Original Article

Features of osteoporosis in male patients with bronchiectasis, a cross-sectional study

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Background: Osteoporosis increases the burden and disease related adverse events of comorbidities in some chronic disease. The relationships between osteoporosis and bronchiectasis are not fully understood. This cross-sectional study explores the features of osteoporosis in male patients with bronchiectasis.

Methods: From January 2017 to December 2019, male patients (age >50 years) with stable bronchiectasis were included, as were normal subjects. Data on demographic characteristics and clinical features were collected.

Results: Totally, 108 male patients with bronchiectasis and 56 controls were analyzed. Osteoporosis was observed in 31.5% (34/108) of patients with bronchiectasis and 17.9% (10/56) of controls (P=0.001). The T-score negatively correlated with age (R=–0.235, P=0.014) and bronchiectasis severity index score (BSI; R=–0.336, P<0.001). BSI score ≥9 was a major factor associated with osteoporosis [odd ratio (OR) =4.52; 95% confidence interval (CI): 1.57–12.96; P=0.005]. Other factors associated with osteoporosis included body-mass index (BMI) <18.5 kg/m^2 (OR =3.44; 95% CI: 1.13–10.46; P=0.030), age ≥65 years (OR =2.87; 95% CI: 1.01–7.55; P=0.033), and a smoking history (OR =2.78; 95% CI: 1.04–7.47; P=0.042).

Conclusions: The prevalence of osteoporosis was higher in male bronchiectasis patients than that in controls. Factors including age, BMI, smoking history, and BSI were associated with osteoporosis. Early diagnosis and treatment might be of great value in prevention and management of osteoporosis in patients with bronchiectasis.

Keywords: Osteoporosis; bronchiectasis; comorbidities; bronchiectasis severity index (BSI); prevalence

Submitted Jul 11, 2022. Accepted for publication Feb 09, 2023. Published online Mar 15, 2023.
doi: 10.21037/jtd-22-887
View this article at: https://dx.doi.org/10.21037/jtd-22-887

Introduction

Bronchiectasis is a chronic airway inflammatory disease (1). Patients with bronchiectasis suffer from recurrent infection, decreased exercise ability, and deterioration of quality of life (2). Bronchiectasis is caused by many diseases, including bacterial infection, post tuberculosis, and due to airway obstruction, to name a few (3). The current treatment modality for stable bronchiectasis includes oral antibiotics and others to improve the healthy status and reduce the frequency of acute exacerbations (2,4). Some studies also reported the use of inhaled corticosteroids (ICS) in patients with bronchiectasis (5,6).

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Osteoporosis is a skeleton metabolism disease. Patients with osteoporosis have decreased bone mineral density (BMD) and increased risk of fractures (7). They suffer from pain, a reduced ability to exercise, and a poor quality of life, burdening both themselves and the society. Osteoporosis increases the burden and disease related adverse events of comorbidities in chronic diseases like coronary heart disease, chronic obstructive pulmonary disease (COPD), and hypertension (8-11). Studies reveal osteoporosis as a comorbidity in patients with bronchiectasis (12-14). The reported prevalence of osteoporosis varies in regions with a range of 5.9–30.1% in patients with bronchietasis (12,15). The mechanism that links bronchiectasis and osteoporosis is still unclear. Some characteristics of bronchiectasis, such as chronic inflammation, use of ICS, malnutrition, and a reduced ability to exercise, may lead to an increased prevalence of osteoporosis (16-19). To improve the quality of life, it might be of great value to understand the prevalence and related factors of osteoporosis in patients with bronchiectasis.

Boonen *et al.* reported a rate of vertebral fracture of 4.9% for male osteoporosis patients (over 50 years old) in 24 months (20). Osteoporosis in men may be ignored despite reports of a high yearly fracture rate (21,22). Moreover, the understanding of osteoporosis in men is mostly inferred from that of osteoporosis in women. As osteoporosis is common in postmenopausal women due to estrogen deficiency, the aetiology of osteoporosis in men is different from that in women. In women, many clinical studies have revealed the disease characteristics of post-menopausal osteoporosis, leading to the development of new drugs to manage osteoporosis and complications. Given the lower prevalence, osteoporosis in men is underestimated, and its diagnosis and treatment are insufficient (21-23). There is evidence that men with osteoporosis prone to more complications and higher fracture-related mortality than women (21,24). Therefore, clarifying the characteristics of male osteoporosis is the key to promote personalized treatment, which is critical for disease management.

