

# Bronchiectasis as a Comorbidity of Chronic Obstructive Pulmonary Disease: Implications and Future Research

Ya-Hong Chen, Yong-Chang Sun

Department of Respiratory and Critical Care Medicine, Peking University Third Hospital, Beijing 100191, China

**Key words:** Bronchiectasis; Chronic Obstructive Pulmonary Disease; Comorbidity; Computed Tomography

Chronic obstructive pulmonary disease (COPD) is a heterogeneous disease with high morbidity and mortality.<sup>[1]</sup> With increasing use of computed tomography in the assessment of patients with COPD, the presence of previously unrecognized radiological bronchiectasis is being identified.<sup>[2]</sup> Accumulating evidence shows that bronchiectasis has an important impact on the natural history of COPD. Moderate-severe COPD with comorbid bronchiectasis has more severe symptoms, higher frequency of exacerbations, and increased mortality.<sup>[3]</sup> Given the prognostic implications of bronchiectasis in COPD, its detection could serve as a guide to better management and eventually improved survival.<sup>[1]</sup> Therefore, bronchiectasis was proposed as a comorbidity of COPD by Global Initiative for Chronic Obstructive Lung Disease (GOLD) updated 2014.

The prevalence of bronchiectasis in COPD is highly varied, mostly due to patient inclusion criteria such as different GOLD stages, and different definitions of bronchiectasis. Evaluation of COPD Longitudinally to Identify Predictive Surrogate Endpoints revealed a prevalence of bronchiectasis in 4% of COPD patients with all GOLD stages,<sup>[4]</sup> but much higher prevalence of bronchiectasis in COPD patients was reported, ranging from 20% to 58% in both primary and secondary care.<sup>[2,5,6]</sup> In a study from Spain, bronchiectasis was found in 57.6% of patients with moderate to severe COPD,<sup>[7]</sup> while in a Turkish study the prevalence was 33%.<sup>[8]</sup> A recent study from the UK showed that 69% of COPD patients with acute exacerbation had some evidence of bronchiectasis, mostly minor or mild in severity; minor 40%, mild 29%, moderate 22%, and severe 8%.<sup>[9]</sup> A nationwide diagnosis-related groups hospital statistics for the years

2005–2011 in Germany indicated that COPD was found in up to 39.2% of hospitalizations with bronchiectasis as the primary diagnosis.<sup>[10]</sup> Recent studies in Chinese patients showed that 34.7% (311/896)<sup>[11]</sup> and 45.8% (87/190)<sup>[12]</sup> of stable COPD patients were coexistent with bronchiectasis revealed by lung high-resolution computed tomography (HRCT).

COPD with comorbid bronchiectasis presents an intriguing model for understanding the complexity of the disease. Some studies found that bronchiectasis was more often in older and male COPD patients with lower prevalence of smokers and smoking index.<sup>[11,13]</sup> These patients tended to have a longer duration of symptoms, more purulent sputum expectoration, and poorer nutritional status.<sup>[9,11,14]</sup> Bronchiectasis may also increase the risk of community-acquired pneumonia in COPD patients.<sup>[15]</sup> Patients with increasing severity of bronchiectasis were independently associated with the number of sputum samples examined, isolation of *Pseudomonas aeruginosa* and atypical mycobacteria, and persistent infection,<sup>[9]</sup> although *Haemophilus influenzae* was the most frequently isolated microorganism in another study.<sup>[5]</sup> The presence of bronchiectasis was associated with increased airway inflammation, such as higher sputum levels of

**Address for correspondence:** Prof. Yong-Chang Sun, Department of Respiratory and Critical Care Medicine, Peking University Third Hospital, Beijing 100191, China  
E-Mail: suny@bjmu.edu.cn

This is an open access article distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 3.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as the author is credited and the new creations are licensed under the identical terms.

© 2016 Chinese Medical Journal | Produced by Wolters Kluwer - Medknow

**Received:** 02-07-2016 **Edited by:** Li-Shao Guo

**How to cite this article:** Chen YH, Sun YC. Bronchiectasis as a Comorbidity of Chronic Obstructive Pulmonary Disease: Implications and Future Research. Chin Med J 2016;129:2017-9.

