Focus on Bronchiectasis/COPD Overlap: An Under-Recognized But Critically Important Condition

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Former "Orphan Disease" Grows in Recognition

Non-cystic fibrosis bronchiectasis (NCFB)[1] is an important disease that remains largely unknown. Once thought to be a rare "orphan" condition—merely the aftermath of infectious diseases that are now readily treated—emerging evidence now shows that NCFB is far more common than originally believed and is closely associated with another better known major respiratory health threat—COPD.[3] Defined as the thickening and enlargement of the airways resulting from chronic inflammation, bronchiectasis damages normal airway clearance mechanisms and results in the accumulation of excess secretions. As a result, patients face chronic cough, excess sputum production, and a recurring cycle of hospitalizations.[2] Appropriate diagnosis and treatment are key to improving quality of life and reducing the need for expensive medical care. Specifically, airway clearance therapy directly addresses the problem of purulent sputum retained in the airways and by "emptying the Petri dish" can help to reduce the risk of future exacerbations without risking exposure to the negative effects of long-term or rotating antibiotics.[4]

Bronchiectasis has rightly been called an "orphan with many parents"[5] because it is the late stage of a number of pulmonary diseases and a disease with a pulmonary component. Among these are infectious diseases such as tuberculosis and nontuberculous mycobacteria (NTM), severe lower respiratory tract infections, chronic aspiration of gastric contents, inhaled foreign objects, and genetic conditions such as cystic fibrosis, alpha-1 antitrypsin deficiency, and primary ciliary dyskinesia. Autoimmune disorders, such as rheumatoid arthritis, sarcoidosis, and granulomatosis with polyangiitis have also been linked to NCFB. Additionally, diseases that affect the immune system, for instance, HIV and common variable immunodeficiency, may lead to chronic or recurrent infections resulting in bronchiectasis in the susceptible host. Despite considerable effort, no identifiable cause is found in 30-50 percent of cases.[6] Once the airways are distended and ciliary transport damaged, a "vicious cycle" will often begin: mucus is retained in the airways becoming a site for bacterial colonization; this in turn provokes an inflammatory response that, if it becomes chronic, causes additional damage.[7] The progression may be slow or swift depending on a number of factors, but once begun, the patient faces an ongoing cycle of recurring infections, resulting in reduction in lung function and quality of life, and the likelihood of ongoing medical care.

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Recognizing Bronchiectasis[2]	• Chronic productive cough • Chronic mucus hypersecretion • Chronic antibiotic use • Frequent hospitalizations • Reduced quality of life

The process is irreversible and there is no known cure—fortunately, appropriate care can substantially improve the lives of affected patients.

While bronchiectasis may be found at any age, it is most often a disease of middle-age and older. The profile of a patient with bronchiectasis is in many ways similar to that of chronic bronchitis.[8] Affected patients often have a chronic productive cough for more than three months of the year along with copious sputum production that is difficult to fully clear. They may have multiple unsuccessful attempts with airway clearance techniques. As a result, their quality of life is often poor due to cough, shortness of breath, and fatigue.[9] Typically, by the time they are diagnosed, patients will have received multiple courses of antibiotics punctuated with frequent exacerbations, often requiring hospitalizations. The gold standard for bronchiectasis diagnosis is the high-resolution CT scan, which can show varying degrees of bronchial wall thickening and dilation of the airways.[2] It is important to note that patients may have radiographic evidence of bronchiectasis but show no symptoms; indeed, they may be stable in the condition for years. However, the airway damage may develop into significant symptoms at any time given the appropriate trigger.

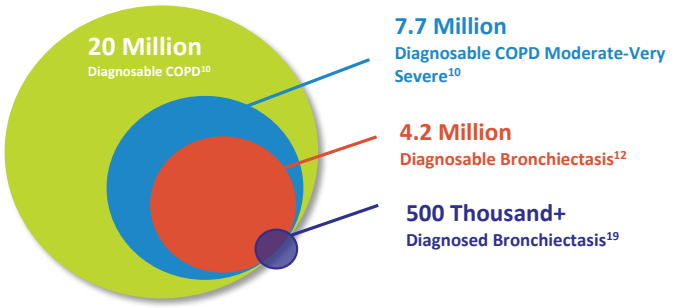

Figure 1 Estimates of the prevalence of diagnosable COPD, diagnosable bronchiectasis, and diagnosed bronchiectasis.

