Factors associated with bronchiectasis in Korea: a national database study

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Background: Many important clinical features of bronchiectasis have been reported. However, the factors were evaluated using a specific disease cohort. Thus, clinical factors associated with bronchiectasis have not been well assessed in comparison to the general population. The aim of this study was to evaluate the factors associated with bronchiectasis using a national representative database.

Methods: We conducted a cross-sectional study using data from the Korean National Health and Nutrition Examination Survey 2007–2009. To evaluate factors associated with bronchiectasis, a multivariable logistic analysis was used with adjustment for demographic and socioeconomic factors.

Results: In the present study, the prevalence of bronchiectasis was 0.4%. Compared with subjects without bronchiectasis, subjects with bronchiectasis were older (55.1 *vs.* 44.4 years, P<0.001) and had lower body mass index (BMI) (23.2 *vs.* 24.2 kg/m^2, P<0.001). The proportions of low family income (70.5% *vs.* 40.2%, P<0.001) and low educational level (less than high school) (85.3% *vs.* 70.6%, P=0.041) were higher in subjects with bronchiectasis than in subjects without bronchiectasis. Regarding comorbidities, subjects with bronchiectasis were more likely to have asthma (17.8% *vs.* 2.9%, P<0.001), previous history of pulmonary tuberculosis (TB) (43.5% *vs.* 5.0%, P<0.001), osteoporosis (19.1% *vs.* 7.8%, P=0.002), and depression (9.3% *vs.* 3.0%, P=0.015) compared with subjects without bronchiectasis. In addition, subjects with bronchiectasis had more respiratory symptoms and poorer quality of life measured using the EuroQoL five dimensions questionnaire (EQ-5D) index (0.87 *vs.* 0.93, P<0.001) than subjects without bronchiectasis. In multivariable logistic regression analysis, low family income (adjusted odds ratio, OR =3.83, 95% confidence interval, CI: 1.46–10.03), asthma (adjusted OR =3.73, 95% CI: 1.29–10.79), pulmonary TB (adjusted OR =7.88, 95% CI: 2.65–23.39), and the presence of airflow limitation (adjusted OR =2.98, 95% CI: 1.01–8.98) were independently associated with bronchiectasis.

Conclusions: Subjects with bronchiectasis suffered from more respiratory symptoms with limited physical

activity and poorer quality of life than the general population. Factors independently associated with bronchiectasis were lower family income and comorbid pulmonary conditions, such as previous pulmonary TB, asthma, and airflow limitation.

Introduction

Non-cystic fibrosis bronchiectasis (hereafter bronchiectasis) is a chronic structural respiratory disease characterized by permanent dilatation of bronchi and chronic respiratory symptoms such as cough, sputum, and dyspnea (1). Although bronchiectasis has been regarded as a neglected lung disease, the prevalence of bronchiectasis is increasing worldwide, and the burden of the disease is significant (2,3).

Fortunately, with a recent interest in this disease, many important clinical characteristics, comorbidity profiles, and socioeconomic factors of bronchiectasis have been elucidated. In several bronchiectasis cohort studies, patients with bronchiectasis were mainly elderly and females were more predominant than males (4-6). Previous pulmonary infectious conditions, such as pneumonia and tuberculosis (TB), chronic obstructive pulmonary disease (COPD), and asthma, are well established pulmonary comorbidities of bronchiectasis (7-12). Extra-pulmonary comorbidities of bronchiectasis include many conditions such as connective tissue disease, inflammatory bowel disease, and immunodeficiency (9,13,14). In addition, low socioeconomic status and low family income were associated with bronchiectasis in subjects 40 years of age or older (12).

In most previous studies, the clinical factors associated with bronchiectasis were evaluated in a specific disease cohort (e.g., asthma, COPD, and inflammatory bowel disease cohort) (15-17), or factors associated with poor outcomes were evaluated in bronchiectasis cohorts (18,19). Furthermore, factors associated with bronchiectasis have not been assessed in the general population. Accordingly, the associated factors for bronchiectasis have not been clarified after adjusting for various clinical and socioeconomic factors. This information could be helpful to provide doctors with clinical clues that can help diagnose bronchiectasis early and manage patients suffering from chronic respiratory symptoms properly.

Therefore, in the present study, we aimed to evaluate the factors associated with bronchiectasis subjects compared with the general population without bronchiectasis using national representative data in Korea. We present the following article in accordance with the STROBE reporting checklist (available at http://dx.doi.org/10.21037/atm-20-4873).

