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The Role of Airway Clearance in Managing Chronic Muco-Obstructive Lung Disease

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Pathogenesis and Clinical Burden of Impaired Mucus Clearance

The impact of chronic muco-obstructive lung diseases is far reaching, contributing to a high symptom burden for patients, in addition to increased utilization of the healthcare system. These impacts are commonly observed in diseases such as chronic obstructive lung disease (COPD), cystic fibrosis (CF), and non-CF bronchiectasis.

COPD, a chronic and progressive lung disease characterized by persistent airway obstruction, is one of the three most common causes of death worldwide.[1] The burden of COPD is expected to further increase in the coming decades.[2] Acute exacerbations of COPD (AECOPD) represent the leading cause of disease-related hospitalizations in Canada and account for the longest mean length of hospital stay of approximately 7.2 days.[3] Currently, COPD costs

the Canadian healthcare system, in Canadian dollars, $1.5 billion annually,[4] and is expected to exceed $9.0 billion by 2030.[5] Chronic Bronchitis (CB), a very common condition in patients with COPD, is classically defined as a chronic productive cough lasting at least three months per year for two consecutive years.

CF is a multi-system disorder caused by pathogenic mutations in the CF transmembrane conductance regulator (CFTR) gene, affecting over 4,513 Canadians.[6] Non-CF bronchiectasis is a heterogenous group of pulmonary diseases characterized by irreversibly damaged and dilated bronchi.[7] The prevalence of non-CF bronchiectasis is rising, and it often remains poorly recognized and managed.

While these three conditions differ in their specific underlying pathophysiology, the chronic presence of excessive mucus located in the diseased airways plays a vital role in each of them. Several mechanisms explain the presence of this excessive mucus, the most important ones being mucus hypersecretion and altered mucus clearance.

Mucus is a gel that exhibits properties of both a soft elastic solid and a viscous fluid, typically composed of 97% water and 3% solids. Mucins are large glycoproteins that account for less than 30% of the solid component; however, mucin overproduction or dysregulation can further increase the concentration of the solid component by up to 15%, leading to viscous and elastic mucus that is not easily cleared.[8,9] Importantly, dehydrated mucus adheres more firmly to the airway wall.[10] When secreted mucin polymers MUC5AC and MUC5B, which are glycopeptides that are upregulated in COPD, generate elevated levels of mucins, airway occlusion may occur.[11] Notably, in the SPROMICS study, participants with severe COPD and elevated glycopeptide concentrations exhibited a CB phenotype and experienced more frequent exacerbations compared to never-smokers.[12]

Additional factors contribute to these complex interactions. The mucociliary barrier environment is fragile and can be easily altered, thus leading to a decrease in its clearance efficiency. In CF, ionic perturbations within the epithelial barrier prevent proper expansion of secreted mucus, leading to thickening.[13] This thicker mucus is more difficult for airway cilia to clear, and its persistent accumulation can lead to infection and inflammation by providing an environment conducive to microbial growth, creating an alteration in the natural airway microbiome.[8]

In diseased states, thick and viscoid mucous can independently lead to airway inflammation and provide a favourable environment for infection. This often leads to a vicious cycle of increased inflammation, recurrent infection, increased mucous production, and airway remodelling, all of which impair effective mucociliary clearance. Maintaining lung health therefore relies on effective mucous clearance.[14] Patients with these illnesses often report dyspnea, and the presence of excess mucous in the airways is thought to be a significant driver of its development. According to Poiseuille's law, a small change in airway radius can have a significant impact on airway resistance,[15] and excess thick mucous physically reduces the airway cross-sectional area. Airway remodelling can also lead to further airway narrowing and flow resistance.[8,11] Indeed, a recent study reported that mucous plugs detected on imaging among a cohort of smokers was linked to exertional hypoxemia.[16]

Rationale and Benefit(s) of Adding Airway Clearance Therapy (ACT)

Management of chronic muco-obstructive lung disease is specific to the underlying disease state. In COPD, the goals of therapy are to improve symptoms of dyspnea and activity limitations, enhance health status, prevent AECOPD, and reduce mortality. Increasingly important is the resultant reduction of hospital admissions and emergency department visits, given the burden on the healthcare system and the increasing costs of preventable resource utilization.

Management includes both pharmacological and non-pharmacological interventions, both playing vital and complementary roles. The recent Canadian Thoracic Society COPD clinical guideline (2023)[17] recommends that all patients with COPD receive long-acting maintenance inhalers as well as short-acting bronchodilators as needed. The choice of long-acting maintenance inhaler(s) would depend on the symptom profile of the patient, severity of obstruction on pulmonary function testing, and history of prior AECOPD. Additional oral pharmacologic therapies may be indicated to further reduce the frequency and severity of AECOPD. Non-pharmacological treatment is similarly multifaceted, involving

self-management education, smoking cessation, promotion of exercise and an active lifestyle, vaccination, pulmonary rehabilitation (PR), the use of airway clearance techniques (ACT), and oxygen therapy if appropriate.[14,17] Self-management is an important category and goal, assimilating many factors such as ensuring proper inhaler technique and selection, assessment of medication adherence, breathing and cough techniques, and the early recognition of AECOPD. Self-management for exacerbations may involve the provision of a written AECOPD action plan, with clear guidance regarding when to implement it.