At present, there were lacking studies on osteoporosis in male patients with bronchiectasis. The purpose of our study was to explore the characteristics of osteoporosis in male patients with bronchiectasis. We also aimed to explore the risk factors of osteoporosis present in these patients. We present the following article in accordance with the STROBE reporting checklist (available at https://jtd.amegroups.com/article/view/10.21037/jtd-22-887/rc).

Highlight box

Key findings

- Factors associated with osteoporosis in males with bronchiectasis include older, low BMI, a smoking history, and a high BSI score.

What is known and what is new?

- Osteoporosis is reported as a comorbidity in patients with bronchiectasis. Studies related to osteoporosis is insufficient in bronchiectasis patients who were not affected by estrogen deficiency.
- The prevalence of osteoporosis was high in male bronchiectasis patients. In these patients not affected by estrogen deficiency, our study found that factors associated with osteoporosis included older, low BMI, a smoking history, and a high BSI score.

What is the implication, and what should change now?

- Considering the high prevalence and the potential disease burden of osteoporosis, early diagnosis of osteoporosis might be of great value in bronchiectasis patients.

Methods

The cross-sectional study was conducted between January 2017 and December 2019. Male patients, over 50 years old, with stable bronchiectasis were admitted to this study from Guangzhou First People's Hospital. Bronchiectasis was diagnosed by high-resolution computed tomography (HRCT) as the presence of bronchial dilatation (4). Stable bronchiectasis refers to an absence of aggravation of symptoms or signs, or acute diseases at least 4 weeks before enrollment. Patients excluded from the study were those with an acute disease or uncontrolled chronic diseases including diabetes, hypertension, myocardial infarction, COPD, and malignancy. Male controls over 50 years old were admitted to our study. Controls subjects were matched for age group and selected from medical examination center in the same hospital. HRCT were performed in all controls, of whom with bronchiectasis were excluded. They suffered no acute diseases at least 4 weeks before enrollment. They did not have a history of uncontrolled chronic diseases including diabetes, hypertension, myocardial infarction, COPD, and malignancy. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Ethics Committee of Guangzhou First People's Hospital (No. K-2018-040-01) and informed consent was taken from all individual participants.