Methods

Participants

Data from the Korea National Health and Nutrition Examination Survey (NHANES) 2007–2009, a nationally representative survey collected by the Korean Ministry of Health and Welfare (n=22,340), were used in this cross-sectional study. Participants with missing weighted variable information were excluded (n=2,489), and 19,851 subjects were included in this study. The participants were classified into two groups based on the presence of physician-diagnosed bronchiectasis: subjects with bronchiectasis (n=78) and subjects without bronchiectasis (n=19,773). The authors are accountable for all aspects of the work and ensure that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. This study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This study was approved by the institutional review board of Chungbuk National University (application No. 2020-03-005). Informed consent was not required because this study was based on the NHANES database, which includes fully anonymized and de-identified data.

Measurements

Data on age; sex; body mass index (BMI); smoking history; physical activity; occupation; EuroQoL five dimensions questionnaire (EQ-5D) index values, which range between 0 (worst imaginable health state) and 1 (best imaginable

health state) (20); and spirometric results were obtained from the Korea NHANES database (21). Absolute values of forced expiratory volume in 1 second (FEV_1) and forced vital capacity (FVC) were obtained, and the percentage of predicted values (% predicted) for FEV_1 and FVC was calculated using the reference equation obtained from analysis of a representative Korean sample (22). Airflow limitation was defined as pre-bronchodilator FEV_1/FVC <0.7 (23). Spirometry was performed in subjects 20 years of age or older. Type of occupation was categorized into four groups according to the 6th Korean Standard Classification of Occupation: manager, professional, office worker or service worker; agriculture or fishery worker; skilled labor or machine operator; and manual laborer (24). Comorbidities were based on questionnaires regarding previous physician diagnosis, which included asthma, pulmonary TB, hypertension, diabetes mellitus, dyslipidemia, cardiovascular disease, osteoporosis, osteoarthritis or rheumatoid arthritis, and depression (25).

Primary and secondary outcomes

The primary outcome was factors associated with bronchiectasis using a representative nationwide database in Korea. The secondary outcome was symptomatic burden of subjects with bronchiectasis. Respiratory symptoms, physical activity limitations due to respiratory diseases, and quality of life measured using the EQ-5D index were compared between subjects with and without bronchiectasis.

Statistical analysis

All statistical analyses were performed using NHANES weights and survey (svy) commands in STATA (release 13.1; StataCorp LP, College Station, TX, USA) to account for the complex multistage probability sampling design. The prevalence and 95% confidence interval (CI) for each variable were calculated for both groups. Intergroup comparisons of continuous variables and categorical variables between the two groups were performed using t-test and chi-squared test, respectively. To evaluate factors associated with bronchiectasis, both univariable and multivariable logistic regression analyses were performed. Model 1 was adjusted for age, sex, BMI, and factors with P values <0.2 in univariable analysis. Model 2 was additionally adjusted for presence of airflow limitation. Subjects with missing values in the pulmonary function test were not included in Model 2. Two-tailed analyses were conducted,

and P values <0.05 were considered significant.

Results

Baseline characteristics

In the present study, the prevalence of bronchiectasis was 0.4%. As shown in *Table 1*, subjects with bronchiectasis were older and had lower BMI than subjects without bronchiectasis. The proportions of low family income and low educational level (less than high school) were higher in subjects with bronchiectasis than in those without bronchiectasis. Significant difference was not observed in type of occupation between the two groups. Regarding comorbidities, subjects with bronchiectasis were more likely to have asthma, previous history of pulmonary TB, osteoporosis, and depression compared with those without bronchiectasis.

Respiratory symptoms and quality of life

As shown in Table S1, subjects with bronchiectasis had more respiratory symptoms including cough, sputum, dyspnea, and limitation in physical activity due to respiratory diseases than did those without bronchiectasis.

Quality of life estimated using the EQ-5D index was lower in subjects with bronchiectasis than subjects without bronchiectasis (0.87 *vs*. 0.93, P<0.001). Among the components of EQ-5D index, subjects with bronchiectasis had more difficulty in mobility, usual activity, pain/discomfort, and anxiety/depression than subjects without bronchiectasis.

