Early View

Original article

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Take-home message:

The prevalence of asymptomatic bronchiectasis appeared to be more common than that of symptomatic bronchiectasis. Female sex, older age, liver disease, COPD, history of tuberculosis, and low FEV1 may be the factors related to asymptomatic bronchiectasis.

Abstract

Despite the burden of bronchiectasis, there is little data from South Korea regarding asymptomatic bronchiectasis. We aimed to investigate the prevalence of bronchiectasis based on computed tomography (CT) findings, with emphasis on asymptomatic bronchiectasis (CT-proven) and its related factors.

We analysed data of individuals who underwent chest CT at a South Korean health screening centre from 2016 to 2017. The prevalence of bronchiectasis was evaluated and adjusted by sex, age, and corresponding year for the Korean general population. Logistic regression analysis was performed to identify factors related to asymptomatic bronchiectasis by comparison between a group without bronchiectasis and a group with symptomatic bronchiectasis.

Among the 27,617 subjects screened, 1,005 were diagnosed with bronchiectasis based on CT findings, representing an adjusted prevalence of 2,329/100,000. The adjusted prevalence of asymptomatic bronchiectasis was 1,235/100,000, and that of symptomatic bronchiectasis was 1,094/100,000. Compared with the non-bronchiectasis group, the factors related to asymptomatic bronchiectasis were female sex (odds ratio [OR], 1.41; 95% confidence interval [CI], 1.18-1.70), older age (OR, 1.06; 95% CI, 1.05-1.07), comorbid liver disease (OR, 1.32; 95% CI, 1.07-1.63) or chronic obstructive pulmonary disease (COPD; OR, 4.99; 95% CI, 2.88-8.64), history of tuberculosis (OR, 1.98; 95% CI, 1.46-2.68), and low forced expiratory volume in 1 second (FEV1; OR, 0.99; 95% CI, 0.98-0.998).

In South Korea, the prevalence of asymptomatic bronchiectasis appeared higher than that of symptomatic bronchiectasis. Female sex, older age, liver disease, COPD, history of tuberculosis, and low FEV1 may be the factors related to asymptomatic bronchiectasis.

Introduction

Bronchiectasis is a chronic respiratory disease characterised by irreversible dilatation of the bronchus and/or its branches, along with recurrent airway inflammation and infection [1]. It is suggested that bronchiectasis may develop by a vicious cycle of impaired mucus clearance, chronic infection, airway obstruction, inflammation, and progressive tissue destruction [2]. For diagnosis of bronchiectasis, chest computed tomography (CT) is now used as a reference standard [3, 4].

Although bronchiectasis might be clinically important as a chronic respiratory disease with irreversible changes, it was once considered as an orphan disease and often neglected [5]. This might be attributed to lack of a standard diagnostic tool and treatment strategy, along with a disinterest and misperception that bronchiectasis was uncommon [6]. Recently, a longitudinal study in UK focusing on older age groups showed an increase in the annual incidence and prevalence of bronchiectasis from 2004 to 2013 [7]. Another study in the United States showed an increase in bronchiectasis prevalence (8.7% per year from 2000 to 2007) [8]. Accordingly, bronchiectasis has imposed a considerable burden on public health, including mortality, hospital admission, and high costs of health care resources [8, 9]. However, previous epidemiological information has been limited to retrospective, cross-sectional studies, with the data mainly extracted using the International Classification of Diseases 10th revision (ICD-10) diagnostic code and mostly based on hospital discharge, medical insurance, or partially *ad hoc* population-based databases [8, 10, 11]. Thus, real-world data on the epidemiology of bronchiectasis is still limited for most countries, including South Korea.

Bronchiectasis is also heterogeneous, showing a wide range of clinical features [12]. Some patients may be asymptomatic, whereas others may have chronic productive cough, dyspnoea, recurrent chest infections, and occasional haemoptysis [13]. The presence of symptoms has clinically important implications. Combined with microbiology, symptoms are used in classifying bronchiectasis phenotypes, with each phenotype having distinctive features regarding quality of life, exacerbations, hospitalisations, and mortality [14]. However, studies on the characteristics of bronchiectasis with clinical symptoms are limited.

Recent studies have shown some advances in the treatment of bronchiectasis, leading to better prognosis [15]. Therefore, it is important to identify and treat bronchiectasis in its early stages, starting from the asymptomatic period. However, there is limited data regarding the prevalence of asymptomatic bronchiectasis and its related factors.

Therefore, we aimed to evaluate the real-world prevalence of bronchiectasis based on chest CT findings at a health screening centre of Asan Medical Centre in South Korea. Furthermore, we aimed to investigate the prevalence and factors associated with asymptomatic bronchiectasis (CT-proven). To identify these related factors, we analysed the group of subjects with asymptomatic bronchiectasis and compared them to the groups without bronchiectasis and with symptomatic bronchiectasis.

Materials and methods

Subjects

This cross-sectional, retrospective study was performed using the database from the in-house electronic medical record system at the Health Screening and Promotion Centre of Asan Medical Centre, Seoul, South Korea, from the years 2016 to 2017. We extracted the data of 27,641 subjects aged ≥18 years who underwent chest CT during their routine medical check-ups. CT scans were performed using multidetector-raw CT (MDCT) scanner.

Identification of bronchiectasis and patients with asymptomatic bronchiectasis

Bronchiectasis was identified by radiologists using chest CT findings of broncho-arterial ratio >1, lack of tapering, or airway visibility within 1 cm of the costopleural surface or touching the mediastinal pleura [4]. Symptoms of bronchiectasis were defined as the presence of at least one of the following five symptoms: cough, sputum production, dyspnoea, wheezing, and haemoptysis [2]. *Asymptomatic bronchiectasis* was defined as the presence of bronchiectatic findings on chest CT with none of the abovementioned symptoms. Contrarily, symptomatic bronchiectasis was defined as the presence of bronchiectatic findings on chest CT with any of the abovementioned five symptoms. As a control group, non-bronchiectasis was defined as the absence of bronchiectatic findings on chest CT and the absence of any of the five respiratory symptoms. We compared the group with asymptomatic bronchiectasis to those with non-bronchiectasis and symptomatic bronchiectasis. Symptomatic patients without bronchiectasis were excluded for comparison.