The COPD Connection

Today a large and growing number of patients with COPD also have been diagnosed with bronchiectasis. More than 20 million people in the US live with COPD[10]; of these more than four million patients may be affected by bronchiectasis, yet only about 500,000 have been diagnosed with the condition, a number rising at an annual rate of 8.7 percent, most likely due to increased awareness and surveillance of the disease.[11] A recent meta-analysis of available data found that over 50 percent of patients with moderate-to-severe COPD also have evidence of bronchiectasis.[12] The causes, treatments, and relationships between comorbid conditions within COPD are controversial and a subject of intensive research. The evidence has led some researchers to propose a "COPD-bronchiectasis overlap syndrome,"[13] while this concept is still debatable.[14] Nonetheless, COPD may be considered a possible cause of bronchiectasis[15], and bronchiectasis is certainly an exacerbating factor in COPD.[16]

It has long been known that COPD patients often experience a cycle of exacerbation followed by temporary recovery. More recently, a study by Suissa et al has shown that exacerbations follow a distinct pattern: after the first event, each subsequent exacerbation follows within a shorter time and tends to be more severe than the last.[17] In this study, risk of a severe exacerbation increased three times after the first exacerbation, and 24 times after the tenth. This finding emphasizes the importance of early intervention in recognizing and treating the disease, particularly when combined with bronchiectasis. A recent meta-analysis by Du et al, of 5,329 COPD patients found a greatly increased exacerbation risk due to comorbid COPD with bronchiectasis compared to COPD alone.[18] Moreover, the risk of exacerbations rose almost two times higher, colonization of the lungs four times higher, severe airway obstruction 30 percent higher, and mortality two times higher. It is not surprising that such elevated risks are also associated with higher healthcare costs. A recent study found that compared to COPD alone, COPD + bronchiectasis resulted in 32 percent more hospitalizations and 27 percent higher hospitalization costs.[19] With these issues at stake, there is a clear need to focus on these at-risk patients.

New Guidelines for Treatment

Given that a sizable fraction of COPD patients who are troubled with excess sputum production may harbor bronchiectasis, it seems prudent to evaluate for the condition using a high-resolution CT scan.

Along with bronchodilators and mucolytics, bronchiectasis patients are sometimes treated with long-term antibiotics such as macrolides. While useful in addressing severe exacerbations, long-term use of such drugs raises the risk of antibiotic resistance and side effects such as cardiac complications and hearing loss.[4] Additionally, a recent study found that bronchiectasis patients are frequently colonized by antibiotic-resistant pathogens.[20] Among NCFB patients who received testing, 69 percent had a positive sputum culture; of these, 20 percent were multiply-drug-resistant organisms (MDR) that are also deemed "urgent" or "serious" threats according to the CDC.[21] MDR organisms are not only difficult to eradicate, but pose a long-term threat to antibiotic stewardship. Therefore, any measure that can reduce the bacterial load in patients' lungs can be valuable in breaking the vicious cycle of infection that such patients face.[15]

New treatment guidelines for bronchiectasis have recently been released by the European Respiratory Society (ERS).[4] This important report contains a broad survey of available evidence, including drug treatments and a discussion of airway clearance. The ERS guidelines state that "before considering the prescription of long-term antibiotics, general aspects of bronchiectasis management need to be optimized such as airway clearance." The list of airway clearance methods includes pulmonary physiotherapy, oscillating positive expiratory pressure (PEP) devices and high-frequency chest wall oscillation (HFCWO or "vest therapy"). As a non-pharmacological method for clearing sputum, airway clearance devices are effective, readily accepted by patients, and support antibiotic stewardship.[22] Aside from directly addressing the needs of symptomatic patients, airway clearance has been shown to reduce the risk of exacerbations[23] and enhance quality of life.[24] A database housing the self-reported outcomes of more than 10,000 bronchiectasis patients shows that after the initiation of vest therapy (inCourage® System, RespirTech, St Paul, Minn.), antibiotic use was reduced by 15 percent and hospitalizations by 59 percent (Figure 2).[25]

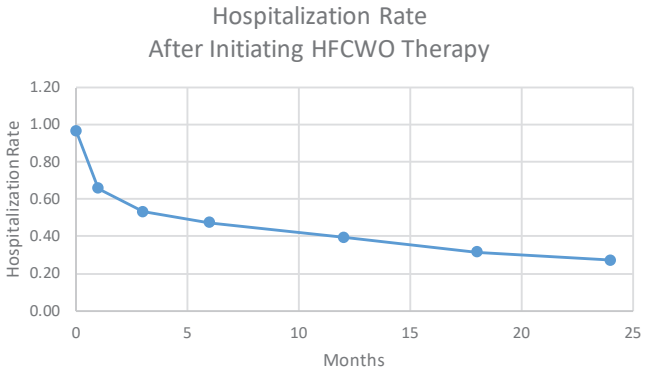

Figure 2 Reduction in hospitalization rate after initiating HFCWO therapy for over 10,000 patients with bronchiectasis.[25]

In summary, bronchiectasis is a progressive disease of the lungs that facilitates a cycle of exacerbation for affected patients. Under-recognized until recently, it is far more common than previously believed. Combined with COPD, bronchiectasis adds substantial risk of hospitalization and early death. Once bronchiectasis is identified, although irreversible, it can be managed by treating the underlying cause (if identified) with appropriate drug therapy and airway clearance devices.

References

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