SIMEOX IN NON-CYSTIC FIBROSIS BRONCHIECTASIS

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SIMEOX CLINICAL NOTEBOOK N°3

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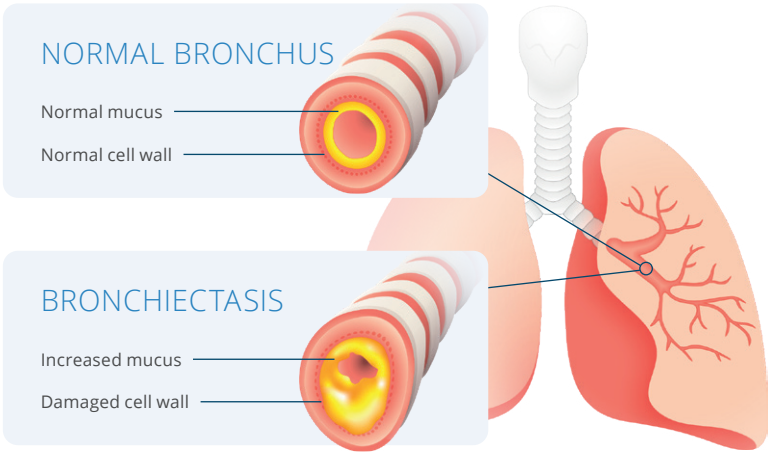
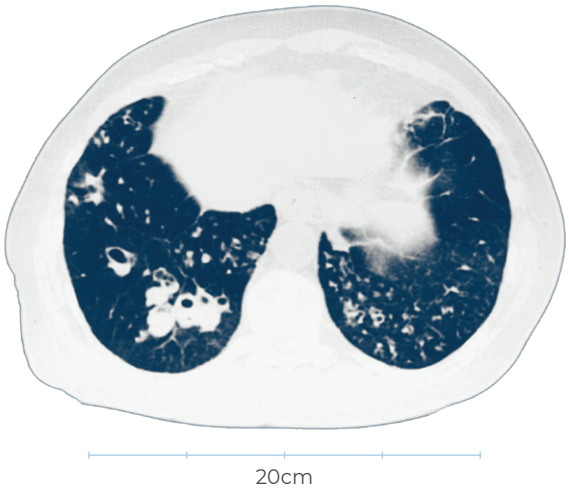
Definition

Bronchiectasis is a chronic respiratory disease characterized by a clinical syndrome of persistent cough, **excessive sputum production** and bronchial infection, and radiologically (confirmed with HRCT-scan) by abnormal and permanent and irreversible dilatation of the bronchi[1]. Cough and sputum production, along with breathlessness are the most frequent symptoms but rhinosinusitis, fatigue, haemoptysis and thoracic pain are also common.

Bronchiectasis is a **frequent comorbidity (50%)** in patients with advanced cystic fibrosis and severe COPD. It is admitted to separate etiologies between patients with and without Cystic fibrosis (non-CF bronchiectasis or NCFB) as CF predisposes patients to bronchiectasis in the majority of them with worsening of the disease, and physiopathology and treatment of bronchiectasis in CF is well characterized.





NCFB can be a consequence of prior lung infection or because of a systemic disorder but a cause is not identified in 50% of patients (idiopathic). Although NCFB is heterogenous and has numerous causes, **idiopathic bronchiectasis and infection-related bronchiectasis** represent the majority of adult cases of NCFB in most series. **COPD is a leading cause in Europe.** In Asia, post-tuberculosis disease is the most frequent underlying cause of NCFB[2].

Pathogens isolated from these patients included nontuberculous mycobacteria (NTM), pseudomonas aeruginosa (PA), and staphylococcus aureus. Patients with PA have a worst prognosis.

In US, patients with NCFB are predominantly women (80%) and never smokers (60%), with a mean age of 64 years[3].

>75% of patients are diagnosed after 50 years old. 50% have airway obstruction (15% severe). Common comorbidities are: history of pneumonia (68%), GERD (47%), asthma (29%), otitis or rhino-sinusitis (25%), COPD (20%), rheumatologic disease (8%), primary deficiency (5%).

More severe and more frequent exacerbations are associated with worse quality of life, daily symptoms, lung function decline, and mortality. Pulmonary exacerbation rate is high with an average of 3 exacerbations in the past 2 years (US registry). 50% of European bronchiectasis patients have two or more exacerbations per year and one third require at least one hospitalization per year. Consequently, the majority of therapeutic interventions **are aimed at reducing exacerbations**.

Bronchiectasis is characterized by a vicious cycle of airway infection and inflammation leading to permanent damage of small airways and lung parenchyma. This model proposed by Cole is not well understood in terms of the underlying biology but **includes deficits in mucociliary clearance** and innate and adaptive immunity[4].

There is amplification of injury processes following anatomical damage to the bronchi leading to progressive worsening of pulmonary physiology and symptoms with associated increase in exacerbations. The host immune response to infection is primarily neutrophilic and neutrophil derived proteases are deleterious and result in further pulmonary damage amplifying a recurrent cycle (Fig.1).