Data for related factors

Information on age, sex, height, weight, comorbidities [malignancy, hypertension, diabetes mellitus (DM), hyperlipidaemia, angina, heart failure (HF), arrhythmia, peripheral vascular disease (PVD), cerebrovascular disease (CVD), osteoporosis, arthritis, dementia, liver disease, kidney disease, chronic obstructive pulmonary disease (COPD), asthma, tuberculosis, gastro-oesophageal reflux disease (GERD), inflammatory bowel disease (IBD), allergic rhinitis], smoking history, and respiratory symptoms at enrolment [dyspnoea, cough (persisting for at least two months), sputum production (persisting for at least three months per year in the past two years), wheezing, haemoptysis] was obtained using standard self-reporting questionnaires developed at the health screening centre during the first visit or CT scan [16]. Body mass index (BMI) was calculated as weight in kilograms divided by the square of height in metres (kg/m^2). According to the National Institutes of Health (NIH), BMI was stratified into three groups: underweight (BMI <18.5 kg/m^2), normal weight (BMI ≥18.5 and <25 kg/m^2), overweight or obese (BMI ≥25 kg/m^2) [17]. Spirometric data, including forced expiratory volume in 1 s (FEV1), forced vital capacity (FVC), and FEV1/FVC were measured. Pulmonary function testing was performed according to the American Thoracic Society/European Respiratory Society Guidelines [18]. Blood haemoglobin and C-reactive protein (CRP) levels were also obtained during stable state.

Prevalence adjustment

The crude prevalence of bronchiectasis was calculated as the number of subjects with bronchiectasis divided by the total number of subjects who underwent chest CT for health screening. To adjust for unequal probabilities of selection and to account for non-participation, the adjusted prevalence was calculated based on the sampling weight. Results were post-stratified to the Korean population as estimated by the Bureau of the Census 2016-2017, with further stratification by either sex or age [19].

Statistical analyses

Continuous data are presented as mean (standard deviation [SD]) or median (25th–75th interquartile range). Categorical data are presented as absolute numbers with percentages in

parentheses. Data among the three groups were compared using the analysis of variance t-test or Kruskal–Wallis test for continuous data and the Chi-square or linear-by-linear test for categorical data. Data between two groups were compared using the Student's t-test or Mann–Whitney test for continuous data and the Chi-square or Fisher's exact test for categorical data. Univariate and multivariate logistic regression analyses were performed to identify risk factors for asymptomatic bronchiectasis. Univariate analyses were performed for all baseline characteristic variables. Multivariate analyses were performed with age, sex, and variables whose p-values were less than 0.10 in univariate analyses. Odds ratios (ORs) and 95% confidence intervals (CIs) were computed for each variable. Statistical analyses were performed using IBM SPSS Statistics Version 24 (IBM Corp., Armonk, NY, USA). A p-value <0.05 was considered statistically significant.

Institutional review board approval and informed consent

This study was approved by the Institutional Review Board (IRB) of Asan Medical Centre (IRB No. 2018-0691). The requirement for informed consent from the subjects was waived because of the retrospective study design.

Results

Study population

A total of 27,617 subjects who underwent chest CT from 2016 to 2017 were included in our study after excluding 24 subjects with missing data (Figure 1). Their mean age was 58.4 (SD, 8.9) years and the proportion of men was greater than women (n=17,511; 63.4%). Among the 27,617 subjects, 1,005 were diagnosed with bronchiectasis based on CT results. Among the 1,005 subjects with bronchiectasis, the mean age was 62.4 (SD, 7.5) years, and the proportion of men was greater than women (n=585; 58.2%). The numbers of subjects were 16143, 566, and 439 in the non-bronchiectasis group, the asymptomatic bronchiectasis group, and the symptomatic bronchiectasis group, respectively.

Baseline characteristics

The baseline characteristics of the three groups are shown in Table 1, Figure 2, and Supplementary Table 1. The proportions of women were different among the three groups, with an increasing trend toward the symptomatic bronchiectasis group (34.4% vs. 39.0% vs. 45.3%, p <0.001), whereas age was greater in the asymptomatic bronchiectasis group than in the other two groups (58.19 vs. 64.24 vs. 62.64, p <0.001). Comorbidities, such as hypertension, hyperlipidaemia, arrhythmia, osteoporosis, arthritis, dementia, liver disease, kidney disease, COPD, asthma, tuberculosis, GERD, and allergic rhinitis, were also different among the three groups. Furthermore, history of smoking (53.2% vs. 46.5% vs. 44.6%, p <0.001) and FEV1 (92.06% of the predicted value vs. 90.42% vs. 85.63%, p <0.001) were different, with decreasing trends toward the symptomatic bronchiectasis group. Regarding laboratory findings, haemoglobin levels were different, with a decreasing trend toward the symptomatic bronchiectasis group (14.61 vs. 14.44 vs. 14.38, p <0.001), whereas CRP levels were relatively higher in the symptomatic bronchiectasis group than in the other groups (0.11 vs. 0.11 vs. 0.16, p <0.001).

Table 1. Baseline characteristics of non-bronchiectasis, asymptomatic bronchiectasis, and symptomatic bronchiectasis

