Effectiveness of chest physiotherapy and pulmonary rehabilitation in patients with non-cystic fibrosis bronchiectasis: a narrative review

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Abstract

Respiratory physiotherapy and rehabilitation are important therapeutic options in non-cystic fibrosis bronchiectasis (NCFB). The aims of this review of clinical trials were to evaluate the safety and the effects on physiologic and clinical outcomes of airway clearance techniques (ACTs) and rehabilitation in NCFB patients, in comparison to usual care. The search was performed on March 2018 by using PubMed and PeDro databases. 33 studies were selected. The use of ACTs for NCFB were effective in increasing sputum volume although no benefit in quality of life (QoL) or pulmonary exacerbations were observed. There were no differences in effectiveness between the several techniques used. Humidification and saline inhalation were able to aid airway clearance. Hypertonic solution (HS) was more effective than isotonic solutions (IS) in improving expectoration and sputum viscosity. Pulmonary rehabilitation (PR) was found to be associated with short term benefits in exercise capacity, dyspnea and fatigue. Exercise training seems to improve quality of life and lower exacerbation rate, but long-term data are not available. Further studies are necessary to identify the most feasible long-term outcomes such as QoL and exacerbation rate.

Introduction

Bronchiectasis is an irreversible and progressive condition of the airways characterized by the presence of bronchial walls dilatation due to alterations in their structure. They may be congenital or more frequently acquired, secondary to a wide variety of conditions including lung infections, as severe pneumonia following measles, pertussis and tuberculosis. Chronic fibrous lung diseases such as those following abnormal pneumonia or inhalation of foreign bodies, harmful gases or particles, also predispose to the development of bronchiectasis. Congenital diseases such as cystic fibrosis, primitive ciliary dyskinesia, α-1 antitrypsin deficiency, and immunodeficiencies can also result in bronchiectasis [1].

Bronchial walls dilatation usually involves segmental or subsegmental bronchioles, and can spread to one or more pulmonary lobes. These anatomical alterations combined with reduced airway clearance expose patients to the risk of bacterial colonization and recurrent infections [2]; the latter, in association with a chronic inflammatory reaction, can cause further airway damage, triggering a vicious circle. The small airways may also be involved as a consequence of proximal obstruction. In fact, in advanced stages of the disease peripheral spaces dilatation and deteriorated respiratory function are also present [3].

Patients with bronchiectasis may have heterogeneous clinical manifestations as repeated bronchial exacerbation episodes, with or without fever, increased cough and mucus production, hemoptysis, and daily production of significant amounts of mucus secretions. Some patients may have dry cough, with little or no expectoration. Bronchiectasis may be associated with other symptoms such as dyspnea, chest pain, fatigue, reduced exercise tolerance and reduced life expectancy [4-6]. Advanced stages of disease progress to the development of chronic respiratory failure and cor pulmonale-related heart failure [7].

Treatment of bronchiectasis is multifaceted and aims to control symptoms, improve life expectancy, prevent progressive pulmonary
damage, reduce the number of exacerbations, and preserve pulmonary function. Recently, a therapeutic approach based on the severity of the disease has been promoted, involving the regular use of respiratory physiotherapy at all levels of the disease [8]. Respiratory physiotherapy goals include: facilitating secretions mobilization, optimizing ventilation efficiency, preserving or increasing exercise tolerance, reducing dyspnea and chest pain, improving patient knowledge about the disease, and optimizing physical performance of the subject and the management of the disease [7].

The aims of this review of clinical trials were to evaluate the safety and the effects on physiologic and clinical outcomes of airway clearance techniques and rehabilitation in patients with non-cystic fibrosis bronchiectasis (NCFB), in comparison of usual care.

Materials and Methods

We searched in MEDLINE and PEDro databases, from 2005 to May 2018, with no language restriction. We also reviewed the references of retrieved articles for additional studies. We performed a literature search according to PRISMA statement (www.prisma-statement.org).

Interventions evaluated were airway clearance techniques (ACTs), humidification, saline inhalation, and pulmonary rehabilitation (PR).

The interventions were compared with a control group (usual medical treatment), no treatment or sham treatment. Outcomes assessed were sputum volume, oxygen saturation, pulmonary function, number of pulmonary exacerbations, quality of life, respiratory symptoms, adverse events. The studies selected were clinical trials, comparative studies, controlled clinical trials and randomized controlled trials (RCT).

As search terms we used: “bronchiectasis” as keyword, which had to be present in the title or abstract of the articles(field). It was then linked via Boolean AND to other key words all in Mesh, inherent to all possible physiotherapy interventions, linked to each other by an OR operator. Through search builder, the final search strip was composed as follows: bronchiectasis[Title/Abstract] AND(physiotherapy OR physical therapy OR respiratory therapy OR exercise OR bronchial hygiene OR pulmonary rehabilitation OR chest therapy OR training OR hypertonic saline OR humidification).

The following filters were applied: humans, type of articles: clinical trial, comparative studies, controlled clinical trial, randomized controlled trial, publication between 1 January 2005 and 31 March 2018.

A subsequent search in the PEDro database allowed us to find additional studies. In this search the keyword “bronchiectasis” was again used, and had to be present in the abstract and title field within advanced search. Other fields were also completed: respiratory therapy (Therapy), clinical trials (Methods), published since 2005, match terms with AND. We found 23 articles.

Results

We identified 126 potentially relevant articles. Of these, 99 were excluded after the abstracts were read.

Finally, 33 studies were included in this review: 27 were found from primary searching and the others identified among the references. The process for selecting studies and exclusion criteria are displayed in Figure 1.