Dual-energy X-ray absorptiometry (Lunar iDXA, GE

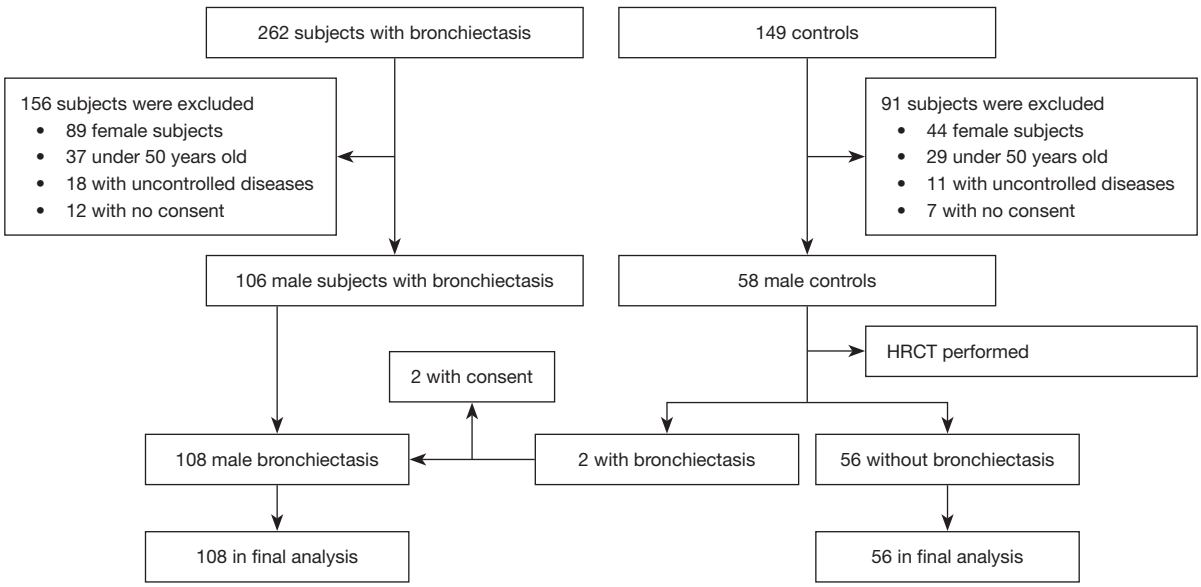

Figure 1 Flow chart of the study. HRCT, high resolution computed tomography.

Healthcare, Massachusetts, USA) was used to test patients' BMD of the Hip, the lumbar spine, and the femoral neck. The diagnosis of osteoporosis was based on BMD (25). In subjects age 50 and older, it is considered as normal BMD when T score ≥–1; osteopenia when –2.5 < T score < –1.0; and osteoporosis when T score ≤–2.5. The lowest T score were recorded and included in the final analysis.

All measurements were performed at the beginning of the study. Demographic and physical characteristics that were recorded included age, body-mass index (BMI), smoking history, alcohol history, exacerbations in previous year, and fracture history. Laboratory findings included sputum culture and assessment of serum levels of C-reactive protein (CRP) and calcium. The 6-minute walking distance (6-MWD) and lung function test were performed on the same day. Dyspnea was measured using the modified British medical research council questionnaire (mMRC). Bronchiectasis severity index (BSI) score was calculated to assess disease severity (26). The HRCT score was calculated to assess radiological severity using the modified Reiff score, with a possible range from 1 to 18 (27).

Statistical analysis

Normally distributed data were evaluated according to Shapiro-Wilk test. In the normal distribution, continuous variables were expressed as mean and standard deviation (SD). In the non-normal distribution, continuous variable were expressed as median and interquartile range (IQR). Independent *t*-test or Wilcoxon rank sum test was processed to test continuous variables. Counts and percentages were used to describe categorical variables. For categorical variables, Chi square test or Fisher exact test was processed. When a P value was 0.10 or less in univariable models, determinants were initially included in the multivariable model and then discarded via backward selection. P value was considered statistically significant if less than 0.05. SPSS 22.0 (IBM, Armonk, NY, USA) was used to process the data.

Results

Differences between patients with bronchiectasis and healthy controls

A total of 108 male patients with stable bronchiectasis and 56 healthy controls (*Figure 1*), average age 61.7 and 62.7 years, respectively (P=0.370), participated in this study (*Table 1*). Osteoporosis was found in 44 subjects, i.e., 34 bronchiectasis patients and 10 healthy controls (31.5% *vs.* 17.9%, P=0.001). The mean T score was lower in bronchiectasis patients than in healthy controls (–1.7 *vs.* –0.9, P<0.001). Compared to healthy controls, bronchiectasis patients were with lower BMI (21.6 *vs.* 23.0, P=0.007). They also had a less 6-MWD (472.8 *vs.* 562.3, P<0.001).

Table 1 Clinical characteristics of the bronchiectasis patients and controls

Clinical characteristics	Bronchiectasis (n=108)	Controls (n=56)	P value*
Age, mean (SD), years	61.7 (6.5)	62.7 (7.2)	0.370
Body-mass index, mean (SD), kg/m^2	21.6 (3.2)	23.0 (2.7)	0.007*
Smoking history, n (%)	37 (34.3)	17 (30.4)	0.240
Alcohol history, n (%)	36 (33.3)	12 (21.4)	0.112
6-MWD, mean (SD), meters	472.8 (92.4)	562.3 (98.1)	<0.001*
Treatment with ICS, n (%)	8 (7.4)	N/A	N/A
Daily ICS dose, median [IQR], μg#	320 [320]	N/A	N/A
ICS duration, median [IQR], months	34 [25]	N/A	N/A
Hip BMD T-score, mean (SD)	−0.8 (1.5)	−0.1 (1.5)	0.003*
Lumbar spine BMD T-score, mean (SD)	−0.9 (1.5)	−0.2 (1.5)	0.002*
Femoral neck BMD T-score, mean (SD)	−1.0 (1.6)	−0.5 (1.5)	0.003*
Lowest T-score, mean (SD)	−1.7 (1.3)	−0.9 (1.5)	<0.001*
Normal, n (%)	31 (28.7)	33 (58.9)	0.001*
Osteopenic, n (%)	43 (39.8)	13 (23.2)	
Osteoporotic, n (%)	34 (31.5)	10 (17.9)	