	Non-bronchiectasis (n=16,143) (A)	Asymptomatic bronchiectasis (n=566) (B)	Symptomatic bronchiectasis (n=439) (C)	p-value			
				A vs B vs C	A vs B	B vs C	A vs C
Female sex	5,555 (34.4%)	221 (39.0%)	199 (45.3%)	<0.001	0.023	0.045	<0.001
Age, years	58.19 (8.58)	64.24 (7.40)	62.64 (7.71)	<0.001	<0.001	0.402	<0.001
BMI, kg/m^2 (n=16,136/566/439)				0.580	0.605	0.249	0.410
Underweight	462 (2.9)	14 (2.5)	16 (3.6)				
Normal weight	10,926 (67.7)	394 (69.6)	286 (65.1)				
Overweight or obesity	4,748 (29.4)	158 (27.9)	137 (31.2)				
Smoking History (non-smoker/ ex-smoker/ current smoker) (n=16,090/563/437)	7,523/5,371/3,196 (46.8%/33.4%/ 19.9%)	301/184/78 (53.5%/32.7%/ 13.9%)	242/125/70 (55.4%/28.6%/ 16.0%)	<0.001	<0.001	0.322	0.002
PFT (FEV1, %) (n=15,747/553/430)	92.06 (11.18)	90.42 (12.07)	85.63 (14.69)	<0.001	0.002	<0.001	0.001
Laboratory test							
Hg, g/dL (n=16,140//566/439)	14.61 (1.41) 14.7 (13.6, 15.6)	14.44 (1.42) 14.3 (13.5, 15.5)	14.38 (1.44) 14.4 (13.4, 15.4)	<0.001	0.006	0.537	<0.001
CRP, mg/dL (n=14,618/517/403)	0.11 (0.16) 0.06 (0.04, 0.1)	0.11 (0.15) 0.06 (0.04, 0.11)	0.16 (0.25) 0.07 (0.05, 0.16)	<0.001	0.363	<0.001	<0.001

*: Linear by Linear test

Continuous variables are presents as mean (SD) or median (interquartile range); categorical variables are presented as number (%).

Abbreviations: BMI, body mass index; COPD, chronic obstructive pulmonary disease; CRP, C-reactive protein; CVD, cerebrovascular disease; DM, diabetes mellitus; FEV1, forced expiratory volume in 1s; GERD, gastroesophageal reflux disease; HF, heart failure; Hg, hemoglobin; IBD, inflammatory bowel disease; PFT, pulmonary function test; PVD, peripheral vascular disease.

Supplementary Table 1. Comorbidities of non-bronchiectasis, asymptomatic bronchiectasis, and symptomatic bronchiectasis

	Non-bronchiectasis (n=16,143) (A)	Asymptomatic bronchiectasis (n=566) (B)	Symptomatic bronchiectasis (n=439) (C)	p-value			
				A vs B vs C	A vs B	B vs C	A vs C
Medical History							
Malignancy	1,401 (8.7%)	58 (10.2%)	35 (8.0%)	0.368	0.194	0.217	0.604
Hypertension	4,177 (25.9%)	164 (29.0%)	146 (33.3%)	0.001	0.098	0.145	0.001
DM	1,682 (10.4%)	72 (12.7%)	55 (12.5%)	0.085	0.079	0.927	0.155
Hyperlipidemia	3,323 (20.6%)	143 (25.3%)	124 (28.2%)	<0.001	0.007	0.289	<0.001
Angina	566 (3.5%)	22 (3.9%)	22 (5.0%)	0.222	0.629	0.388	0.092
HF	28 (0.2%)	1 (0.2%)	2 (0.5%)	0.272*	1.0*	0.584*	0.188
Arrhythmia	468 (2.9%)	26 (4.6%)	23 (5.2%)	0.002	0.019	0.637	0.004
PVD	88 (0.5%)	1 (0.2%)	7 (1.6%)	0.104*	0.375*	0.025*	0.013
CVD	222 (1.4%)	13 (2.3%)	7 (1.6%)	0.178	0.067	0.429	0.698
Osteoporosis	972 (6.0%)	52 (9.2%)	47 (10.7%)	<0.001	0.002	0.423	<0.001
Arthritis	1,326 (8.2%)	59 (10.4%)	69 (15.7%)	<0.001	0.061	0.013	<0.001
Dementia	13 (0.1%)	1 (0.2%)	3 (0.7%)	<0.001*	0.383*	0.324*	0.008
Liver disease	2,764 (17.1%)	123 (21.7%)	105 (23.9%)	<0.001	0.004	0.412	<0.001
Kidney disease	76 (0.5%)	2 (0.4%)	8 (1.8%)	0.004*	1.0*	0.025*	0.002
COPD	82 (0.5%)	18 (3.2%)	25 (5.7%)	<0.001*	<0.001*	0.051	<0.001
Asthma	193 (1.2%)	7 (1.2%)	33 (7.5%)	<0.001	0.929	<0.001	<0.001
Tuberculosis	727 (4.5%)	53 (9.4%)	64 (14.6%)	<0.001	<0.001	0.011	<0.001
GERD	3,161 (19.6%)	125 (22.1.%)	120 (27.3%)	<0.001	0.141	0.055	<0.001
IBD	101 (0.6%)	6 (1.1 %)	5 (1.1%)	0.074*	0.180*	1.0*	0.208

Rhinitis (n=16,142/565/439)	2,770 (17.2%)	99 (17.5%)	119 (27.1%)	<0.001	0.823	<0.001	<0.001

*: Linear by Linear test

Continuous variables are presents as mean (SD) or median (interquartile range); categorical variables are presented as number (%).

Abbreviations: BMI, body mass index; COPD, chronic obstructive pulmonary disease; CRP, C-reactive protein; CVD, cerebrovascular disease; DM, diabetes mellitus; FEV1, forced expiratory volume in 1s; GERD, gastroesophageal reflux disease; HF, heart failure; Hg, hemoglobin; IBD, inflammatory bowel disease; PFT, pulmonary function test; PVD, peripheral vascular disease.

Prevalence of bronchiectasis

The crude prevalence of bronchiectasis was 3,639 per 100,000 subjects, with a higher prevalence among women than men (4,156/100,000 vs. 3,341/100,000; p <0.001). The prevalence of bronchiectasis, adjusted by age, sex, and year, was 2,329/100,000. The crude prevalence of bronchiectasis increased substantially with age (from 0 per 100,000 in ages 20-29 years to 7,210 per 100,000 in ages ≥70 years; p <0.001) (Figure 3). Across all age ranges with 10-year intervals, the prevalence of bronchiectasis was higher in women than in men, especially within the range of 50-59 years (3,641 per 100,000 vs. 2,409 per 100,000; p <0.001).