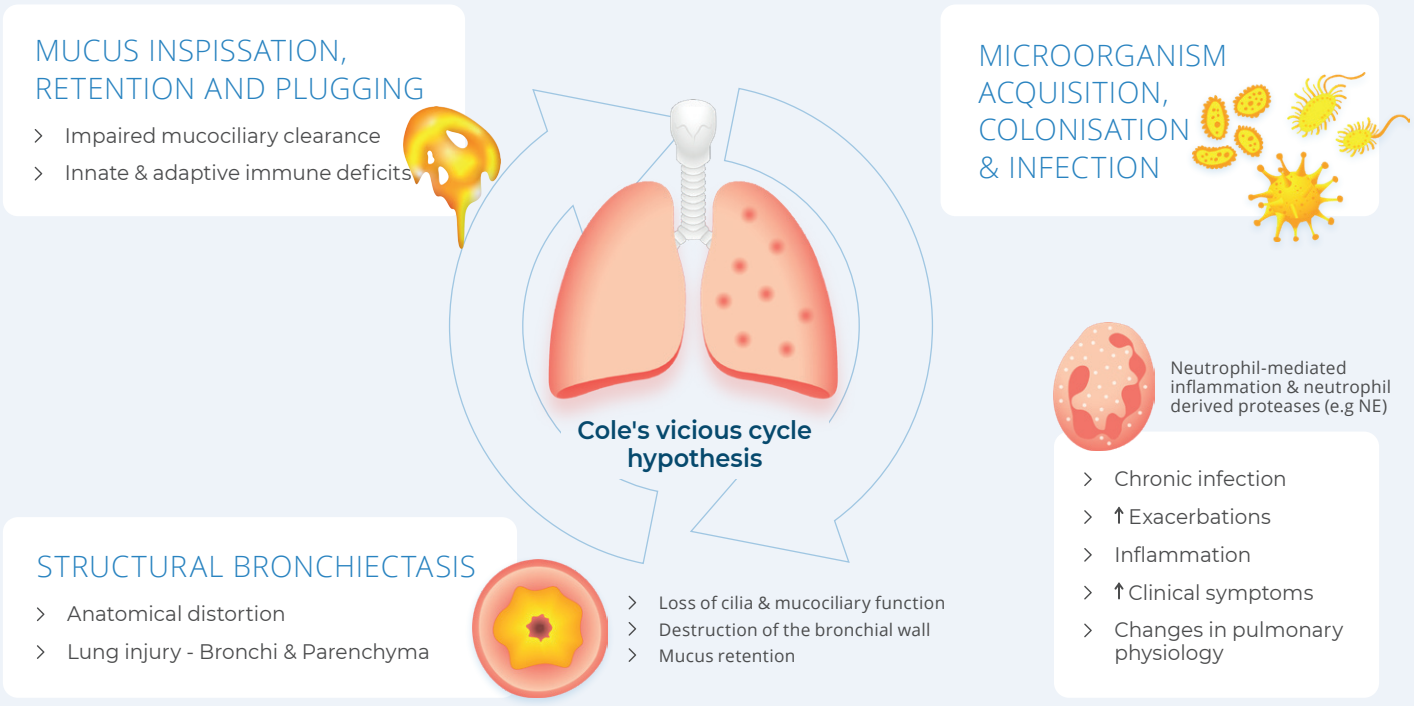


Fig. 1 - A modern interpretation of Cole's vicious cyde hypothesis. Abbreviations: NE - Neutrophil elastase - Increased

[1] Polverino E et al. European Respiratory Society guidelines for the management of adult bronchiectasis. Eur Respir J 2017; 50: 1700629.

[2] Chandrasekaran R et al. Geographic variation in the aetiology, epidemiology and microbiology of bronchiectasis. BMC Pulm Med. 2018 May 22;18(1):83. doi:10.1186/s12890-018-0638-0

[3] Aksamit TR et al. Bronchiectasis Research Registry Consortium. Adult Patients With Bronchiectasis: A First Look at the US Bronchiectasis Research Registry. Chest. 2017 May;151(5):982-992. doi:10.1016/j.chest.2016.10.055

[4] O'Donnell AE. Bronchiectasis update. Curr Opin Infect Dis. 2018 Apr;31(2):194-198. doi: 10.1097/QCO.0000000000000445.

Physiopathology of pulmonary obstruction

It is well recognized that **obstruction of small airways** in peripheral lungs plays a significant role in this deleterious process. Excessive mucus and inflammatory mediators promote luminal occlusion and bronchoconstriction that are amplified by airway remodeling.

Aberrant epithelial remodeling with impaired mucociliary architecture is present in both large and small airways in patients with refractory non-CF bronchiectasis (Fig.2)[5].

Airway dilation in bronchiectasis is due to **morphological changes of airway epithelial cells with cellular hyperplasia** and proliferation of club cells, and led to loss of cilia and MCC impairment. **In bronchiectasis, the mucus itself is often abnormal and more complex.** These structural abnormalities in small airways allow for mucus stasis, which favors continued chronic infection and the persisted vicious cycle in patient with bronchiectasis.

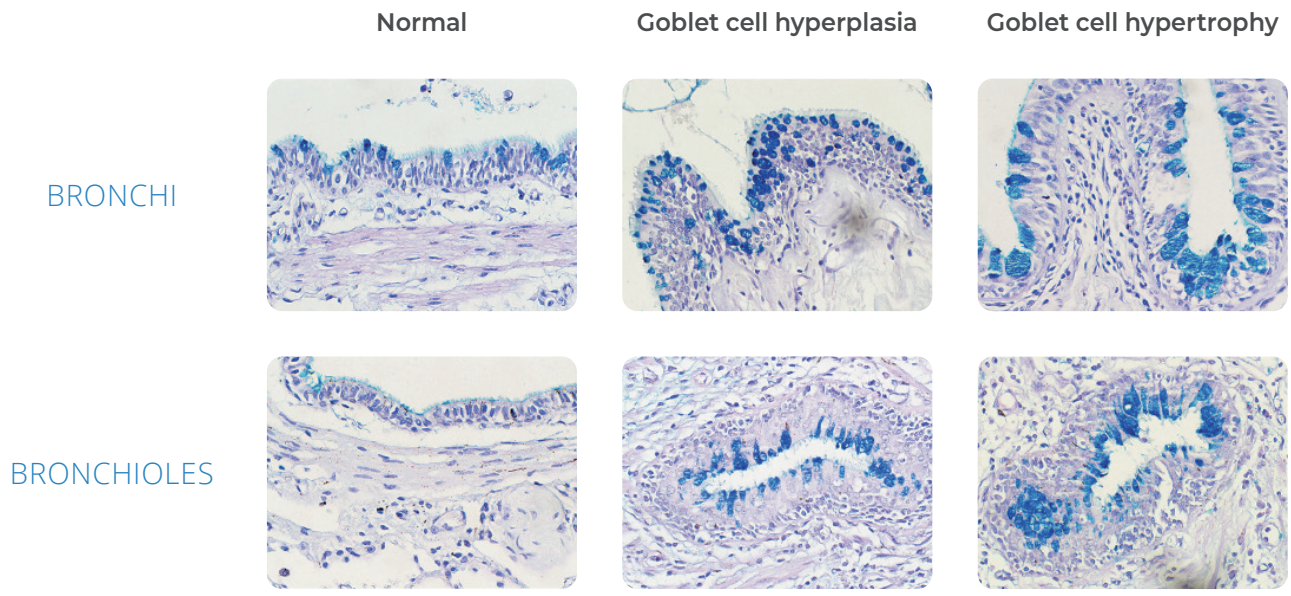


Fig. 2

[5] Chen ZG et al. Aberrant epithelial remodeling with impairment of cilia architecture in non-cystic fibrosis bronchiectasis. J Thorac Dis. 2018 Mar;10(3):1753-1764. doi: 10.21037/jtd.2018.02.13.
[6] Weycker D, Hansen GL, Seifer FD. Prevalence and incidence of noncystic fibrosis bronchiectasis among US adults in 2013. Chron Respir Dis. 2017 Nov;14(4):377-384. doi: 10.1177/1479972317709649
[7] Lin JL, Xu JF, Qu JM. Bronchiectasis in China. Ann Am Thorac Soc. 2016 May;13(5):609-16. doi:10.1513/AnnalsATS.201511-740PS

Prevalence and incidence

Prevalence

NCFB prevalence has been rising since 2000. Similarly, bronchiectasis is also being detected more frequently in all parts of the world. NCFB is seen in all age groups but the **highest prevalence of disease is seen in the older age range (greater than 60 years).** Bronchiectasis is an age-associated disease and a marked increase in prevalence, particularly of severe disease is observed in the elderly.

Women are disproportionately affected in Western countries with higher prevalence than in men. Conversely, as pulmonary tuberculosis occurs more frequently in men, NCFB prevalence is higher in men than women in countries where tuberculosis is a common cause of NCFB like China or India.

NCFB prevalence in US is about 140 patients per 100 000 people > 45 years according to age and gender (fig. 3)[6] and **may affect > 450 000 patients in US.** Prevalence is 500 per 100 000 of people >65 years. Similar prevalence can be estimated in Europe. Some studies reported 67 per 100 000 in Germany and 362 per 100 000 in Spain.