Smoking history: a history of smoking or ever smoking. #, different ICS were calculated into equivalent doses of budesonide; *, P<0.05. SD, standard deviation; 6-MWD, 6-minute walking distance; ICS, inhaled corticosteroids; N/A, not applicable; IQR, interquartile range; BMD, bone mineral density.

Differences between patients with osteoporosis and without

In comparison to those without osteoporosis, patients with osteoporosis were older (64.8 *vs.* 60.3 years, P=0.001; *Table 2*). They also had a lower BMI (20.4 *vs.* 22.2 kg/m^2, P=0.004) and a less 6-MWD (441.4 *vs.* 487.3 meters, P=0.016). The disease severity evaluated by BSI score was more serious in patients with osteoporosis (9.0 *vs.* 4.0, P<0.001). They also suffered more acute exacerbations (1.0 *vs.* 0, P=0.023). The sputum culture (12 *vs.* 14, P=0.065) were not significantly different between the two groups. There was no difference in the use of ICS between the two groups (3 *vs.* 5, P>0.999).

Factors associated with osteoporosis

All possible variables associated with osteoporosis were assessed by univariable analysis. These variables comprised age, BMI, smoking history, 6-MWD, mMRC score, sputum culture results, exacerbations in the previous year, and BSI score (*Table 3*). Variables included in the multivariable analysis were age ≥65 years, BMI <18.5 kg/m^2, smoking history, 6-MWD ≤425 meters, mMRC ≥4, BSI score ≥9, and positive bacterial culture. In the multiple regression model (*Table 4*), BSI score ≥9 was a major factor associated with osteoporosis [odd ratio (OR) =4.52; 95% confidence interval (CI): 1.57–12.96; P=0.005]. Other factors associated with osteoporosis included BMI <18.5 kg/m^2 (OR =3.44; 95% CI: 1.13–10.46; P=0.030), age ≥65 years (OR =2.87; 95% CI: 1.01–7.55; P=0.033), and a smoking history (OR =2.78; 95% CI: 1.04–7.47; P=0.042).

Correlations between T score and others

T score associated with the disease severity evaluated by BSI score (R=−0.336, P<0.001; *Figure 2*). It was also consistent with physical exercise ability, as it positively correlated with FEV1 % pred (R=0.197, P=0.041) and 6-MWD (R=0.331, P<0.001). Other factors correlated with T score included age (R=−0.235, P=0.014) and BMI (R=0.225, P=0.008). There was no correlation between T score and HRCT score.

Discussion

Our study illustrated the prevalence of osteoporosis in

Table 2 Differences between bronchiectasis patients with osteoporosis and those without