Based on the presence of respiratory symptoms, there were 566 cases of asymptomatic bronchiectasis and 439 cases of symptomatic bronchiectasis among the total 27,617 subjects. The crude prevalence in the asymptomatic bronchiectasis group was 2,050/100,000, which was higher than that of the symptomatic group (1,590/100,000). The prevalence of asymptomatic bronchiectasis, adjusted by age, sex, and year, was 1,235/100,000, which was also higher than that in the symptomatic group (1,094/100,000).

Factors related to asymptomatic bronchiectasis

Factors related to asymptomatic bronchiectasis were evaluated and compared with those in the non-bronchiectasis group (Figure 4). Univariate analysis revealed the following ORs for the variables: female sex (OR, 1.22; 95% CI, 1.03-1.45), age in years (1.06; 1.05-1.07), hypertension (1.17; 0.97-1.41), DM (1.25; 0.97-1.61), hyperlipidaemia (1.3; 1.08-1.58), arrhythmia (1.61; 1.08-2.42), CVD (1.69; 0.96-2.97), osteoporosis (1.58; 1.18-2.12), arthritis (1.3; 0.99-1.71), liver disease (1.34; 1.10-1.65), COPD (6.43; 3.84-10.79), tuberculosis (2.19; 1.64-2.94), smoking history (ex-smoker: 0.86; 0.71-1.03/current smoker: 0.61; 0.47-0.79), FEV1 (%) (0.99; 0.98-0.995), and haemoglobin (0.92; 0.87-0.98). Among these variables, multivariate analysis (presented as ORs; 95% CIs) showed that female sex (1.41; 1.18-1.70), older age (1.06; 1.05-1.07), comorbid liver disease (1.32; 1.07-1.63) and COPD (4.99; 2.88-8.64), history of tuberculosis (1.98; 1.46-2.68), and lower FEV1 (%) (0.99; 0.98-0.998) were related to asymptomatic bronchiectasis.

Factors related to the presence of respiratory symptoms in bronchiectasis

Factors related to respiratory symptoms in bronchiectasis were evaluated, with comparison

between the symptomatic bronchiectasis and asymptomatic bronchiectasis groups (Supplementary Figure 1).

Factors related to symptomatic bronchiectasis

Factors related to symptomatic bronchiectasis were evaluated, with comparison to the non-bronchiectasis group (Supplementary Figure 2).

Discussion

Our study reports the prevalence of bronchiectasis in South Korea based on CT findings, using the 2016–2017 database at a health screening centre of Asan Medical Centre. The data were further adjusted by age, sex, and the corresponding year for the Korean general population. Furthermore, this is the first study to evaluate the prevalence of asymptomatic bronchiectasis and its related factors, which were female sex, advanced age, comorbid liver disease and COPD, history of tuberculosis, and low FEV1.

In our study, the adjusted prevalence of bronchiectasis in South Korea was 2,329/100,000, with female predominance and an increase with age. Some studies in South Korea have shown a lower prevalence of bronchiectasis than that reported in this study. A study by Choi et al. reported the prevalence of bronchiectasis as 464 per 100,000 population in South Korea [20]. It was based on the 2012–2017 Health Insurance Review and Assessment Service, National Patient Sample (HIRA-NPS) database and the ICD-10 diagnostic code, which could underestimate the true prevalence of bronchiectasis. A study by Yang et al. showed that the prevalence of bronchiectasis in subjects aged 40 or more years was 0.8%, which was based on the 2007–2009 Korean National Health and Nutrition Examination Survey database [21]. However, there was a possibility of recall bias and exclusion of patients with severe symptoms and inability to respond to the survey. Our study estimated the prevalence of bronchiectasis based on CT findings in all subjects, adjusted to the Korean general population. Thus, our study may provide a more accurate prevalence of bronchiectasis in South Korea.

Previous studies on the prevalence of bronchiectasis were mostly limited to western countries, producing a result lower than that reported in our study. The annual prevalence of bronchiectasis has been reported to be 486 (for men) to 566 (for women) per 100,000 population in the UK from 2004 to 2013 [7], 163 per 100,000 population in Italy from 2002 to 2015 [22], 95 per 100,000 population in Germany from 2009 to 2017 [9], and 139 per 100,000 population in the US in 2013

[23]. This inconsistency might be partially explained by ethnicity; Asians showed 2.5- and 3.9-fold higher prevalence of bronchiectasis than Caucasian and African-American populations among people aged ≥ 65 years with one available CT scan, indicating a predisposition toward bronchiectasis in the Asian population [8]. The inconsistency might also be attributed to differences in the aetiology of bronchiectasis worldwide. In Asia, the prevalence of pulmonary infection and pulmonary tuberculosis were reported to be much higher than that in western countries and accounted for the major aetiologies of bronchiectasis [24]. Further CT-based studies with international multicentric cohorts and a focus on genetic susceptibility and aetiologies of bronchiectasis are warranted to support a higher prevalence of bronchiectasis in Asia.

Another important finding of our study is that the adjusted prevalence of asymptomatic bronchiectasis was 1,235/100,000, which was higher than that of the symptomatic group (1,094/100,000). Previous studies were mostly based on the ICD-10 diagnostic code, which might have excluded patients with asymptomatic bronchiectasis not requiring hospital visits [9, 20, 22, 23]. One study showed that asymptomatic bronchiectasis accounted for 46% of all bronchiectasis cases, but the total study population was small (n=1,409) [25]. Our study emphasises the high burden of asymptomatic bronchiectasis with stronger evidence because our large cohort from the health screening centre was likely more attentive to health issues during the asymptomatic period. Thus, our study indicates the need for increased awareness of asymptomatic bronchiectasis to prevent disease onset and slow progression. Further studies are warranted to evaluate the impact of asymptomatic bronchiectasis on the overall clinical course of bronchiectasis.