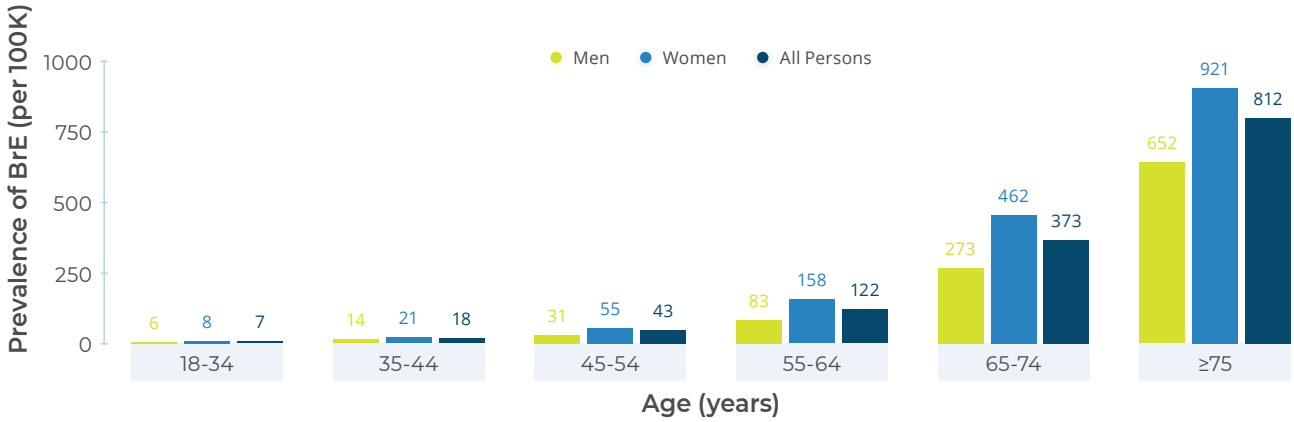


Fig. 3 - Prevalence of bronchiectasis among US adults, by age and sex.

A report estimated that NCFB prevalence in China may be **greater than 1.2% of people > 40 years** (fig.4)[7] so approximatively 7 Million people affected.

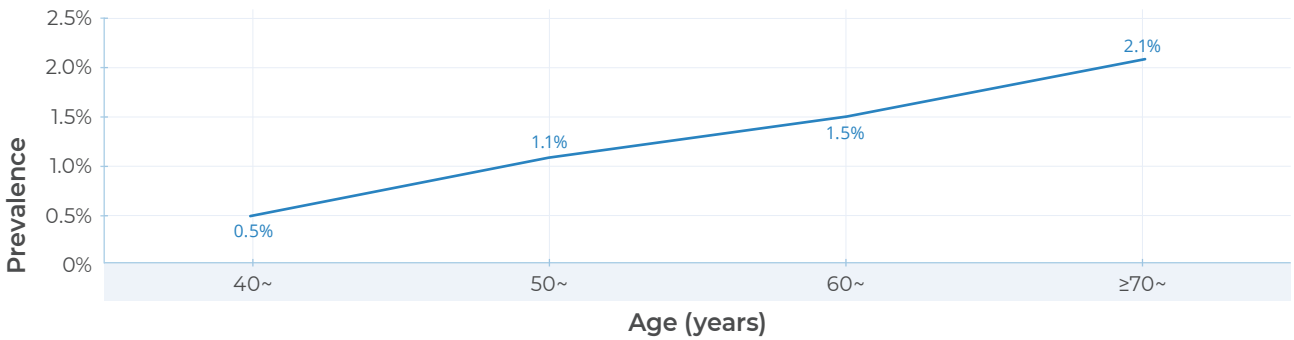


Fig. 4 - NCFB prevalence in China

Prevalence and incidence

Prevalence of NCFB in COPD

There is a significant overlap between COPD and NCFB. **NCFB prevalence in COPD is estimated overall at 20%[8].** In more severe COPD patients, 20-40% of GOLD III and IV patients may have NCFB. But bronchiectasis diagnosis is not systematic in COPD and clinical symptoms are very similar that explains the underestimate of COPD prevalence in NCFB. However, expansion of lung cancer screening with CT-scan allows to identify more and more bronchiectasis in COPD.

By including COPD patients, projection of overall prevalence of NCFB suggests that about **4.2 million adults over 40 years old may have bronchiectasis in the US[5].**

COPD patients with NCFB have a **greater production and purulence of sputum,** more severe and frequent exacerbations, and increased prevalence of Pseudomonas aeruginosa colonization.

Incidence

The overall annual incidence (new cases per year) of NCFB in US is estimated to be **29 cases per 100 000 US adults (+ new 70 000 patients per year)** and was estimated to be higher for women (34 per 100 000) versus men (23 per 100 000).

The incidence increases also with age (fig. 5).

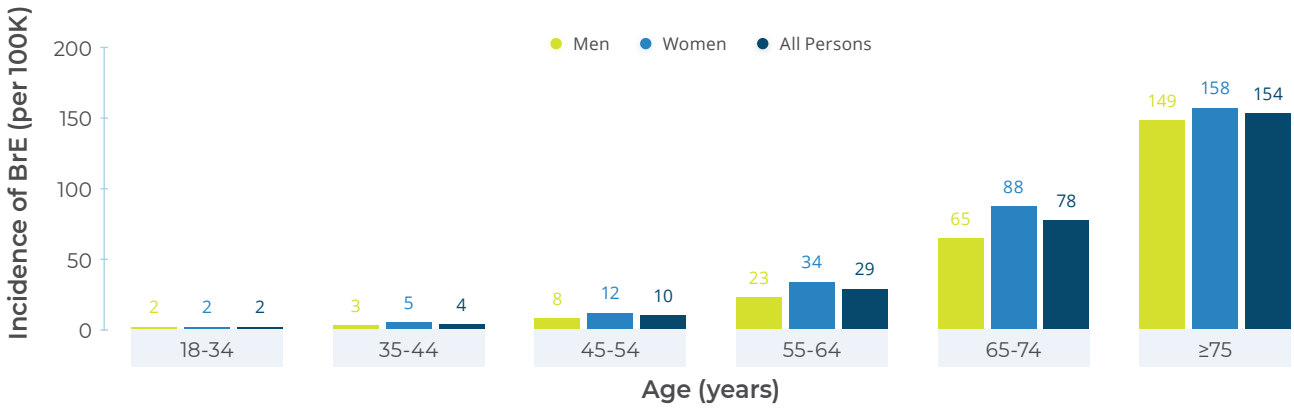


Fig. 5 - Incidence (annual) of bronchiectasis among US adults, by age and sex.

Similar incidence in Europe was reported in some studies: 20 cases per 100 000 (+17 000 / year) in Germany (2013)[9] and 48 cases per 100 000 (+20 000/ year) in Spain.

Incidence in Asia is unknown.

[2] Chandrasekaran R et al. Geographic variation in the aetiology, epidemiology and microbiology of bronchiectasis. BMC Pulm Med. 2018 May 22;18(1):83. doi:10.1186/s12890-018-0638-0

[5] Chen ZG et al. Aberrant epithelial remodeling with impairment of cilia architecture in non-cystic fibrosis bronchiectasis. J Thorac Dis. 2018 Mar;10(3):1753-1764. doi: 10.21037/jtd.2018.02.13.