PR is a comprehensive intervention based on an initial thorough patient assessment and patient-tailored therapies that include, but are not limited to, exercise training, education, and behaviour change. These components are intended to improve the physical and psychological wellbeing, and to promote long-term adherence to health-enhancing behaviours.[18,19] PR is the standard of care for patients with moderate, severe, or very severe COPD who remain symptomatic despite bronchodilator therapies.[19-21] In patients with COPD, PR has been shown to reduce dyspnea, increase exercise capacity, improve quality of life, and reduce health care resource use.[22,23] For COPD patients at risk of exacerbation, PR has also been shown to reduce the risk of hospital readmission.[24,25] Unfortunately, access to PR remains extremely limited. One report from 2015 revealed that only 0.4% of Canadian patients with COPD had access to PR26 – an astonishingly low figure given its unchallenged benefits in COPD management.

Comprehensive management of CF involves nutritional counselling and support, promotion of exercise and healthy lifestyle, and often includes pharmacotherapy management with inhaled therapies such as hypertonic saline or Dornase alfa, chronic maintenance oral azithromycin, and CFTR modulating therapies. CFTR-targeted therapies are a relatively new and exciting treatment option for many patients with CF, significantly improving morbidity and mortality and markedly enhancing outcomes for many patients with CF. Management of CF also includes screening and treatment of extra-pulmonary disease, such as of the pancreas, sinuses, and intestines.[27] Management of non-CF bronchiectasis shares some similarities and involves investigation and management of the underlying cause, occasional long-term antibiotic use, and supportive care such as vaccinations, healthy lifestyle promotion, smoking cessation, and dietary support.[28]

ACT is critical for the management of chronic muco-obstructive lung diseases, and is recognized an important standard of care. ACT involves techniques and devices used to help clear and remove mucus from the airways. While the skills of trained personnel for can optimize benefits, most ACT therapies can be properly performed independently in the home setting, by either patients or their caregivers. ACT may be appropriate for both acute management of exacerbations and for ongoing maintenance. ACT has long been a central aspect of care in CF and non-CF bronchiectasis, and there is a growing body of literature and interest in its role for COPD, particularly in individuals with CB who frequently produce sputum.

ACT can be delivered through various methods to enable an individualized approach. Common options summarized in **Table 1** include oscillating positive expiratory pressure (OPEP) devices, active cycle of breathing techniques, autogenic drainage, high frequency chest wall oscillation devices, and exercise. Generally, more active methods such as OPEP are favoured over less active methods such as high frequency chest wall oscillation devices,[29] and it is often recommended to combine and individualize therapies to achieve targeted goals of therapy.[30]

Spotlight on Oscillating Positive Expiratory Pressure (OPEP) Therapy

While various forms of ACT exist, more active methods using OPEP are often central to management of excess mucus clearance. OPEP devices are typically hand-held, easy to use, medication free, and patient initiated. When a patient exhales through the device, intermittent resistance creates a unique pressure-oscillation dynamic, which expands the airways and helps to mobilize mucus toward the upper airways, where it can be more easily expectorated.[31] Numerous OPEP devices available, including *Aerobika®, Acapella®, Flutter®, Long Flute®, PocketPEP®, Quake®, RC-Cornet®, ShurClear®, Vibralung®, vPEP*, and *VibraPEP®*. These devices have demonstrated benefits in both acute and chronic management of muco-obstructive lung diseases, as discussed below.

Method	Technique	Considerations
Active Cycle of Breathing Teczhniques	Comprises three components: breathing control, thoracic expansion exercises, and forced expiration technique.	• Requires no equipment • May be combined with other techniques
Oscillating Positive Expiratory Pressure Devices	Various devices which, when exhaling through, produce intra-thoracic oscillations via positive pressure oscillations.	• Multiple different devices available • Significant body of evidence supporting benefit
Autogenic Drainage	Comprises three stages: mucous 'unsticking' with slow and deep breathing manoeuvres, collecting with slightly faster breathing, and evacuating with deeper, more forceful breathing.	• Requires no equipment • May be better tolerated as a gentle technique
High Frequency Chest Wall Oscillation	Air pulse generator connected to an inflatable jacket or vest, creating external oscillations to the chest wall.	• Passive technique • Cost and inconvenience • Proven evidence of benefit
Exercise	Various approaches that increase tidal volume and respiratory rate.	• Requires no equipment • Impactful health benefits independent of sputum clearance • May/should be combined with other methods