Interestingly, female sex was associated with asymptomatic bronchiectasis and also with the presence of respiratory symptoms in bronchiectasis. Female predominance in the prevalence of non-cystic bronchiectasis was previously reported, although there were conflicting results for sex predominance in the elderly population [7, 22, 23, 26]. This might be due to changes in the aetiologies of bronchiectasis, such as increased non-tuberculous mycobacterial infection and connective tissue disease, which are predominant in women [27-29]. Furthermore, some studies suggested that female anatomy and sex hormone factors might contribute to sex differences because of early bacterial colonisation and its conversion to the Pseudomonas phenotype in bronchiectasis, which might lead to development of respiratory symptoms [30, 31]. Thus, women are likely to have a relatively high risk of future bronchiectasis, as well as respiratory symptoms when bronchiectasis develops. More attention should be paid to this population, and further prospective cohort studies are warranted to evaluate the causal relationships with bronchiectasis.

Furthermore, liver disease was positively correlated with bronchiectasis, which might be mostly

attributed to asymptomatic bronchiectasis. Among the aetiologies of liver disease, fatty liver disease was the most common cause in our study, comprising 75.2% (2,078/2,764) in non-bronchiectasis, 71.5% (88/123) in asymptomatic bronchiectasis, and 71.5% (88/123) in symptomatic bronchiectasis groups. Non-alcoholic fatty liver disease (NAFLD) was previously reported to be highly prevalent in patients with COPD [32, 33] and positively associated with impaired lung function [34, 35], indicating a close relationship with airway disease. This might be attributed to systemic inflammation associated with NAFLD and interleukin-8, tumour necrosis factor alpha, leptin, and oxidative stress [36-38], which might induce recurrent bronchial inflammation and the development of bronchiectasis. Thus, liver disease could be used to identify subjects with a high risk of developing asymptomatic bronchiectasis. Further prospective studies are warranted to evaluate the relationship between these factors and asymptomatic bronchiectasis.

Our study has some limitations. First, this study was based on voluntary participants at a tertiary centre, which may have caused a selection bias. Furthermore, this may have influenced the presence of certain comorbid conditions. However, this was a large population-based study adjusted to the standard population and may be representative of the general health screening population of South Korea. Second, true causality of the factors related to asymptomatic bronchiectasis could not be identified due to the retrospective and cross-sectional study design. Therefore, further prospective, longitudinal cohort studies are needed to confirm the true causal relationship of the potential risk factors for asymptomatic bronchiectasis. Third, we could not estimate the impact of asymptomatic bronchiectasis on clinical outcomes, such as mortality, hospitalisation, exacerbations, and quality of life, due to the nature of data obtained from a health screening centre with a short study period. Further studies with adequate, longitudinal data on clinical outcomes are thus warranted to evaluate the association with asymptomatic bronchiectasis. Fourth, comorbidities might have been underestimated due to the retrospective nature of our study. Future studies with various aetiologies of bronchiectasis are needed to evaluate their effects on asymptomatic bronchiectasis. Fifth, in asymptomatic bronchiectasis, there was a limitation in discriminating dry bronchiectasis from early stage of symptomatic bronchiectasis due to the retrospective nature and absence of etiological testing. Further studies are needed to define and evaluate the pre-clinical stage of symptomatic bronchiectasis.

Conclusion

Bronchiectasis might not be a rare disease in South Korea, where asymptomatic bronchiectasis

appeared to be more common than symptomatic bronchiectasis. Female sex, older age, liver disease, COPD, history of tuberculosis, and low FEV1 might be related to asymptomatic bronchiectasis. Therefore, the related factors should be further explored.

Acknowledgments

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Figure Legends

27,641 participants included at
Asan Medical Center Health Screening
Center (2016-2017) with

1. Age ≥ 18 years
2. Available chest CT

24 participants excluded
due to missing data regarding

1. Respiratory symptoms
2. Available medical chart

Exclusion

27,617 participants with

1. Respiratory symptoms
2. Available medical chart

1. Radiology
- Bronchoarterial ratio >1
- Lack of tapering
- Airway visibility within 1cm of
costal pleural surface or
touching mediastinal pleura