[6] Weycker D, Hansen GL, Seifer FD. Prevalence and incidence of noncystic fibrosis bronchiectasis among US adults in 2013. Chron Respir Dis. 2017 Nov;14(4):377-384. doi: 10.1177/1479972317709649

[8] Martinez-Garcia MA, Miravitlles M. Bronchiectasis in COPD patients: more than a comorbidity? Int J Chron Obstruct Pulmon Dis. 2017 May 11;12:1401-1411. doi:10.2147/COPD.S132961

[9] Ringshausen FC, de Roux A, Diel R, Hohmann D, Welte T, Rademacher J. Bronchiectasis in Germany: a population-based estimation of disease prevalence. Eur Respir J. 2015 Dec;46(6):1805-7. doi: 10.1183/13993003.00954-2015

Etiologies

In Western countries, **post-infection bronchiectasis** is the most commonly identifiable cause for disease development. However, bronchiectasis caused by immune-related mechanisms including autoimmunity, immunodeficiencies and hematologic malignancies is identified as predominant etiologies in the US probably due to systemic evaluation in these diseases.

COPD and asthma are also significant contributors in Europe[2].

In Asia and Latin America, **predominant etiology is chronic pulmonary infection** and especially post-tuberculosis disease. In China the main causes have shifted from pertussis, measles, and tuberculosis to bacterial, mycoplasma, and viral pneumonia. Others significant etiologies include infection, COPD and allergic bronchopulmonary aspergillosis[6].

In Japan, an inflammatory disease associated with rhino-sinusitis has been particularly studied (Sino-bronchial Syndrome).

Potential genetic predisposition to bronchiectasis may account for the increased disease prevalence in indigenous communities in the Asia-Pacific region. The influence of the environment and its accompanying climate may also influence microorganisms and/or pathogens that affect the bronchiectasis airway.

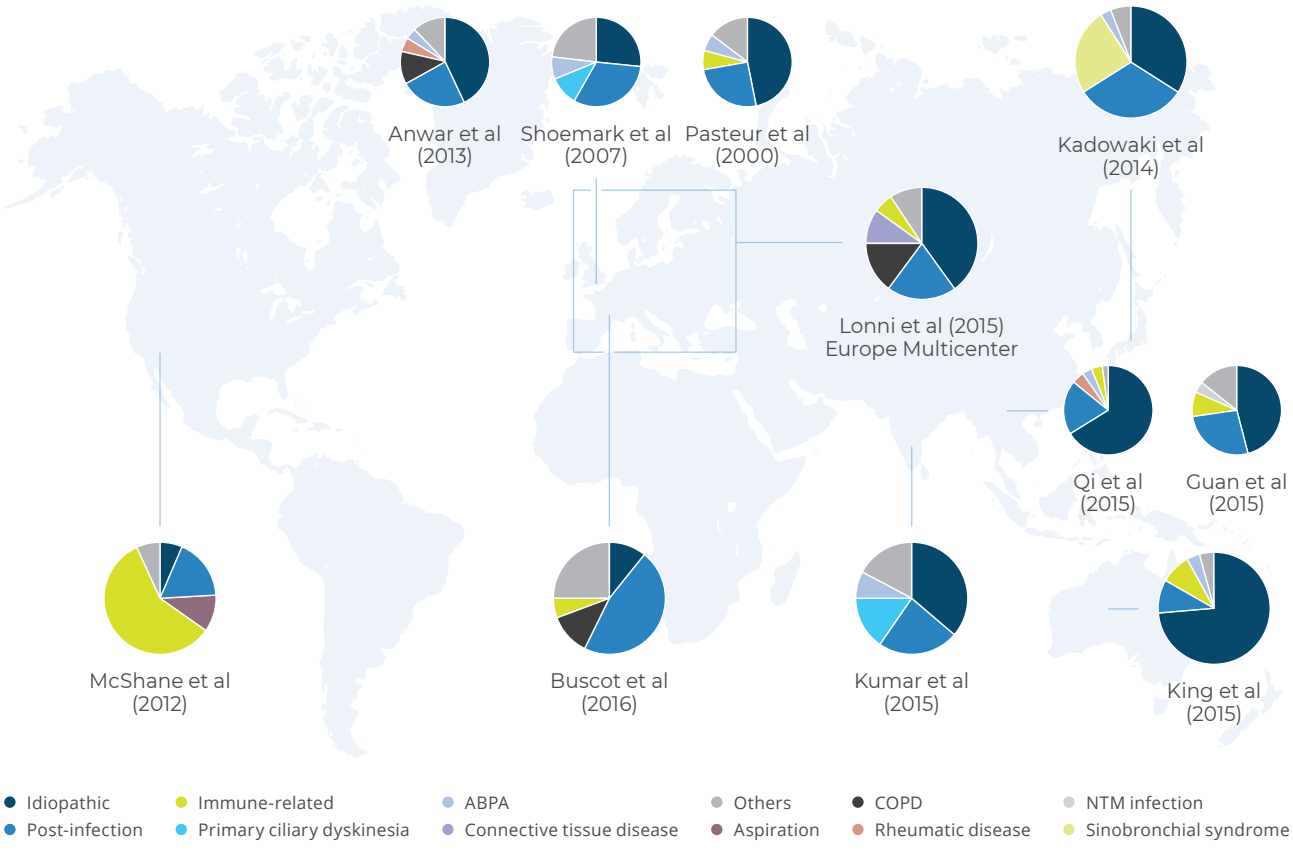


Fig. 2 - Predominant aetiologies across different geographic regions and ethnic populations. The individual pie charts indicate the top aethologies (top 4 or 5) in each cohort. Abbreviations: ABPA - Allergic Broncho-Pulmonary Aspergillosis, COPD - Chronic Obstructive Pulmonary Discorder, NTM - Non-Tuberculosis Mycobacteria, GERD - Gastro-Esophageal Reflux Disease

Airway clearance therapies

Treatment is primarily based on the principles of preventing or suppressing acute and chronic bronchial infection, improving mucociliary clearance and reducing the impact of structural lung disease. Mucociliary clearance is impaired by the impact of structural bronchiectasis, airway dehydration, excess mucus volume and viscosity. More than 70% of bronchiectasis patients expectorate sputum daily with highly variable sputum volumes. Treatment aims to prevent mucus stasis and the associated mucus plugging, airflow obstruction and progressive lung damage.