Table 1. Airway Clearance Methods; *courtesy of Jeffrey D. Marciniuk, MD, FRCPC, Sophie Bergeron-Kermelly, MD, FRCPC, Pierre Landry, MSc, MD, FRCPC, and Darcy D. Marciniuk, MD, FRCPC, FCAHS, Master FCCP, FAEM.*

In COPD patients who produce sputum daily or most days, OPEP therapy may enhance mucous mobilization, alleviate symptoms, and improve quality of life (QOL).[32] Among patients with bronchiectasis, OPEP devices have been shown to improve sputum expectoration and QOL compared to no OPEP treatment.[33] Furthermore, the British Thoracic Society clinical guideline for bronchiectasis in adults reports a greater patient preference for OPEP compared with active cycle of breathing techniques, with or without gravity-assisted positioning.[28] In CF, a Cochrane review confirmed an improvement in lung function with ACT versus no therapy. However, in the 2020 review, OPEP devices did not demonstrate better improvements compared with other clearance techniques regarding frequency of infectious exacerbations, sputum volume or weight, and patient preference. The low quality of evidence from included randomized controlled trials at the time may partially explain the lack of observed differences between clearance techniques and OPEP devices.[34]

While OPEP devices have demonstrated benefits in both reducing symptoms and improving disease-specific QOL, several small studies have also suggested cost benefits. In COPD, use of the *Aerobika®* device was estimated to save $694 CAN per patient, modelled on a Canadian provincial (Alberta) health care system, driven in part by reduced exacerbations.[35] Similar cost-savings have also been demonstrated in United States healthcare delivery systems.[36] Moreover, reductions in hospitalizations, driven by reduced re-admissions, have been documented across various respiratory disease conditions, including COPD and CB.[37]

New Evidence in Patient-Centred Care: *Aerobika®* Quality of Life (QOL) Data

Evidence supporting the benefits of *Aerobika®*, an OPEP device manufactured by a Canadian company, in patients with chronic muco-obstructive lung disease continues to grow, with several recent studies examining various QOL outcomes.

A recent study[38] evaluated the daily use of *Aerobika®* in patients with COPD and chronic sputum production. Patients used the *Aerobika®* device for 21–28 days, and outcomes included pulmonary function testing, six-minute walk test distance (6MWD), St. George Respiratory Questionnaire (SGRQ) and Patient Evaluation Questionnaire (PEQ) scores. The SGRQ is a 50-item self-administered questionnaire that measures health status and QOL in people with chronic respiratory diseases. The PEQ evaluates cough frequency, cough severity, chest discomfort, dyspnea, bronchodilator use, and ease of sputum expectoration. Daily use of the *Aerobika®* device in patients with COPD and chronic sputum production was shown to improve the SGRQ and PEQ scores, forced vital capacity, and 6MWD.[38]

In addition to QOL data, several studies have evaluated the effect of the Aerobika OPEP device on AECOPD frequency. A 2017 study[37] assessed 30-day rates of moderate to severe exacerbations in COPD patients treated with *Aerobika®* versus a matched control group in a real-world setting. Patients in the *Aerobika®* use group experienced a 28% reduction in moderate to severe exacerbation frequency compared to those receiving usual care (control group).

In patients with non-CF bronchiectasis and a history of frequent exacerbations, twice-daily use of the *Aerobika®* device resulted in a decreased rate of exacerbations.[39] Among patients with COPD or CB following discharge from initial hospitalization, *Aerobika®* device users were less likely to experience ≥1 severe AECOPD exacerbation within 30 days and at 12 months post-discharge compared to controls.[40] They also had fewer (≥1) all-cause inpatient visits within these timeframes than that experienced by *Acapella®* device users. These recently published results confirm the benefits of the *Aerobika®* device across studies, lending reassurance to its validity in the populations examined. Nonetheless, it should be kept in mind that these studies involved small sample sizes and were not double-blinded due to the nature of the intervention.

Additional information and supporting data regarding the *Aerobika®* device are available here.[31]

Summary

Chronic muco-obstructive lung disease encompasses a heterogenous group of conditions with distinct pathophysiology that share one common feature: difficulty managing excessive mucus in the airways. The presence of excess sputum has a significant negative impact on QOL, increases the risk of exacerbations, and contributes to mortality. In this regard, airway clearance techniques are central to effective treatment. These inexpensive, drug-free devices highlight the benefit(s) of often neglected non-pharmacologic components of treatment. OPEP devices have been demonstrated to be safe and efficacious and are appropriate for use across various disease states, and are associated with improvements in respiratory symptoms. By empowering patients to actively participate in their care, OPEP devices are an essential tool. We advocate for their appropriate and widespread use in the treatment of patients with chronic muco-obstructive disease.

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