2. Code 142 designated by
health screening center

Criteria of
bronchiectasis

No

Yes

Symptomatic
without bronchiectasis
n=10,469

Exclusion

Bronchiectasis
n=1,005

Non-bronchiectasis
n=16,143

Asymptomatic
bronchiectasis
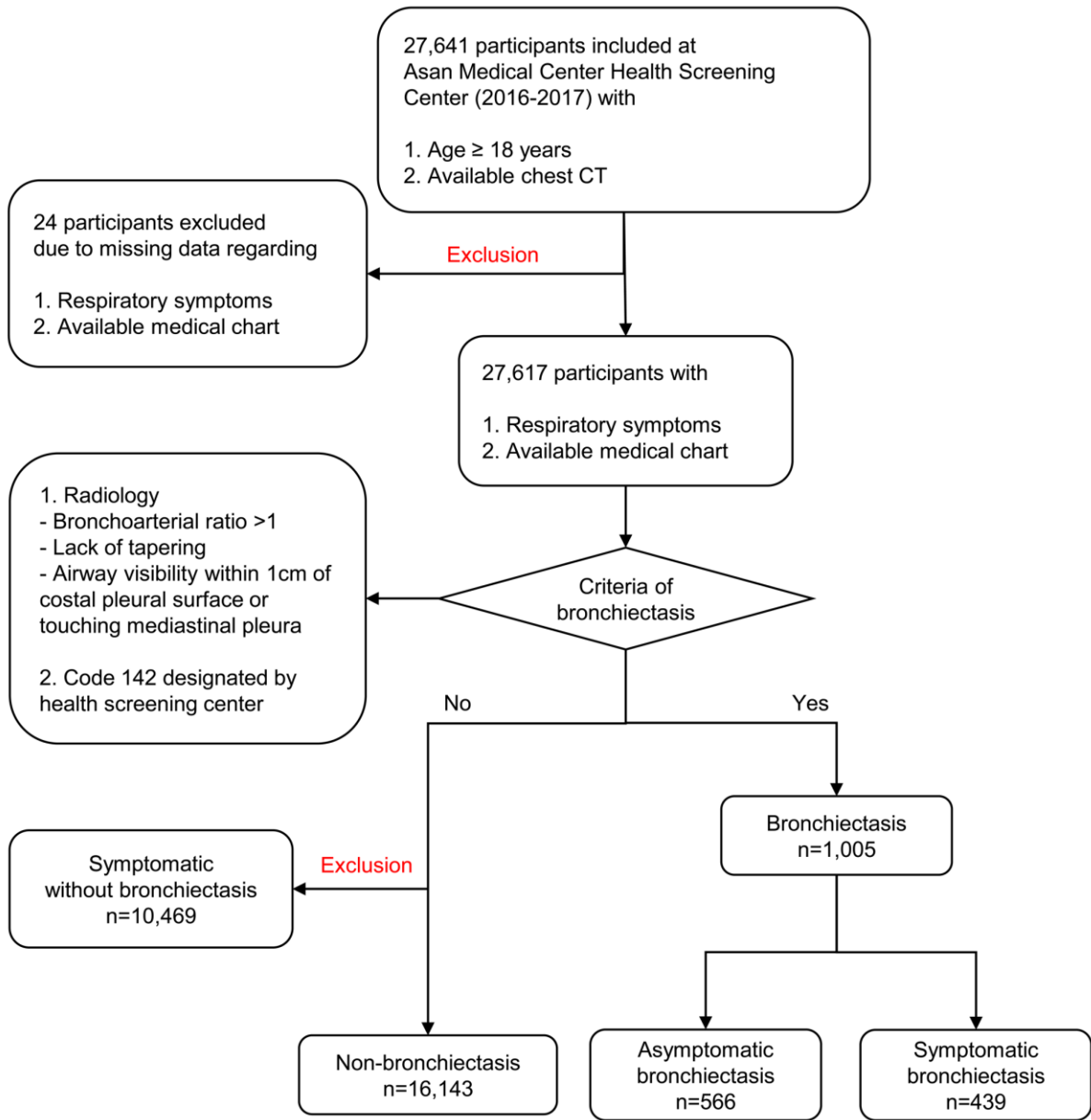n=566

Symptomatic
bronchiectasis
n=439

Figure 1. Flow chart of the study population
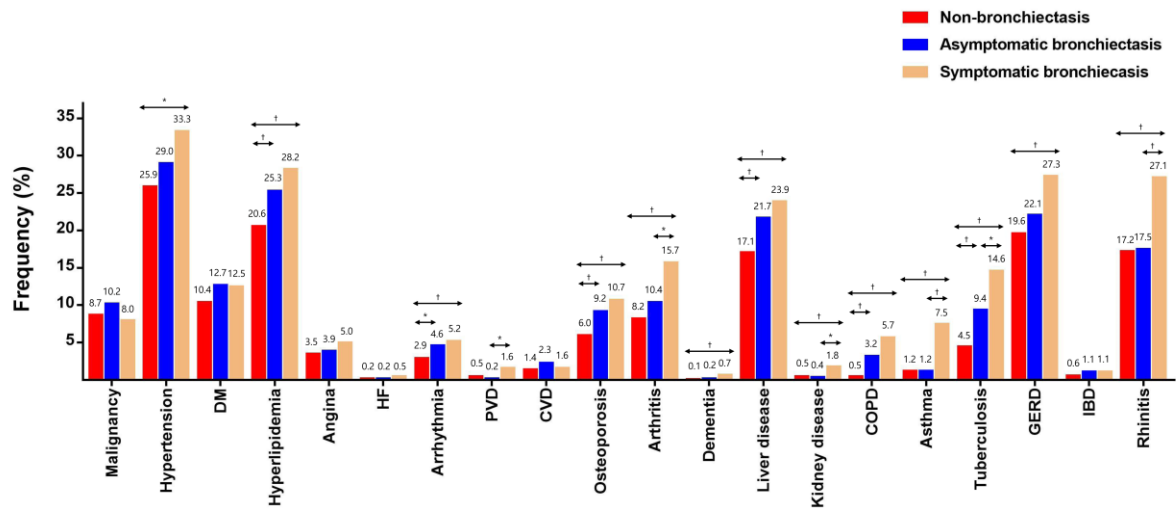
Figure 2. Frequency of comorbidities among non-bronchiectasis, asymptomatic bronchiectasis, and symptomatic bronchiectasis