Factors associated with bronchiectasis

In univariable analysis, age (unadjusted odds ratio, OR =1.04, 95% CI: 1.02–1.05), BMI (unadjusted OR =0.90, 95% CI: 0.83–0.98), low family income (unadjusted OR =3.54, 95% CI: 1.85–6.78), low educational level (unadjusted OR =2.42, 95% CI: 1.01–5.79), asthma (unadjusted OR =4.07, 95% CI: 1.46–11.37), pulmonary TB (unadjusted OR =8.93, 95% CI: 3.30–24.17), and airflow limitation (unadjusted OR =6.13, 95% CI: 3.24–11.59) were significant factors associated with bronchiectasis (*Table 2*).

In multivariable analysis when the pulmonary function test was not included (Model 1), age (adjusted OR =1.03, 95% CI: 1.00–1.08), low family income (adjusted OR =4.03, 95% CI: 1.45–11.19), asthma (adjusted OR =5.75, 95%

Table 1 Baseline characteristics

Characteristics	Subjects without bronchiectasis (n=19,773)	Subjects with bronchiectasis (n=78)	P value
Age, years	44.4 (43.8–44.9)	55.1 (51.4–58.7)	<0.001
Sex, male	49.5 (48.2–50.9)	50.5 (49.1–51.8)	0.884
BMI, kg/m^2	24.2 (24.1–24.3)	23.2 (22.4–23.9)	<0.001
Smoking history			0.483
Never-smoker	54.3 (53.0–55.7)	48.5 (32.7–64.5)	
Current- or ex-smoker	45.7 (44.3–47.0)	51.5 (35.5–67.3)	
Family income			<0.001
Low	40.2 (38.3–42.3)	70.5 (55.4–82.1)	
High	59.7 (57.7–61.7)	29.5 (17.9–44.6)	
Educational level			0.041
High school or less	70.6 (68.9–72.2)	85.3 (70.6–93.3)	
College or above	29.4 (27.7–31.1)	14.7 (6.7–29.3)	
Type of occupation			0.079
Manager/professional/office worker/service worker	59.2 (57.1–61.4)	46.3 (24.3–69.9)	
Agriculture/fishery worker	8.8 (7.2–10.6)	23.3 (10.7–43.4)	
Skilled labor/machine operation	18.8 (17.3–20.4)	11.1 (3.2–31.9)	
Manual laborer	13.2 (11.9–14.5)	19.3 (7.4–41.8)	
Comorbidities			
Pulmonary comorbidity			
Asthma	2.9 (2.5–3.3)	17.8 (9.5–30.9)	<0.001
Pulmonary TB	5.0 (4.5–5.6)	43.5 (28.7–59.6)	<0.001
Extra-pulmonary comorbidity			
Diabetes mellitus	8.7 (8.0–9.5)	9.1 (3.6–12.1)	0.921
Hypertension	26.9 (25.6–28.4)	26.7 (14.9–43.1)	0.968
Dyslipidemia	39.5 (38.1–40.9)	44.3 (28.8–61.0)	0.563
Cardiovascular disease	2.6 (2.2–2.9)	4.3 (1.1–1.6)	0.451
Osteoporosis	7.8 (7.1–8.7)	19.1 (10.3–32.7)	0.002
Osteoarthritis or rheumatoid arthritis	10.8 (10.1–11.6)	26.4 (15.2–42.0)	0.061
Depression	3.0 (2.5–3.4)	9.3 (3.6–22.2)	0.015
Spirometry			
FVC, L	3.75 (3.72–3.78)	3.36 (3.11–3.61)	0.009
FVC, % predicted	92.8 (92.4–93.2)	87.6 (83.6–91.6)	0.001
FEV$_1$, L	3.02 (2.99–3.05)	2.47 (2.27–2.73)	<0.001
FEV$_1$, % predicted	91.9 (91.5–92.3)	81.9 (75.8–88.1)	<0.001
FEV$_1$/FVC ratio	0.81 (0.80–0.81)	0.73 (0.69–0.77)	<0.001

Table 1 (*continued*)

Table 1 (*continued*)

Characteristics	Subjects without bronchiectasis (n=19,773)	Subjects with bronchiectasis (n=78)	P value
Spirometric pattern*			<0.001
Normal	80.9 (79.7–82.0)	50.0 (34.3–65.7)	
Restrictive	11.1 (10.1–12.1)	15.1 (6.5–31.3)	
Obstructive	8.0 (7.4–8.7)	34.9 (22.2–50.1)	

Data are presented as weighted mean (95% confidence interval) or weighted percentage (95% CI). *, spirometric pattern was classified as follows: normal spirometry was defined as pre-bronchodilator $FEV_1/FVC \geq 0.70$ and FVC ≥80% predicted, the restrictive spirometric pattern was defined as pre-bronchodilator $FEV_1/FVC \geq 0.7$ and FVC <80% predicted, the obstructive spirometric pattern was defined as pre-bronchodilator $FEV_1/FVC < 0.7$. BMI, body mass index; TB, tuberculosis; FVC, forced vital capacity; FEV_1, forced expiratory volume in 1 second; CI, confidence interval.