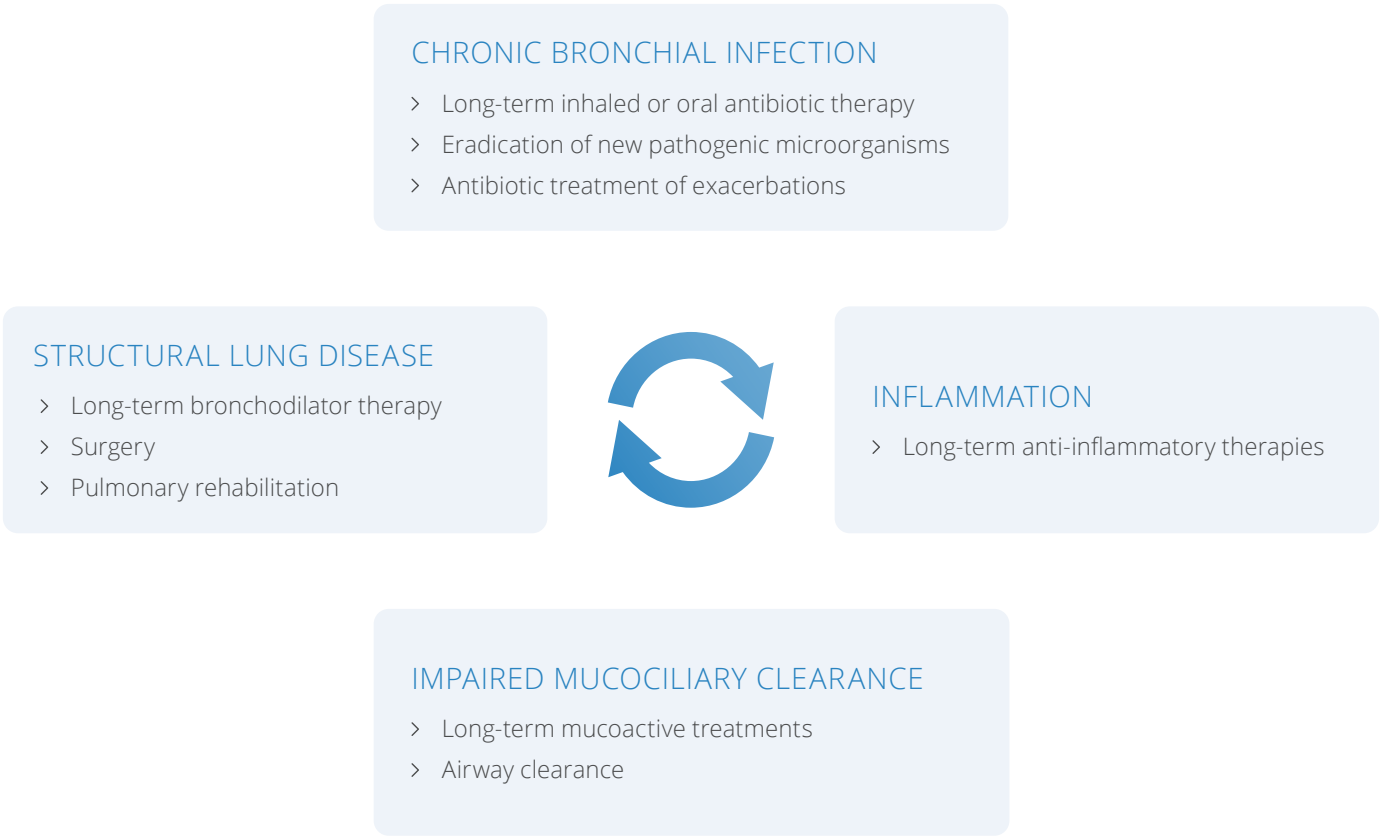


Fig. 1 - Treatments for bronchiectasis considered in this guideline according to the vicious cycle concept of bronchiectasis.

Medical treatment consists in suppressive ATB, bronchodilators, ICS, mucolytic agents (only if Airway clearance Technique failed). Dornase alpha (Pulmozyme) is not recommended. Before considering the prescription of long-term antibiotics, general aspects of bronchiectasis management need to be optimized, **such as airway clearance** and treating modifiable underlying causes[1].

According to ERS guidelines, **patients with chronic productive cough or difficulty to expectorate sputum** should be taught an ACT by a trained respiratory physiotherapist to perform **once or twice daily.**

ACTs are safe and enhance mucus clearance in BE. There are a few evidences to suggest some benefits on lung function, pulmonary exacerbation or health-related quality of life. **Patients with BE may be good responders to ACT.** Available clinical evidences showed that no ACT demonstrated to be superior to others and that the **prescription of ACTs should be individualized based on patient preference.**

ERS guidelines propose the following flow chart for ACT interventions in bronchiectasis:

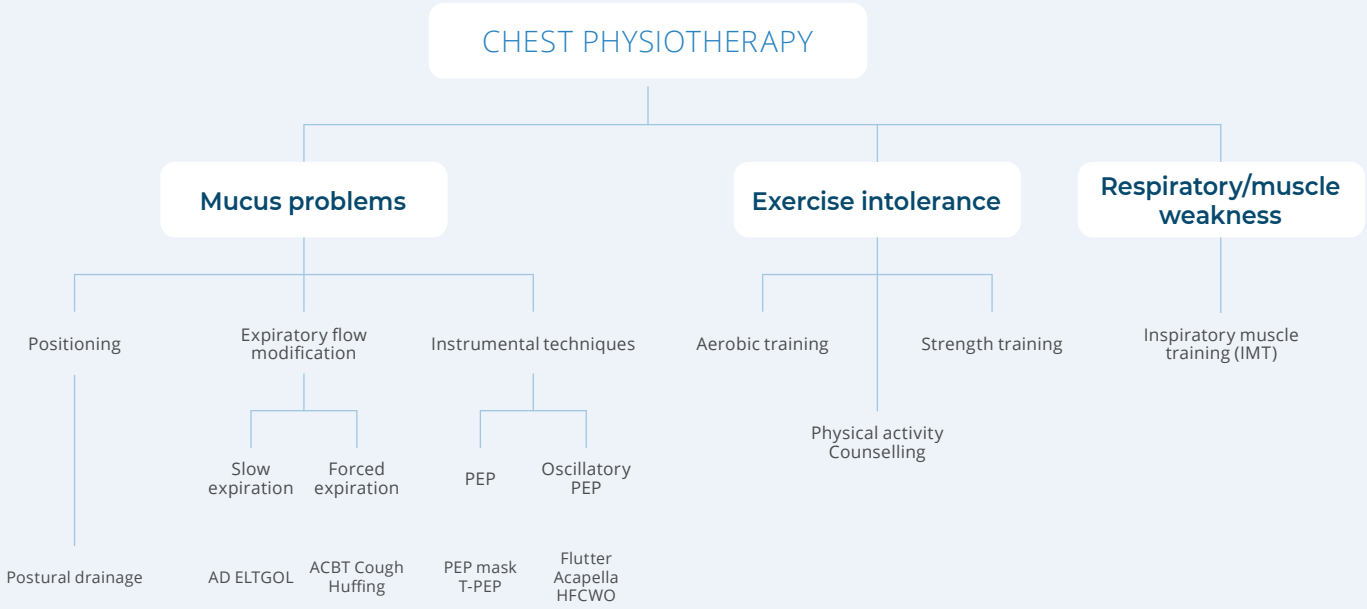


Fig. 6 - Chest physiotherapy interventions flow chart based on clinical experience from the task force panel. AD: autogenic drainage; ELTGOL: total slow expiration with open glottis and infralateral position; ACBT: active cycle of breathing techniques; PEP: positive expiratory pressure; T-PEP: temporary positive expiratory pressure; HFCWO: high frequency chest wall oscillation.

Data from US registry[3] showed that 55% of patients with BE have ACT:

- 16% chest percussion, postural drainage
- 50% PEP, flutter
- 15% HFCWO (uncommon outside US: 1-2%)

[1] Polverino E et al. European Respiratory Society guidelines for the management of adult bronchiectasis. Eur Respir J 2017; 50: 1700629.