* p <0.05

† p <0.01
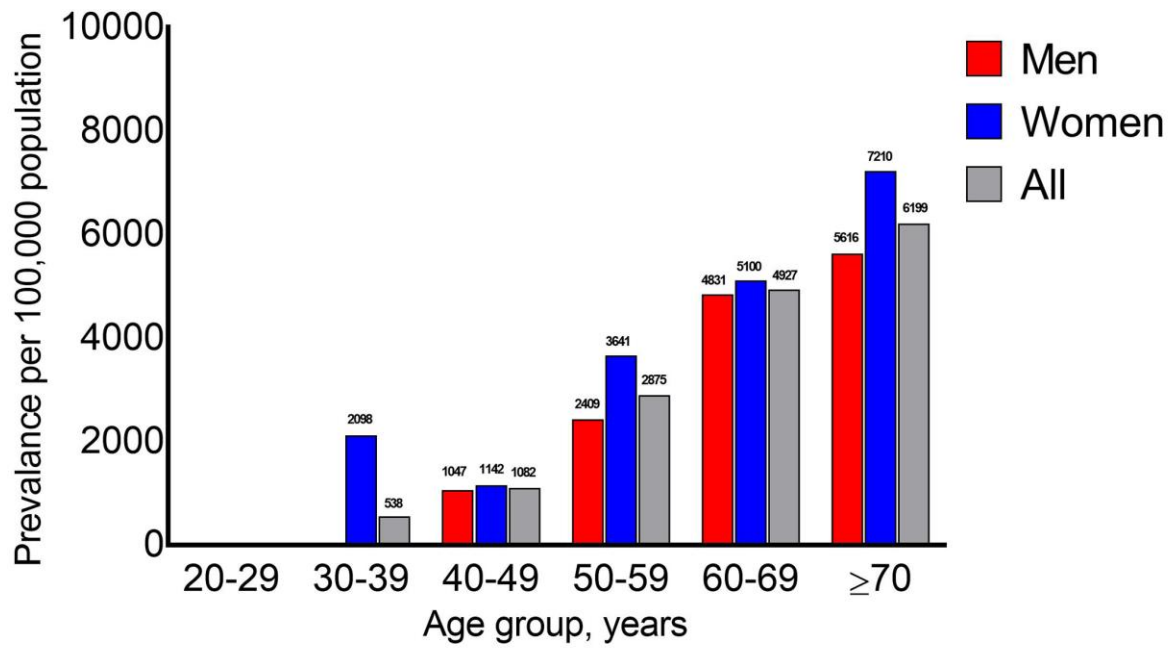
Figure 3. Prevalence of bronchiectasis based on age group and sex in South Korea during 2016–2017
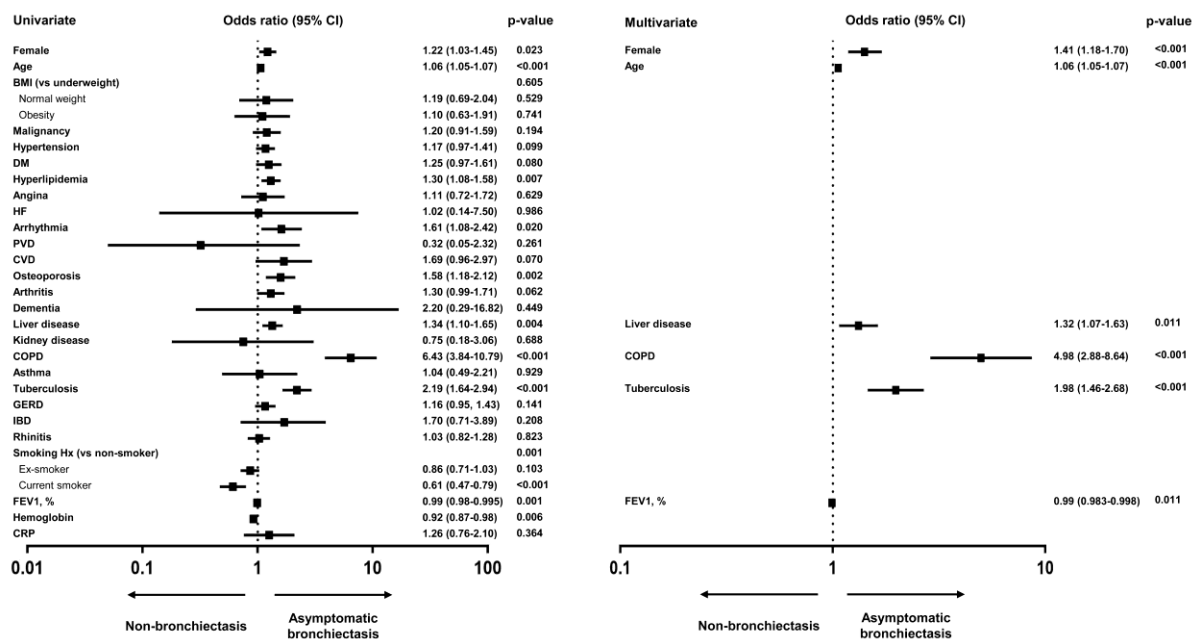
Figure 4. Factors related to asymptomatic bronchiectasis

Abbreviations: BMI, body mass index; COPD, chronic obstructive pulmonary disease; CRP, C-reactive protein; CVD, cerebrovascular disease; DM, diabetes mellitus; FEV1, forced expiratory volume in 1 s; GERD, gastro-oesophageal reflux disease; HF, heart failure; Hg, haemoglobin; IBD, inflammatory bowel disease; PVD, peripheral vascular disease.

Supplementary Figure legends

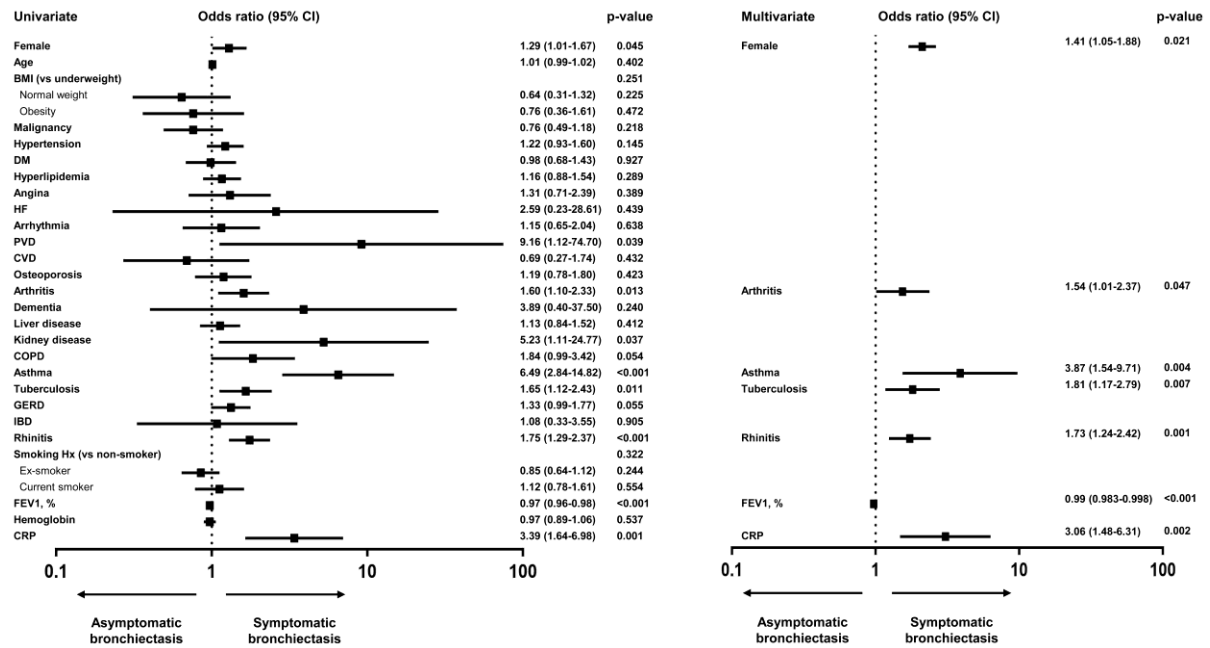| Univariate	Odds ratio (95% CI)	p-value
Female	1.29 (1.01-1.67)	0.045
Age	1.01 (0.99-1.02)	0.402
BMI (vs underweight)		0.251
Normal weight	0.64 (0.31-1.32)	0.225
Obesity	0.76 (0.36-1.61)	0.472
Malignancy	0.76 (0.49-1.18)	0.218
Hypertension	1.22 (0.93-1.60)	0.145
DM	0.98 (0.68-1.43)	0.927
Hyperlipidemia	1.16 (0.88-1.54)	0.289
Angina	1.31 (0.71-2.39)	0.389
HF	2.59 (0.23-28.61)	0.439
Arrhythmia	1.15 (0.65-2.04)	0.638
PVD	9.16 (1.12-74.70)	0.039
CVD	0.69 (0.27-1.74)	0.432
Osteoporosis	1.19 (0.78-1.80)	0.423
Arthritis	1.60 (1.10-2.33)	0.013
Dementia	3.89 (0.40-37.50)	0.240
Liver disease	1.13 (0.84-1.52)	0.412
Kidney disease	5.23 (1.11-24.77)	0.037
COPD	1.84 (0.99-3.42)	0.054
Asthma	6.49 (2.84-14.82)	<0.001
Tuberculosis	1.65 (1.12-2.43)	0.011
GERD	1.33 (0.99-1.77)	0.055
IBD	1.08 (0.33-3.55)	0.905
Rhinitis	1.75 (1.29-2.37)	<0.001
Smoking Hx (vs non-smoker)		0.322
Ex-smoker	0.85 (0.64-1.12)	0.244
Current smoker	1.12 (0.78-1.61)	0.554
FEV1, %	0.97 (0.96-0.98)	<0.001
Hemoglobin	0.97 (0.89-1.06)	0.537
CRP	3.39 (1.64-6.98)	0.001

