			
Sinusitis (yes vs no)	16.22	6.70 to 25.74	.001			
Exacerbations (yes vs no)	−0.25	−3.19 to 2.68	.87			
Pseudomonas (yes vs no)	−1.70	−14.61 to 11.22	.80			
FVC, % predicted	0.004	−0.044 to 0.052	.87			

* Estimates were derived from a model incorporating all variables with specified results. Variables eliminated in the model-selection process are shown without estimates.
D_{LCO}/V_A = diffusing capacity of the lung for carbon monoxide, adjusted for alveolar lung volume
MRC = Medical Research Council
FVC = forced vital capacity

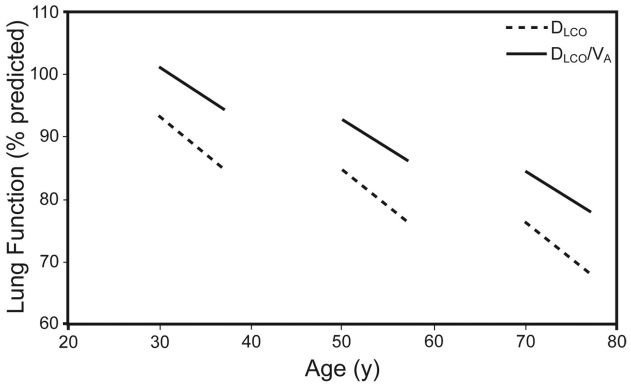

Fig. 2. Percent-of-predicted diffusing capacity of the lung for carbon monoxide (D_{LCO}) and the ratio of D_{LCO} to alveolar volume (V_A) in typical patients with bronchiectasis, ages 30, 50, and 70 years, followed for 7 years.

Previous investigators found that a low D_{LCO} is the most sensitive indicator of resting hypoxia and exercise-induced hypoxia in COPD.[21-23] Failure of gas exchange is a feature of end-stage CF and non-CF bronchiectasis. Interestingly, studies of patients with gas-exchange failure have generally described only moderate D_{LCO} impairment, compared to the FEV_1.[24,25] Those results may imply that the D_{LCO} measured in CF and bronchiectasis is not as accurate an assessment of gas exchange as it is in other conditions, such as COPD or pulmonary fibrosis.

The single-breath D_{LCO} is influenced by several factors. It is an expression of the overall integrity of the alveolar membrane and red cell volume within pulmonary capillaries. Preservation of the ventilation-perfusion relationship, secondary to regional hypoxic pulmonary vasoconstriction, might have operated in the more severely affected patients in this series.[26] It has also been suggested that the forced inspiratory effort in the presence of air flow obstruction associated with the performance of tests may transiently increase the pulmonary capillary volume.[27] Loss of effective membrane surface area and ventilation-perfusion mismatch are the major factors that reduce D_{LCO} in emphysema. The studies by Whitwell and Loubeyre found localized parenchyma destruction in bronchiectasis,[7,8] and our present findings are consistent with that process.

In the present study, our multivariate analysis found factors associated with D_{LCO} and $D_{LCO}/_{VA}$ decline. Greater age was associated with greater D_{LCO} decline, and a recent study highlighted the role of age in COPD.[28] There was a significant association between the decline in D_{LCO} and FEV_1. Previous studies showed that D_{LCO} is low only in subjects with more severe disease. As both FEV_1 and D_{LCO} progressively declined in our cohort, it suggests that the change in D_{LCO} occurs later in bronchiectasis. This is consistent with the inflammatory process causing airway obstruction spreading beyond the bronchi to cause parenchymal damage.

Limitations

Our mean follow-up period of 7 years was similar to studies of pulmonary function in COPD.[29,30] We used a linear mixed model that was established by previous investigators. A weakness of this study is that there was variability in the duration of follow-up and the number of tests for each patient, because it was difficult to simultaneously assemble a large cohort of subjects with bronchiectasis. This study would have been further strengthened by longitudinal CT data, which we would expect to dem-

onstrate progressive parenchymal lung damage. Lung-volume data would also have been helpful for determining the roles of air trapping and restrictive lung disease in the pathophysiology. Also, underlying conditions such as asthma and COPD may have affected outcome, but our number of subjects was too small to analyze that effect. Bronchiectasis is also a heterogeneous condition.

Conclusions

There is an excessive D_{LCO} decline in adult patients with bronchiectasis, in both D_{LCO} and D_{LCO}/V_A. Associated factors in this decline are age and FEV_1 decline.

ACKNOWLEDGMENTS

We thank Michael Pain MD, Department of Respiratory Medicine, Royal Melbourne Hospital, Melbourne, Australia, for reviewing this manuscript, and Jacob Twiss MD, Department of Respiratory Medicine, Auckland Starship Children's Hospital, Auckland, New Zealand for advice.

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