Table 2 Factors associated with bronchiectasis using univariable and multivariable analysis

Variable	Univariable analysis (n=78)		Multivariable analysis	
			Model 1 (n=78)	Model 2 (n=67)
	Unadjusted OR	P value	Adjusted OR (95% CI)	Adjusted OR (95% CI)
Age	1.04 (1.02–1.05)	<0.001	1.03 (1.001–1.08)	1.02 (0.99–1.07)
Male	0.95 (0.48–1.88)	0.884	0.53 (0.18–1.55)	0.64 (0.18–2.20)
BMI, kg/m^2	0.90 (0.83–0.98)	0.018	3.09 (0.57–16.79)	2.62 (0.47–14.65)
Family income				
High	Ref		Ref	Ref
Low	3.54 (1.85–6.78)	<0.001	4.03 (1.45–11.19)	3.83 (1.46–10.03)
Educational level				
>High school	Ref		Ref	Ref
High school or less	2.42 (1.01–5.79)	0.048	1.13 (0.31–4.19)	1.09 (0.42–2.86)
Type of occupation				
Manager/professional/office worker/service worker	Ref	0.074	Ref	Ref
Agriculture/fishery worker	3.40 (1.14–10.12)		0.69 (0.10–4.66)	0.58 (0.09–3.93)
Skilled labor/machine operation	0.75 (0.17–3.30)		0.50 (0.08–2.98)	0.47 (0.07–2.85)
Manual laborer	1.87 (0.52–6.69)		0.72 (0.13–3.93)	0.56 (0.11–2.79)
Pulmonary comorbidity				
Asthma	4.07 (1.46–11.37)	<0.001	5.75 (1.89–17.46)	3.73 (1.29–10.79)
Pulmonary TB	8.93 (3.30–24.17)	<0.001	8.95 (2.97–26.95)	7.88 (2.65–23.39)
Pulmonary function				
Without airflow limitation	Ref	<0.001	–	Ref
With airflow limitation	6.13 (3.24–11.59)		–	2.98 (1.01–8.98)

Data are presented as ratio (95% CI). Age, sex, BMI, family income, educational level, type of occupation, and pulmonary comorbidities (asthma and TB) were adjusted in Model 1. Variables in Model 1 and presence of airflow limitation were adjusted in Model 2. OR, odds ratio; CI, confidence interval; Ref, reference; BMI, body mass index; TB, tuberculosis.
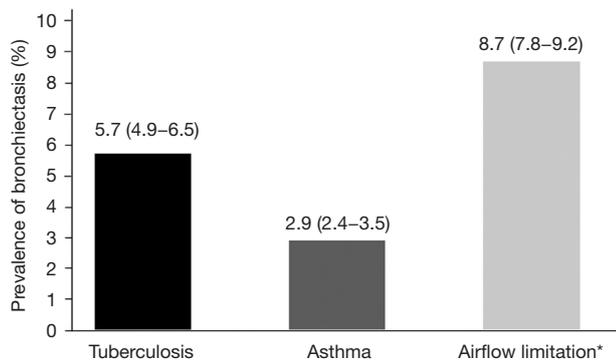
Figure 1 The prevalence of bronchiectasis in subjects with TB, asthma, and airflow limitation based on Korean NHANES 2007–2009 data. The prevalence is presented as weighted percentage (95% CI). *, airflow limitation was defined as pre-bronchodilator $FEV_1/FVC <0.7$. TB, tuberculosis; NHANES, National Health and Nutrition Examination Survey; CI, confidence interval; FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity.
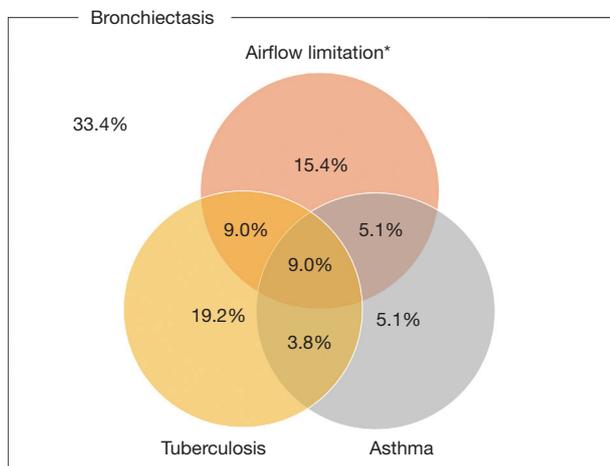