Clinical characteristics	With osteoporosis (n=34)	Without osteoporosis (n=74)	P value*
Age, mean (SD), years	64.8 (6.2)	60.3 (6.2)	0.001*
Body-mass index, mean (SD), kg/m^2	20.4 (3.3)	22.2 (2.9)	0.004*
Smoking history, n (%)	18 (55.9)	19 (25.7)	0.006*
Alcohol history, n (%)	12 (35.3)	24 (32.4)	0.232
6-MWD, mean (SD), meters	441.4 (81.2)	487.3 (94.2)	0.016*
mMRC score, median (IQR)	2.5 (2.3)	1.5 (2.0)	0.019*
C-reactive protein >6.0 mg/dL, n (%)	11 (32.4)	16 (21.6)	0.232
Serum calcium, mean (SD), mmol/L	2.42 (0.29)	2.39 (0.26)	0.700
HRCT score, median (IQR)	7.0 (4.3)	7.0 (6.0)	0.958
AE in previous year, median (IQR)	1.0 (3.0)	0 (2.0)	0.023*
Fracture history, n (%)	1 (2.9)	1 (1.4)	>0.999
BSI, median (IQR)	9.0 (7.5)	4.0 (2.0)	<0.001*
Positive bacterial culture, n (%)	12 (35.3)	14 (18.9)	0.065
Pulmonary function, mean (SD)			
FEV1 % pred	63.5 (13.0)	68.6 (12.6)	0.055
FEV1/FVC % pred	73.7 (8.8)	75.4 (7.9)	0.307
Treatment, n (%)			
Mucoactive treatment	14 (41.2)	27 (36.5)	0.641
Theophylline	9 (26.5)	21 (28.4)	0.837
Long-term oral antibiotics	7 (20.6)	10 (13.5)	0.348
Inhaled corticosteroids	3 (8.8)	5 (6.8)	>0.999
Long β2-receptor agonists	3 (8.8)	4 (5.4)	>0.999

Smoking history: a history of smoking or ever smoking. *, P<0.05. SD, standard deviation; 6-MWD, 6-minute walking distance; mMRC, modified British medical research council questionnaire; IQR, interquartile range; HRCT, high resolution computed tomography; AE, acute exacerbation; BSI, bronchiectasis severity index; FEV1, forced expiratory volume in one second; FVC, forced vital capacity.

male bronchiectasis patients. The prevalence was 31.5%, significantly higher than that in healthy controls. The present study revealed that BMD was low in patients with bronchiectasis. Previous studies have indicated that potential factors might lead to low BMD, including poor nutritional status, reduced physical activity, chronic inflammation, and glucocorticoid use (18,19,28,29), which overlap with the characteristic features associated with bronchiectasis. In our study, patients with bronchiectasis exhibited low BMI and a reduced ability to exercise compared to healthy controls. This indicates that bronchiectasis might increase the risk of osteoporosis.

Several studies reported osteoporosis as a comorbidity in patients with bronchiectasis (12-14). Choi *et al.* found that the prevalence of osteoporosis in bronchiectasis was higher than that in COPD (13). The prevalence of osteoporosis varies in regions or age. Lee *et al.* reported the prevalence was highest in Australians (23.1%), followed by Koreans (11.7%), Europeans (7.4%) and Indians (5.9%) (14). In the study performed by Diehl *et al.*, 30.1% bronchiectasis patients were with osteoporosis in America (15). Our study found that osteoporosis was present in 31.5% of male patients in South China. The prevalence of osteoporosis increases with age. In the study by Contreras-Bolívar *et al.*, osteoporosis was present in 38.9% patients over 65 years old, 18.7% patents aged 45–65, and 2.7% under 45 years old (30).

Table 3 Determinants associated with osteoporosis in bronchiectasis patients

Determinants	With osteoporosis (n=34)	Without osteoporosis (n=74)	Univariable models, OR (95% CI)	P value
Age ≥65 years	20	22	3.38 (1.45–7.87)	0.005*
BMI <18.5 kg/m^2	14	10	4.48 (1.73–11.63)	0.002*
Smoking history	18	19	3.26 (1.39–7.63)	0.007*
6-MWD, meters				
≤425	16	20	2.40 (1.03–5.60)	0.043*
426–550	15	36	0.83 (0.37–1.89)	0.661
≥550	3	18	0.30 (0.08–1.10)	0.070
mMRC ≥4	12	13	2.56 (1.02–6.45)	0.046*
BSI score				
0–4	4	13	0.63 (0.19–2.08)	0.445
5–8	12	51	0.24 (0.10–0.58)	0.001
>9	18	10	7.20 (2.79–18.57)	<0.001*
AE ≥2/year	14	20	1.89 (0.80–4.44)	0.144
Positive bacterial culture	12	14	2.34 (0.94–5.82)	0.068*
FEV1 % pred				
<50	5	8	1.42 (0.43–4.72)	0.565
50–80	23	49	1.07 (0.45–2.53)	0.884
≥80	6	17	0.72 (0.26–2.02)	0.531

Smoking history: a history of smoking or ever smoking. *, variables included in the multivariable analysis. OR, odd ratio; CI, confidence interval; BMI, body-mass index; 6-MWD, 6-minute walking distance; mMRC, modified British medical research council questionnaire; BSI, bronchiectasis severity index; AE, acute exacerbation; FEV1, forced expiratory volume in one second.