## Access this article online

### Quick Response Code:



**Website:**  
www.cmj.org

**DOI:**  
10.4103/0366-6999.189071

interleukin (IL-6) and IL-8.<sup>[16]</sup> Systemic inflammatory markers, including CRP and fibrinogen, and the serum level of total IgE were significantly elevated in COPD patients with bronchiectasis.<sup>[5,11,12,16]</sup>

The imaging features of bronchiectasis in COPD were consistent from different studies, mostly tubular and varicose in appearance, mild to moderate in severity, while cystic changes are uncommon.<sup>[1]</sup> Gatheral *et al.* found that increasing severity of bronchiectasis was strongly associated with increasing severity of bronchial wall thickening, but not emphysema.<sup>[9]</sup> Their findings suggest there are two different phenotypes within the phenotypes of COPD with bronchiectasis. One is the presence of mild bronchiectasis with severe emphysema (the patients may suffer from dyspnea and lower exercise tolerance), and the other is a diffuse bronchiectatic pattern associated with bronchial wall thickening (the patients may present with daily sputum production and frequent exacerbations). Although several radiological scores such as the Smith and the Bhalla *et al.* scores are being used for evaluation of bronchiectasis, and there is also an online calculation tool for bronchiectasis severity index ([www.bronchiectasisseverity.com](http://www.bronchiectasisseverity.com)), these systems still need to be tested in well-designed prospective studies in patients with and without COPD.<sup>[8,9,17]</sup>

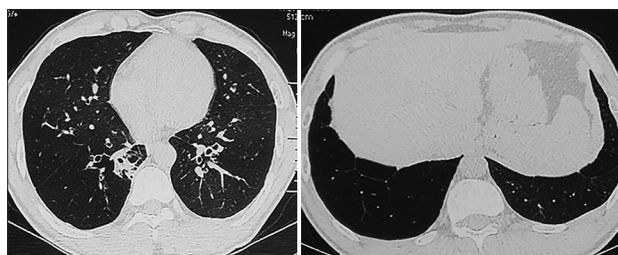
Bronchiectasis in COPD may indicate a poor prognosis, especially in terms of exacerbation frequency and mortality.<sup>[3]</sup> Mao *et al.* found that COPD patients with bronchiectasis were 1.77 times more likely to die compared with those without bronchiectasis after 5 years of follow-up.<sup>[11]</sup> Increasing severity of bronchiectasis in COPD patients was independently associated with annual respiratory admissions and annual inpatient days for respiratory causes.<sup>[5]</sup> It was an independent risk factor for all-cause mortality in patients with moderate-to-severe COPD.<sup>[18]</sup>

It needs to be noted that, in patients with a primary diagnosis of COPD, the finding of radiological bronchiectasis may have different implications. Bronchiectasis may be a consequence of COPD, as in most cases, likely through “vicious cycle” of airway inflammation and repeated infections [Figure 1]. Another scenario is that bronchiectasis and COPD are two independent disease entities (overlap), a less common but not rare situation [Figure 2]. A history of recurrent respiratory infections before the age of 40 years in a smoker, combined with HRCT patterns, may help making the diagnosis of this overlap, although it may be difficult to distinguish the two entities in some cases.

There is no consensus about the management strategies for COPD coexistent with bronchiectasis.<sup>[1]</sup> Treatments beneficial in COPD may not be so in bronchiectasis and vice versa. Inhaled corticosteroids are widely used in COPD but not recommended in most patients with bronchiectasis. GOLD strategy suggested that treatment



**Figure 1:** Radiological bronchiectasis in chronic obstructive pulmonary disease. A 69-year-old male patient with chronic cough, expectoration for 20 years, exertional dyspnea for 5 years. He had smoked for 40 years with one pack per day. Postbronchodilator forced expiratory volume in 1 s/forced vital capacity 30% and forced expiratory volume in 1 s percentage 26%. Chest computed tomography showed lower lobe bronchial wall thickening, mild tubular bronchiectasis and emphysema.



**Figure 2:** Chronic obstructive pulmonary disease and bronchiectasis overlap. A 45-year-old male patient with exertional dyspnea for 3 years. He had had “pneumonia” in his twenties and had cough and mild hemoptysis for several times before. He smoked for 20 years with 30–40 cigarettes/day. Postbronchodilator forced expiratory volume in 1 s/forced vital capacity 49% and forced expiratory volume in 1 s percentage 52%. Bronchiectasis and emphysema in both lower lobes on chest computed tomography.

of bronchiectasis in patients with COPD should be along conventional lines for bronchiectasis with the addition of usual COPD strategies where indicated. Whether prevention of exacerbations requires more long-term use of oral or inhaled antibiotics rather than bronchodilators or inhaled, corticosteroid therapy remains unknown.<sup>[14]</sup> Azithromycin maintenance treatment in noncystic fibrosis bronchiectasis improved the quality of life and decreased exacerbations.<sup>[19]</sup> Extrapolating this to COPD-associated bronchiectasis needs further investigation.

## REFERENCES

1. Global Initiative for Chronic Obstructive Lung Disease (GOLD); 2016. Available from: [www.goldcopd.org](http://www.goldcopd.org). [Last accessed on 2016 Jun 18].
2. O'Brien C, Guest PJ, Hill SL, Stockley RA. Physiological and radiological characterisation of patients diagnosed with chronic obstructive pulmonary disease in primary care. *Thorax* 2000;55:635-42. doi:10.1136/thorax.55.8.635
3. Du Q, Jin J, Liu X, Sun Y. Bronchiectasis as a comorbidity of chronic obstructive pulmonary disease: A systematic review and meta-analysis.