Figure 2 Venn diagram showing the rate of TB, asthma, and airflow limitation in subjects with bronchiectasis. *, airflow limitation was defined as pre-bronchodilator $FEV_1/FVC <0.7$. TB, tuberculosis; FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity.

CI: 1.89–17.46), and pulmonary TB (adjusted OR =8.95, 95% CI: 2.97–26.95) were significantly associated with bronchiectasis (Pseudo $R2 =0.165$). In Model 2, in which the presence of airflow limitation was further adjusted, low family income (adjusted OR =3.83, 95% CI: 1.46–10.03), asthma (adjusted OR =3.73, 95% CI: 1.29–10.79), pulmonary TB (adjusted OR =7.88, 95% CI: 2.65–23.39),

and presence of airflow limitation (adjusted OR =2.98, 95% CI: 1.01–8.98) were significant factors associated with bronchiectasis (Pseudo $R2 =0.174$) (*Table 2*).

Prevalence of bronchiectasis in the context of pulmonary comorbidities

Figure 1 shows the prevalence of bronchiectasis in subjects with TB, asthma, and airflow limitation. Weighted percentage (95% CI) was 5.7% (4.9–6.5%) in subjects with TB, 2.9% (2.4–3.5%) in subjects with asthma, and 8.7% (7.8–9.2%) in subjects with airflow limitation. *Figure 2* is a Venn diagram showing the proportions of TB, asthma, and airflow limitation in subjects with bronchiectasis. Among subjects with bronchiectasis (n=78), 9.0% had asthma, TB, and airflow limitation simultaneously.

Discussion

To the best of our knowledge, this is the first study to evaluate factors associated with bronchiectasis using a nationally representative database. Factors associated with bronchiectasis included respiratory symptoms such as airflow limitation, pulmonary TB, a lower family income/educational level, and poorer quality of life, compared with subjects without bronchiectasis. Considering that bronchiectasis is still under-recognized, it is important to elucidate factors associated with bronchiectasis, which would help clinicians diagnose and manage bronchiectasis early in patients with chronic respiratory symptoms.

The most notable finding of this study was the factors associated with bronchiectasis. The factors comprised comorbid pulmonary conditions such as previous pulmonary TB, asthma, and presence of airflow limitation and low family income. Most previous studies focused on the clinical characteristics of bronchiectasis accompanying other diseases, including COPD or asthma (6,8,26,27). Older age, lower BMI, more severe respiratory symptoms, and more frequent exacerbations were observed in COPD or asthma patients with bronchiectasis compared to those without bronchiectasis (7,15,27). In addition, in terms of pulmonary function tests, COPD patients with bronchiectasis showed more severe airflow limitation than subjects without bronchiectasis (8,27). In contrast, the clinical features, comorbidities, pulmonary function, and quality of life associated with bronchiectasis in the general population were evaluated in the present study. In

addition, socioeconomic factors were incorporated with clinical features of subjects with bronchiectasis, which provides clinicians a more complete picture of subjects with bronchiectasis.

In the present study, pulmonary comorbidities of asthma, previous pulmonary TB, and airflow limitation were independently associated with presence of bronchiectasis. In agreement with our findings, asthma and COPD were common etiologies and comorbidities in individuals with bronchiectasis in previous studies (5,6,18). In a recent cohort study performed in Finland, asthma was associated with 68% of the study population and was an estimated cause of bronchiectasis in one-fourth of the study population (6). In addition to the previous report, asthma was significantly associated with bronchiectasis in the present study. Furthermore, the rate of post-infectious bronchiectasis was reportedly 15–50% (28-30), and previous TB was the most well-known etiology of bronchiectasis among various factors (31). In agreement with the previous study, previous pulmonary TB was associated with bronchiectasis even after adjustment for various socioeconomic factors in the present study.