[3] Aksamit TR et al. Bronchiectasis Research Registry Consortium. Adult Patients With Bronchiectasis: A First Look at the US Bronchiectasis Research Registry. Chest. 2017 May;151(5):982-992. doi:10.1016/j.chest.2016.10.055

CLINICAL RESULTS WITH SIMEOX

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Effect of a new ACT versus manual physiotherapy in COPD 15
Mihaltan et al, National Institute of Pneumology Marius Nasta - Bucharest (Romania)

Simeox feasibility and safety evaluation in patients with bronchiectasis 16
Kolek et al, Palacky University Hospital, Olomouc (Czech Republic)

Benefits of SIMEOX Airway clearance technology in non-CF patients with Bronchiectasis 17
Sliwinski et al, Institute of Tuberculosis and Lung Diseases, Warsaw (Poland)

Feasibility and benefits of an innovative Airway Clearance Technology in COPD patients hospitalized for acute exacerbation 18
Solovic et al, National Institute for TB, Lung Diseases and Thoracic Surgery, Vyšné Hágy (Slovakia)

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Preliminary data for Simeox in non-CF Bronchiectasis

The following clinical documentation brings together the Simeox experience of several recognized national centers of medical expertise and research from different EU countries (Poland, Czech Republic, Romania, Slovakia) in the management of patients with non-CF bronchiectasis suffering from pulmonary congestion and requiring airway clearance.

Each center performed a pilot prospective study with the aim of assessing short-term benefits and safety of Simeox technology compared to conventional physiotherapy in patients hospitalized for acute pulmonary exacerbation. Patients with acute exacerbation were treated for chest congestion with Simeox for 5-7 days (1 or 2 sessions per day) during hospitalization while receiving optimal drug therapy. Pulmonary function tests, symptoms, mucus clearance, SpO2, usability, quality of life and adverse events were evaluated during the study.

The body of clinical evidence in non-CF bronchiectasis is summarized in the following Table:

Study Title/Authors	References	Study Design/Population
Effect of a new Airway Clearance Technology versus manual physiotherapy in COPD Mihaltan et al.	ERS 2018: F. Mihaltan, L. Morin, C. Borcea, A. Costantin, A. Pahontu, L. Marinescu, V. C. Cosei, Effects of a new Airway Clearance Technology versus manual physiotherapy in COPD, ERJ 2018 52: Suppl. 62, PA4047 (poster)	Prospective comparative study of 10 COPD patients (70% with bronchiectasis) hospitalized for AECOPD, comparing manual ACT versus ACT using Simeox, 5 patients per group
Benefits of SIMEOX Airway clearance technology in non-CF patients with Bronchiectasis Sliwinsky et al.	ERS 2018: K. Iwan, D. Klatka, A. Gladzka, L. Morin, P. Sliwinski, Benefits of Simeox airway clearance technology in non-CF patients with bronchiectasis, ERJ 2018 52: Suppl. 62, PA805 (poster) ATS 2019: P. Sliwinski, D. Klatka , A. Gladzka , L. Morin , K. Iwan , Benefits of Simeox airway clearance technology in non-CF patients with bronchiectasis, American Journal of Respiratory and Critical Care Medicine 2019;199:A5720 (oral communication)	Prospective comparative study of 21 patients with non-CF bronchiectasis hospitalized for PEx, Comparing manual chest therapy (n=8) Vs Simeox (n=13)
Feasibility and safety evaluation of Simeox airway clearance technique in patients with bronchiectasis V Kolek et al.	ERS 2019: Vitezslav Kolek, Petr Jakubec, Jana Doleželová, Laurent Morin, Jiří Kufa European Respiratory Journal 2019 54: PA601; DOI: 10.1183/13993003.congress-2019.PA601 (poster)	Prospective comparative study of 12 patients with CF or non-CF bronchiectasis hospitalized for PEx, comparing conventional ACT versus ACT using Simeox, 6 patients per group
Feasibility and benefits of an innovative Airway Clearance Technology in COPD patients hospitalized for acute exacerbation I Solovic et al.	Internal data (abstract submitted to ERS 2020)	Prospective comparative study of 32 patients with COPD (37% bronchiectasis) hospitalized for AECOPD, comparing standard care (n=13) Vs Simeox (n=19)

The studies listed on Table above are further described thereafter:

Effect of a new ACT versus manual physiotherapy in COPD

Mihaltan et al, National Institute of Pneumology Marius Nasta - Bucharest (Romania)

STUDY METHODOLOGY

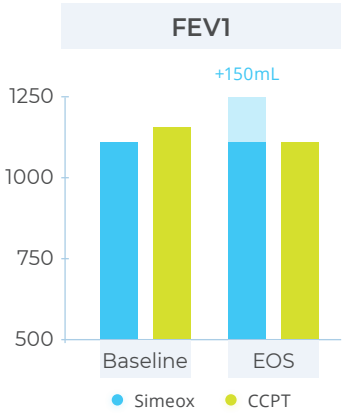
Comparative non-randomized prospective series (conducted in 2018) of 10 COPD patients (FEV1>20%) with bronchiectasis and Acute Exacerbation of COPD (AECOPD) who reported excessive mucus congestion and difficulties to clear airways despite optimal bronchodilator therapy.

Patients were treated for 5 days (2 sessions of 20-min/day) during hospitalization with either Simeox technology or conventional chest physiotherapy (5 patients in each group). Pulmonary Functional Tests (PFTs: spirometry), respiratory symptoms, CAT score, usability and safety were compared between the 2 groups.

STUDY RESULTS

While mucus clearance and evolution of respiratory symptoms were similar between the two groups after 5 days of therapy, all PFTs variables improved from baseline for the Simeox group. FEV1(L) improved by +0.15±0.10L (FEV1% +5±2%) and FEV1/FVC increased from 52.5±2.4% to 58.0±12.8% in the device group but remained stable in the manual physiotherapy group.

CAT score improved in the device group only from 20.2±6.4 to 17.0±4.6. From usability perspective, all the patients of Simeox group acquired quickly autonomous usage. The device was well tolerated with no adverse event nor pain reported.



Variables	Device group values (N=5)		Manual Physiotherapy group values (N=5)	
	Baseline	EOS**	Baseline	EOS*
CAT score Mean ±SD	20.2 ± 6.4	17.0 ± 4.6	17.2 ± 5.4	18.6 ± 4.0
Drainage improvment (N, %)	5 (100%)		4 (80%)	
Dyspnea improvment (N, %)	4 (80%)		4 (80%)	
Fatigue improvment (N, %)	4 (80%)		4 (80%)	
Autonomy in execution	5 (100%)		4 (80%)	

*End of Study (EOS) : 2 sessions of 20 minutes per day, for 5 days
**End of Study (EOS) : 2 sessions of 20 minutes per day, intensity 50-75% for 5 days

CONCLUSION

The study concluded that the preliminary data suggest safety and additional benefits of use of Simeox airway clearance technology for COPD with severe chronic bronchitis symptoms or bronchiectasis.