Table 4 Multivariable analysis of determinants associated with osteoporosis in bronchiectasis patients

Determinants	OR	95% CI	P value
Age ≥65 years	2.87	1.01–7.55	0.033
BMI <18.5 kg/m^2	3.44	1.13–10.46	0.030
Smoking history	2.78	1.04–7.47	0.042
BSI score ≥9	4.52	1.57–12.96	0.005

Smoking history: a history of smoking or ever smoking. OR, odd ratio; CI, confidence interval; BMI, body-mass index; BSI, bronchiectasis severity index.

To further investigate the factors related to osteoporosis, we conducted a multivariable analysis. We found that factors associated with osteoporosis included age, low BMI, smoking history, and high BSI score, consistent with results of previous studies (30,31). This suggests that the comorbidity of osteoporosis and bronchiectasis may be linked to a variety of mechanisms. It might also provide us with some potential interventions, such as enhancing nutrition, increasing physical activity, and smoking cessation. In fact, some of these measures have proven effective in treating osteoporosis (7,25).

In our study, the treatment for stable bronchiectasis included ICS and others. ICS are widely used in respiratory inflammatory diseases including asthma and COPD. They

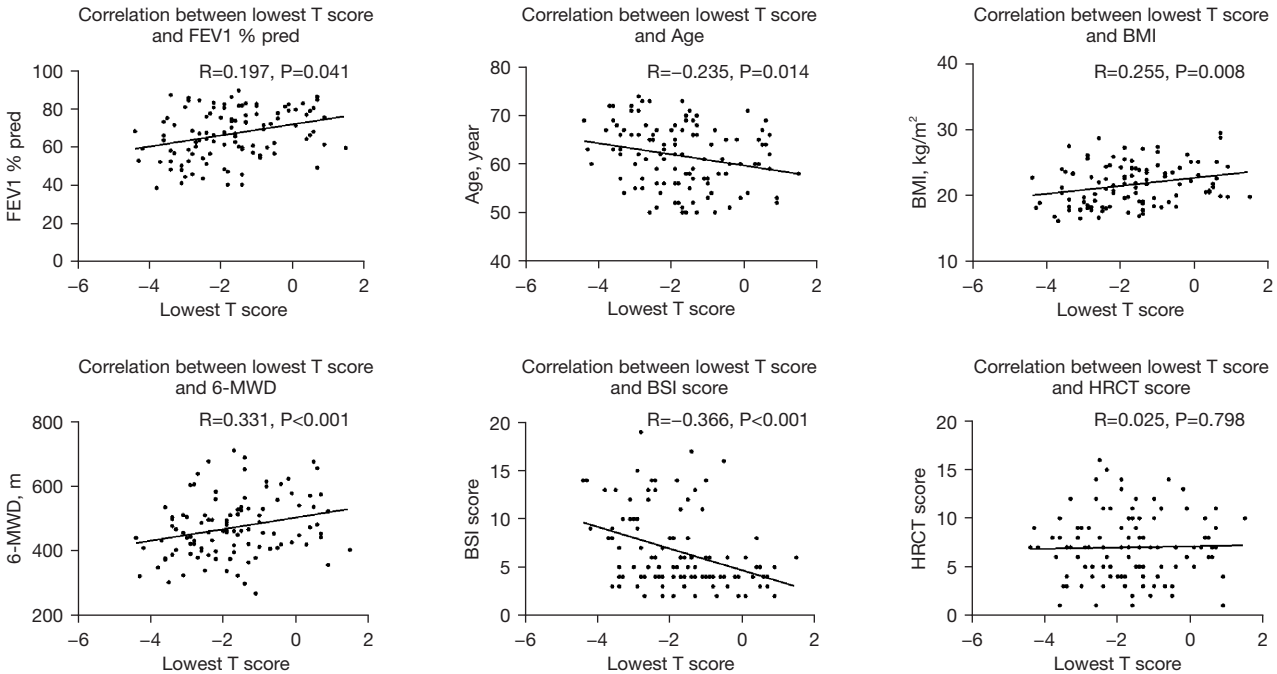

Figure 2 Correlations between the lowest T score and clinical characteristics. The lowest T score: the lowest value of BMD among hip, lumbar spine, and femoral. FEV1, forced expiratory volume in one second; BMI, body-mass index; 6-MWD, 6-minute walking distance; BSI, bronchiectasis severity index; HRCT, high resolution computed tomography; BMD, bone mineral density.