In this study, subjects with bronchiectasis showed more respiratory symptoms, physical activity limitations, and poorer quality of life. Patients with bronchiectasis are known to suffer from more respiratory symptoms, including purulent sputum and recurrent respiratory infections (13,32-35). In addition to respiratory symptoms, physical activity limitation and poorer quality of life were observed more frequently in subjects with bronchiectasis than in subjects without bronchiectasis. Hypothetically, quality of life impairment and physical activity limitations may be more negatively affected by additional respiratory symptoms in subjects with bronchiectasis. However, among the EQ-5D index components, pain/discomfort and anxiety/depression were especially present in subjects with bronchiectasis in the present study. These results indicate that poorer quality of life may not be solely explained by more respiratory symptoms in subjects with bronchiectasis. Future studies are warranted to determine the underlying mechanisms of the phenomenon, which may help clinicians discover measures to improve the quality of life in subjects with bronchiectasis.

Bronchiectasis is often underreported or underdiagnosed (36) although it is associated with a significantly increased health burden worldwide, an annual exacerbation frequency of up to 3 per patient per year, and a clear attributable mortality (37). From this point of view, revealing factors associated with bronchiectasis would be very helpful in reducing the bronchiectasis-related health burden through early diagnosis and management of this disease. Our study showed that asthma and the presence of airflow limitation are associated with bronchiectasis. As comorbid bronchiectasis results in a poorer disease control and more frequent exacerbation in patients with COPD or asthma (7,38), our results strongly suggest that clinicians should suspect the presence of bronchiectasis when they encounter patients with poorly controlled airway diseases. Consistent with a previous report (39), this study also emphasizes that bronchiectasis is significantly associated with a previous history of pulmonary TB. Thus, bronchiectasis should be considered as a differential diagnosis when patients have persistent respiratory symptoms even after completion of TB treatment.

Another interesting finding is that subjects with bronchiectasis showed a lower family income and lower educational level. Due to the cross-sectional design, we could not fully explain the causal relationship between bronchiectasis and socioeconomic status. One possible explanation is that a low socioeconomic status could contribute to the development of bronchiectasis. Many studies have shown that a lower socioeconomic family is associated with respiratory infection, including TB, which is a well-known risk factor for bronchiectasis (1,40). In contrast, bronchiectasis could contribute to a low socioeconomic status in these patients. Patients with bronchiectasis could be at risk of disability and low work productivity (work loss, reduced work hours, absenteeism, and early retirement) due to substantial symptomatic burden, as shown in studies evaluating disability and job status in subjects with COPD (24). An increased medical burden in subjects with bronchiectasis could also contribute to their low socioeconomic status. Thus, long-term and large-scale prospective cohort studies are warranted to elucidate the causal inference of this phenomenon in the future.

The present study results have several important clinical implications. First, individuals with bronchiectasis experience more respiratory symptoms and poorer quality of life than subjects without bronchiectasis. Accordingly, this indicates that early diagnosis and adequate treatment are critical in individuals with bronchiectasis. Second, asthma and airflow limitations were the main factors associated with presence of bronchiectasis. Therefore, it is important for

clinicians to determine whether bronchiectasis is co-existent in subjects with uncontrolled or airway diseases with airflow limitation. Third, pulmonary TB was a significant factor associated with bronchiectasis. From this perspective and considering the high prevalence of TB in many Asian countries, clinicians should carefully assess the development of bronchiectasis after TB treatment.

The present study had several limitations. First, due to the nature of the cross-sectional study design, evaluating a cause-and-effect relationship between bronchiectasis and associated factors was not possible. Second, because this study was conducted in the Korean population, the results might not be generalized to other races or ethnic groups. Third, bronchiectasis was diagnosed based on physician diagnosis. Therefore, more symptomatic subjects may have been included in the study, and subjects with minor symptoms may not have been included. Fourth, compared with the control group, the number of bronchiectasis subjects was relatively small, which may have led to some important factors lacking statistical significance.

In conclusion, subjects with bronchiectasis were more likely to be older, have lower BMI, lower family income, lower educational level, more pulmonary comorbidities, and decreased lung function compared with those without bronchiectasis. Subjects with bronchiectasis suffer from more respiratory symptoms with physical activity limitation and decreased quality of life than those without bronchiectasis. Furthermore, lower family income and pulmonary comorbidities of previous pulmonary TB, asthma, and presence of airflow limitation were independently associated with bronchiectasis. Appropriate management to reduce disease burden associated with respiratory symptoms, poor quality of life, and comorbid pulmonary conditions is needed in subjects with bronchiectasis.

Acknowledgments

Footnote

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