- PLoS One 2016;11:e0150532. doi: 10.1371/journal.pone.0150532.
4. Agusti A, Calverley PM, Celli B, Coxson HO, Edwards LD, Lomas DA, *et al.* Characterisation of COPD heterogeneity in the ECLIPSE cohort. *Respir Res* 2010;11:122. doi: 10.1186/1465-9921-11-122.
  5. Martínez-García MÁ, Soler-Cataluña JJ, Donat Sanz Y, Catalán Serra P, Agramunt Lerma M, Ballestín Vicente J, *et al.* Factors associated with bronchiectasis in patients with COPD. *Chest* 2011;140:1130-7. doi: 10.1378/chest.10-1758.
  6. Bafadhel M, Umar I, Gupta S, Raj JV, Vara DD, Entwisle JJ, *et al.* The role of CT scanning in multidimensional phenotyping of COPD. *Chest* 2011;140:634-42. doi: 10.1378/chest.10-3007.
  7. Blasi F, Chalmers JD, Aliberti S. COPD and bronchiectasis: Phenotype, endotype or co-morbidity? *COPD* 2014;11:603-4. doi: 10.3109/15412555.2014.974744.
  8. Smith IE, Jurriaans E, Diederich S, Ali N, Shneerson JM, Flower CD. Chronic sputum production: correlations between clinical features and findings on high resolution computed tomographic scanning of the chest. *Thorax* 1996;51:914-8. doi: 10.1136/thx.51.9.914.
  9. Gatheral T, Kumar N, Sansom B, Lai D, Nair A, Vlahos I, *et al.* COPD-related bronchiectasis; independent impact on disease course and outcomes. *COPD* 2014;11:605-14. doi: 10.3109/15412555.2014.922174.
  10. Ringshausen FC, de Roux A, Pletz MW, Hämäläinen N, Welte T, Rademacher J. Bronchiectasis-associated hospitalizations in Germany, 2005-2011: A population-based study of disease burden and trends. *PLoS One* 2013;8:e71109. doi: 10.1371/journal.pone.0071109.
  11. Mao B, Lu HW, Li MH, Fan LC, Yang JW, Miao XY, *et al.* The existence of bronchiectasis predicts worse prognosis in patients with COPD. *Sci Rep* 2015;5:10961. doi: 10.1038/srep10961.
  12. Jin J, Yu W, Li S, Lu L, Liu X, Sun Y. Factors associated with bronchiectasis in patients with moderate severe chronic obstructive pulmonary disease. *Medicine (Baltimore)* 2016;95:e4219. doi:10.1097/MD.00000000000004219.
  13. Ni Y, Shi G, Yu Y, Hao J, Chen T, Song H. Clinical characteristics of patients with chronic obstructive pulmonary disease with comorbid bronchiectasis: A systemic review and meta-analysis. *Int J Chron Obstruct Pulmon Dis* 2015;10:1465-75. doi: 10.2147/COPD.S83910.
  14. Hurst JR, Elborn JS, De Soyza A; BRONCH-UK Consortium. COPD-bronchiectasis overlap syndrome. *Eur Respir J* 2015;45:310-3. doi: 10.1183/09031936.00170014.
  15. Lin SH, Ji BC, Shih YM, Chen CH, Chan PC, Chang YJ, *et al.* Comorbid pulmonary disease and risk of community-acquired pneumonia in COPD patients. *Int J Tuberc Lung Dis* 2013;17:1638-44. doi: 10.5588/ijtld.13.0330.
  16. Patel IS, Vlahos I, Wilkinson TM, Lloyd-Owen SJ, Donaldson GC, Wilks M, *et al.* Bronchiectasis, exacerbation indices, and inflammation in chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 2004;170:400-7. doi: 10.1164/rccm.200305-648OC.
  17. Bhalla M, Turcios N, Aponte V, Jenkins M, Leitman BS, McCauley DI, *et al.* Cystic fibrosis: Scoring system with thin-section CT. *Radiology* 1991;179:783-8. doi: 10.1148/radiology.179.3.2027992.
  18. Martínez-García MA, de la Rosa Carrillo D, Soler-Cataluña JJ, Donat-Sanz Y, Serra PC, Lerma MA, *et al.* Prognostic value of bronchiectasis in patients with moderate-to-severe chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 2013;187:823-31. doi: 10.1164/rccm.201208-1518OC.
  19. Altenburg J, de Graaff CS, Stienstra Y, Sloos JH, van Haren EH, Koppers RJ, *et al.* Effect of azithromycin maintenance treatment on infectious exacerbations among patients with non-cystic fibrosis bronchiectasis: The BAT randomized controlled trial. *JAMA* 2013;309:1251-9. doi: 10.1001/jama.2013.1937.