were also reported in the treatment of bronchiectasis in previous studies (5,6). Osteoporosis induced by glucocorticoids remains common and complex (32). Whether ICS can lead to osteoporosis remains controversial (32,33). Previous studies showed that osteoporosis induced by glucocorticoids is related to the daily dosages of glucocorticoids (32). In our study, the median daily doses of ICS were about 320 mg/day, and the median duration were 37 months. The daily dose of ICS were defined as low dose according to the standard of American College of Rheumatology (32). The low daily doses might be the reason why there was no relationship between ICS and low BMD.

Comorbidities of chronic diseases are common and increase with age. In osteoporosis, the comorbidities include cardiovascular disease, hypertension, diabetes mellitus, COPD, and others (34,35). Osteoporosis increases the burden of comorbidities in chronic diseases (8). It also increases disease related adverse events and mortality. Similar with previous studies (31,32), we reveal osteoporosis as a comorbidity of bronchiectasis. Osteoporosis and bronchiectasis show overlapping characteristics, including low BMI and a reduced ability to exercise. Bronchiectasis patients with osteoporosis have more severe disease and decreased exercise ability. Therefore, actions should be taken to prevent or treat osteoporosis in bronchiectasis patients. Despite its higher prevalence, osteoporosis in male patients is easily ignored (22). Some patients with osteoporosis may be asymptomatic or lack typical symptoms (36,37) that lead to the misdiagnosis of osteoporosis. Therefore, studies on the relationships between osteoporosis and bronchiectasis are needed. To benefit the patients with associated factors, early screening and diagnosis might be reasonable and appropriate.

Chalmers *et al.* provided a clinical prediction tool named BSI to assess the severity of the disease (26). It performed well in predicting mortality and hospitalization. A high BSI score indicates a more severe disease and a worse prognosis. The BSI score of patients with osteoporosis is high, which means a higher risk of mortality and hospitalization in these patients. Therefore, more attention should be paid to them.

Our study has the following limitations. First, the single-center nature limits the scope of the conclusion. Second, the sample size in this study is small. Third, the nature of the cross-sectional study makes it difficult to elucidate the causal relationship between bronchiectasis and osteoporosis. Hence, more intervention studies, with large sample size,

should be performed to confirm the causal relationships and clarify the underlying mechanisms of association between bronchiectasis and osteoporosis.

Conclusions

The prevalence of osteoporosis in male patients with bronchiectasis was high. Factors associated with osteoporosis in males with bronchiectasis include older, low BMI, a smoking history, and a high BSI score. These data provides valuable insights into osteoporosis associated with bronchiectasis in males.

Acknowledgments

Funding: This work was supported by the Guangzhou Municipal Health Commission (Nos. 20191A010014, 201704020105).

Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://jtd.amegroups.com/article/view/10.21037/jtd-22-887/rc

Data Sharing Statement: Available at https://jtd.amegroups.com/article/view/10.21037/jtd-22-887/dss

Peer Review File: Available at https://jtd.amegroups.com/article/view/10.21037/jtd-22-887/prf

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://jtd.amegroups.com/article/view/10.21037/jtd-22-887/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Ethics Committee of Guangzhou First People's Hospital (No. K-2018-040-01) and informed consent was taken from all individual participants.

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Cite this article as: Xu G, Zhao J, Liu F, Cai D, Feng C, Wang L, Zeng Y, Liu Y, Wu S, Chen Y, Ma W. Features of osteoporosis in male patients with bronchiectasis, a cross-sectional study. J Thorac Dis 2023;15(3):1177-1185. doi: 10.21037/jtd-22-887