Benefits of SIMEOX Airway clearance technology in non-CF patients with Bronchiectasis

Sliwinski et al, Institute of Tuberculosis and Lung Diseases, Warsaw (Poland)

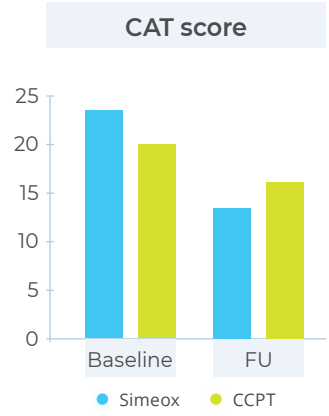
STUDY METHODOLOGY

Comparative non-randomized prospective series (conducted in 2018) of 21 patients with non-CF bronchiectasis hospitalized for severe pulmonary exacerbation, undergoing ACT with either Simeox (n=13) versus conventional chest physiotherapy (CCPT, n=8) followed for 7 days. Change in respiratory symptoms, lung function, disease-specific quality of life questionnaire (CAT score) and 6-minute walking distance test (6MWT) were compared between both groups.

STUDY RESULTS

The results confirmed the significant improvement from baseline after 7 days of therapy in the Simeox group in CAT score which was reduced by 8 points (p=0.008) in Simeox group. No significant change was observed in control group. Also cough intensity, chest congestion and perceived dyspnea decreased significantly in Simeox group (p<0.05) while only cough intensity improved in control group.

Furthermore, 6MWT improved also significantly from baseline in the Simeox group (n=10, 74±117 m; 23%); oxygen desaturation during exercise improved also significantly from baseline in the Simeox group (reduction of -0.9±1.2 %; p<0.05). In contract, changes in control group were not significant.



Group		ΔSaO2 (%) during exercise	Distance covered (m)	Δ Borg scale during exercise
Device N=10	at admission	4.8 ± 7.2	334 ± 119	0.9 ± 1.3
	after 7 days	4.4 ± 7.6	412 ± 87	1.1 ± 2.3
	Δ	-0.9 ± 1.2	74 ± 117	0.2 ± 1.8
	p value	**<0.05**	**0.036**	**NS**
Control N=8	at admission	2.1 ± 1.6	382 ± 232	1.1 ± 1.9
	after 7 days	1.6 ± 1.9	438 ± 188	0.6 ± 1.8
	Δ	-0.5 ± 1.9	56 ± 110	-0.4 ± 1.1
	p value	**NS**	**NS**	**NS**

Results of 6MWT before and after 7 days of ACT with device or CP (control).

CONCLUSION

The study concludes that Patients with non-CF bronchiectasis of different origin may benefit from the use of Simeox during acute exacerbation in hospital setting. Easy to use and efficient airway clearance technology may quickly and significantly improve quality of life and exercise capacity of these patients. Simeox technology was well tolerated by all studied patients and proved to be safe and easy to handle even for older and disabled person.

Simeox feasibility and safety evaluation in patients with bronchiectasis

Kolek et al, Palacky University Hospital, Olomouc (Czech Republic)

STUDY METHODOLOGY

The objectives of this randomized controlled trial were (1) to demonstrate non-inferiority of the Simeox device compared to traditional manual physiotherapy technique for airway clearance of hospitalized patients suffering from bronchiectasis in cystic fibrosis, COPD and idiopathic pulmonary fibrosis, (2) to evaluate clinical outcomes of Simeox procedure measured by pulmonary functional tests, and (3) to consider daily autonomous use of Simeox technology in patients with various obstructive lung diseases. Feasibility of Simeox procedure was the primary endpoint. Secondary endpoints were: Safety of the procedure with regard to respiratory and other complications, PFTs results (FEV1, RV), chest expansion measured on xiphoid processus level (in cm), SpO2 measured by pulse oximetry (%), 24-hour collected mucus amount (ml).

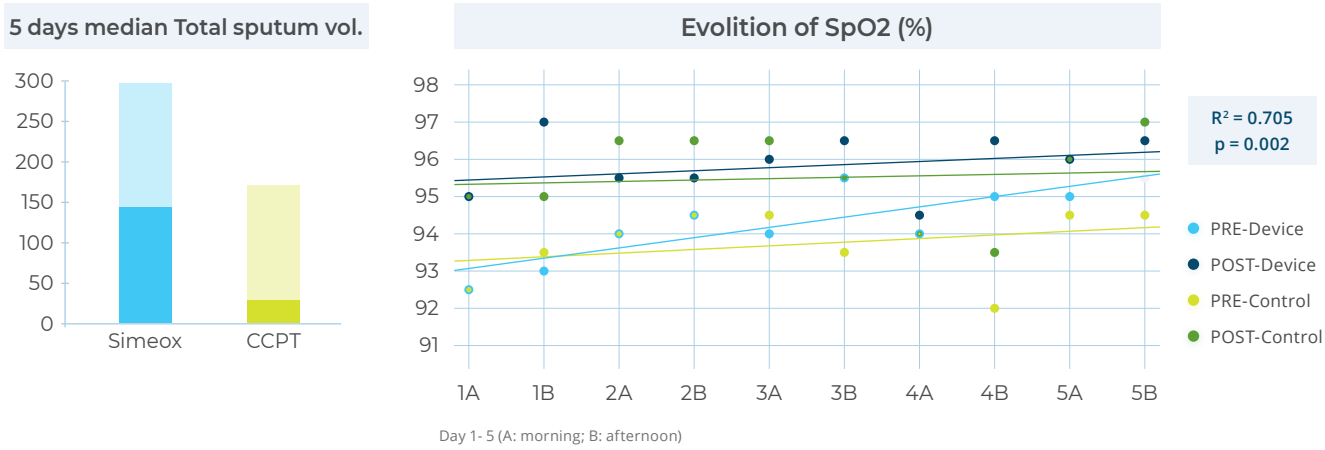
Patients between 18-75 years, with bronchiectasis and diagnosis of cystic fibrosis, COPD or idiopathic pulmonary fibrosis (IPF) reporting symptoms of excessive mucus production and difficulties to clear the mucus were enrolled into the study in consecutive manner and were randomized to either conventional chest physiotherapy (CCPT, control) or Simeox procedure. Both procedures were conducted for 5 days with 2 sessions per day (morning and afternoon). Each session lasted 20 minutes minimum. Measurement of pulmonary function tests, chest expansion, oxygen saturation of hemoglobin was performed before and after session, and mucus was collected daily.

All patients achieved planned procedures.

STUDY RESULTS

12 patients were included from March to April 2018. 7 men, 5 women; Mean age 46.5 y. Lung diseases: 7 CF+BE (Control: 5, Simeox: 2), 3 COPD+BE (Control: 1, Simeox: 2); 2 IPF+BE (Control:0, Simeox:2). After 5 days of therapy, there was a similar trend in FEV1 improvement between Simeox (+2.5%; +70ml) and Control (+1.5%; +40ml). Chest expansion and SpO2 increased significantly to a similar extent in both groups. Total sputum production (median [Min; Max]) seemed to be higher with the device (+143ml [25; 300]) than Control (+30ml [20; 180]) but the difference between groups was not statistically significant.

A longitudinal rise of SpO2 pre-therapy leading to less negative SpO2 variations between ACT sessions was observed during the 5 days in the device group only (R2=0.705; p = 0.002), suggesting a persistent effect of therapy with the device on oxygen saturation. Simeox procedure was tolerated by all patients. Functions of Simeox were easily understood and proper handling was simple for every patient. No safety signal was detected. Patients appreciated the device and found it comfortable.