Multivariate	Odds ratio (95% CI)	p-value
Female	1.41 (1.05-1.88)	0.021
Arthritis	1.54 (1.01-2.37)	0.047
Asthma	3.87 (1.54-9.71)	0.004
Tuberculosis	1.81 (1.17-2.79)	0.007
Rhinitis	1.73 (1.24-2.42)	0.001
FEV1, %	0.99 (0.983-0.998)	<0.001
CRP	3.06 (1.48-6.31)	0.002

Supplementary Figure 1. Factors related to the presence of respiratory symptoms in bronchiectasis
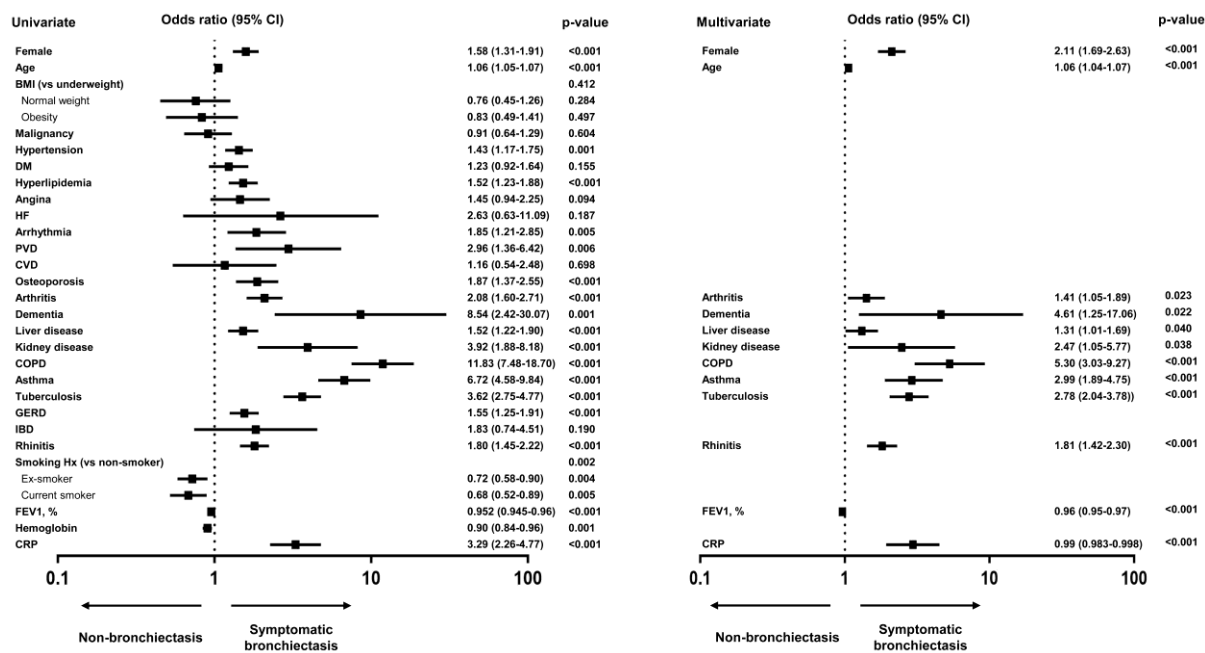
Abbreviations: BMI, body mass index; COPD, chronic obstructive pulmonary disease; CRP, C-reactive protein; CVD, cerebrovascular disease; DM, diabetes mellitus; FEV1, forced expiratory volume in 1 s; GERD, gastro-oesophageal reflux disease; HF, heart failure; Hg, haemoglobin; IBD, inflammatory bowel disease; PVD, peripheral vascular disease.

Supplementary Figure 2. Factors related to symptomatic bronchiectasis

Abbreviations: BMI, body mass index; COPD, chronic obstructive pulmonary disease; CRP, C-reactive protein; CVD, cerebrovascular disease; DM, diabetes mellitus; FEV1, forced expiratory volume in 1 s; GERD, gastro-oesophageal reflux disease; HF, heart failure; Hg, haemoglobin; IBD, inflammatory bowel disease; PVD, peripheral vascular disease.