CONCLUSION

The investigators concluded that these preliminary data showed non-inferiority of Simeox procedure compared to manual chest physiotherapy in patients with bronchiectasis of various origins hospitalized for PEx. Simeox technology was considered safe and feasible for airway clearance management during hospitalization of different lung diseases with mucus retention.

Feasibility and benefits of an innovative Airway Clearance Technology in COPD patients hospitalized for acute exacerbation

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STUDY METHODOLOGY

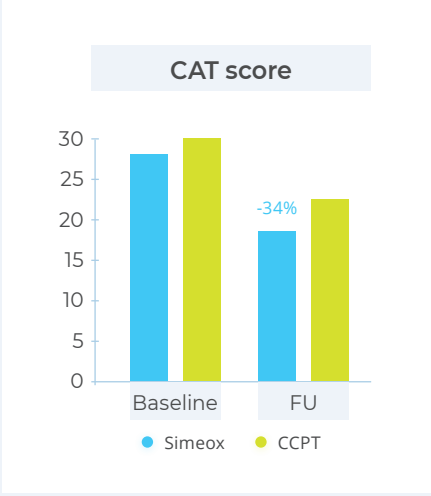
This comparative prospective study conducted in 2018-2019 aimed to assess feasibility and effects of Simeox in COPD patients with acute exacerbation of COPD and suffering from chest congestion despite adherent medication and conventional chest physiotherapy. Patients were included from 13 March 2018 to 20 Sept. 2019. Objectives were to assess ability to properly use the device, safety, tolerance, patients reported outcomes (CAT score), changes in mucus production, and spirometry. Inclusion criteria were: age >18yr, patient with AECOPD reporting symptoms of excessive mucus and difficulties to clear the mucus despite usual manual physiotherapy technique performed by the physiotherapist. Patient had one daily bronchial drainage session with Simeox or conventional chest physiotherapy (CCPT) and pulmonary rehabilitation program session for 6 days. Three successive programs were performed during each device session: 4x6 expiratory cycles, 4x8 expiratory cycles and 4x10 expiratory cycles. Power selection was 25 or 50%. Expectoration were monitored by clinical team during each session and the patient monitored himself the expectoration after the session.

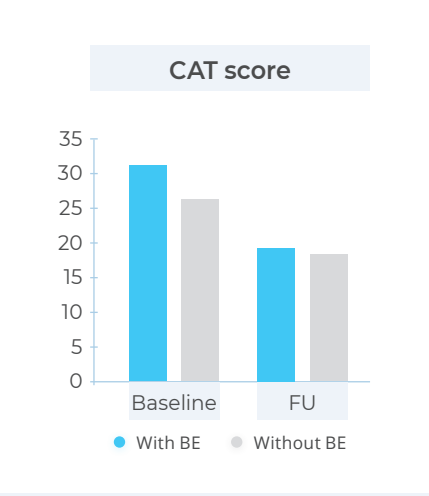
STUDY RESULTS

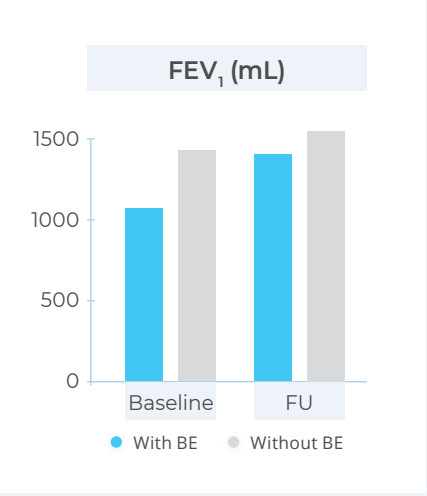
32 patients hospitalized for AECOPD who reported symptoms of excessive mucus congestion were treated with Simeox device (n=19) or manual CP (n=13). The cohort (67y, 68% of male) included a majority of very symptomatic patients with high risk of exacerbation (based on GOLD grading). The duration of clearance therapy session with Simeox was between 15-25 min. Patients were able to use the device after a 15-min of training during the first session.

No adverse event nor pain was reported. Mucus clearance was improved in all patients. FEV1 increased significantly from baseline by +170±60 ml (p=0.0017) and +220±100 ml (p<0.001) in Control and Simeox, respectively (Control vs Simeox NS).

Improvement of CAT score was significantly higher in Simeox than in Control group (-9.6±3.0, -34±9% versus -7.2±1.2, -24±4% respectively; p=0.02). Moreover, in COPD patients with bronchiectasis (BE) comorbidity treated with Simeox, FEV1 and CAT score improvement was even higher (with BE: FEV1 +300±90 ml, CAT -11.7±2.9 vs without BE: FEV1 +180±80, CAT -8.3±2.5; p<0.05).







CONCLUSION

The authors concluded that these results confirmed the feasibility of managing airway clearance in patients with COPD and chest congestion with Simeox device. This technology may contribute to respiratory symptoms and quality of life improvement especially in COPD patients with bronchiectasis without worsening fatigue or pain during chest physiotherapy.

Conclusion on preliminary clinical evidences in bronchiectasis

PhysioAssist has conducted several studies in recognized national centers in various EU countries (Poland, Czech Republic, Romania, Slovakia). These studies included hospitalized patients with non-CF bronchiectasis suffering from pulmonary congestion and requiring airway clearance. Pulmonary function tests, respiratory symptoms, mucus clearance, SpO2, usability, quality of life, exercise capacity and adverse events were evaluated.

Based on the various studies described above, Simeox has been used in 4 clinical studies including patients with non-CF bronchiectasis (Simeox n=41; Control n=34). The results are listed in the following table:

STUDIES	NBR. OF PATIENTS	ETIOLOGY	THERAPY	RESULTS
Mihaltan et al.	10	COPD (7 with BE)	Simeox vs CPT, 5 days	FEV1 (+150 ml) and CAT (3) score seemed to improve with Simeox only
Sliwinsky et al.	21	Non-CF BE	Simeox vs CPT, 7 days	6MWT (+23%, p<0.05) and CAT score (p=0.008) improved with Simeox only
Kolek et al.	12	7 CF and 5 non-CF with BE	Simeox vs CPT, 5 days	Higher increase in sputum vol. with Simeox (+143 vs 30 ml). Less negative SpO2 variation with Simeox.
Solovic et al.	32	COPD (12 with BE)	Simeox vs CPT, 6 days	Higher improvement in CAT score with Simeox (10 vs 7, p=0.02). Simeox seemed to increase FEV1 in COPD with BE (+300 ml)

Findings are summarized below

Patients with BE can acquire quickly autonomous usage of the device during hospitalization after a short training by physiotherapists. The technology is very well tolerated and most patients find it comfortable and easy to use. No side effect related to Simeox device is reported. **Mucus clearance improves at least to the same extent as manual physiotherapy. Moreover, Simeox device may provide also additional benefits on respiratory symptoms, lung function and quality of life in patients with non-CF bronchiectasis.** While the clinical studies discussed above are conducted in hospitalized patients, the data provide confidence in home use for Simeox in these patients after proper training.

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