A total of 33 articles were included as they addressed the three main areas of intervention: tracheo-bronchial clearance (20 studies), airway humidification and saline inhalation (6 studies), and exercise (7 studies).

Bronchial airway clearance

ACTs are now recommended in bronchiectasis aimed at improving airway clearance [9-11]. Only in recent years we have witnessed a gradual increase in specific studies on NCFB.

The first studies were focused on the direct comparison of two main techniques: Oscillatory Positive Expiratory Pressure techniques (O-PEP) (Flutter and Acapella), and controlled breathing techniques [Active Cycle of Breathing Technique (ACBT)] and Breathing Control (BC) with or without posture changes (Table 1). Three crosstudies [12-14], and 2 RCTs [15,16] have showed similar outcomes in respiratory function parameters and sputum weight. There were no significant differences in efficacy between the techniques proposed, both in acute [15,16] and chronic patients [12-14]. In a single study the forced expiratory volume in 1 s (FEV1) improved with flutter (P<0.03) [12]; in another study ACBT associated with posture changes was associated with improved secretions drainage than flutter [14]. Several studies have found that O-PEP device was the preferred technique both in chronic (in 65%, 70% and 44%, respectively) [12-14] and in acute patients, because it was considered more effective (Flutter vs BC p=0.011) [15]. However, no statistically significant difference in tolerance and duration of treatment was observed (Acapella vs ACBT P<0.06) [16]. The main limitations in comparing the results of these studies are the use of different scales for subjective measurements (chronic respiratory questionnaire (CRQ), Borg dyspnea, visual analogic scale (VAS), Likert Scale). Also, different application techniques time ranging from single daily treatment to twice or more times per day, for a total time that never exceeded 4 weeks have been used [13,14].

In 2009, Murray proposed a three-month crossover study to evaluate the effectiveness of regular chest physiotherapy [17]. There was a significant difference in medium to long term sputum volume using Acapella twice per day compared to the group not treated with airway clearance. The increase in the sputum volume was associated with higher exercise tolerance (Incremental Shuttle Walking Test (ISWT) p<0.001) and improved quality of life (QoL) [Leicester Cough Questionnaire (LCQ) p<0.002, Saint George Respiratory Questionnaire (SGRQ) p<0.005]. However, there were no spirometric parameters and number of exacerbations improvement.

Guimaraes performed a crossover-controlled study [18], and although there was a single treatment session for each technique (Expiration Lente Totale Glotte Ouverte en infraLateral (ELTGOL) and flutter), static volumes significantly decreased after only 15 minutes compared to the control group in the treatment with ELTGOL [total lung capacity (TLC) 9.66%, Functional residual capacity (FRC) 14.48%, residual volume (RV) 18.72%] and with Flutter (TLC 18.27%, FRC 25.81% and RV 29.55%). The authors concluded that these techniques were equally useful in reducing the degree of hyperinflation in obstructive syndromes. Moreover, the ELTGOL technique allowed faster secretions drainage than the flutter did (p<0.05). The first study of long-term effectiveness of ELTGOL in cleaning secretions was described in a recent randomized placebo-controlled trial [19]. Performance of the
ELTGOL technique twice-daily over a 1-year period increased overall 24-h sputum volume (during first intervention and 24 h later) by 17 mL compared to placebo (p<0.001). The trial reported lower exacerbation rate (p=0.042), an improvement in QoL (SGRQ p<0.001), and a reduction in the impact of coughing (LCQ p<0.001). This study is the first long-term randomized controlled trial of an ACT. Finally, two recent studies have analyzed the efficacy and comfort of ACBT compared to postural drainage (PD), concluding that there were no significant differences in sputum volume [20]; nevertheless, ACBT was the preferred technique [21].

Several studies have analyzed the use of alternative techniques to enhance airway clearance (Table 2). Naraparaju compared Acapella with an Inspiratory Muscle Training instrument (IMT), concluding on the superiority of the O-PEP device with a sputum amount of 7.16 ±1.12 mL vs 6.4±1.08 ml (p=0.014) [22]. A study on a population of 78 patients with chronic obstructive pulmonary disease (COPD) and 20 with bronchiectasis evaluated the efficacy of temporary PEP (T-PEP) on several outcomes. A statistically significant improvement in inspiratory capacity (IC) was observed in the T-PEP group compared to the control group, in which only manual techniques were performed [23].

Limitations in this study were the treatment time (20 min for manual treatment vs 20 min + 15 min for the T-PEP group) and population data (bronchiectasis patients were not described separately in the study). Herrero-Cortina et al. [24] investigated the efficacy of T-PEP compared to other manual techniques [autogenic drainage (AD) and ELTGOL] in a more homogeneous group of patients. The authors emphasized the equal effectiveness of the three techniques in draining secretions over 24 h after physiotherapy. Furthermore, a progressively lower production of sputum in daily life compared to baseline (p<0.001) was observed. Whereas AD and ELTGOL were associated with faster sputum drainage, sometimes within the same session, T-PEP appeared capable of generating a constant drainage, even after the application. The study of D’Abrasca et al. [25] confirmed the efficacy of T-PEP on pulmonary function parameters. The author additionally observed a reduction in oxygen requirement among patients on long-term oxygen therapy compared to the group treated with PEP Mask.

A recent RCT investigated the short-term efficacy of high frequency chest wall oscillation (HFCWO). HFCWO applied for 30 min twice per day at a frequency of 13-15 Hz was compared with a commonly used ACTs (PEP, ELTGOL) and with medical therapy.
Table 1. Studies evaluating the use of oscillating positive expiratory pressure (PEP) and controlled breathing techniques (ACBT, BC, ELTGOL).

| Reference          | No. of patients (FEV1) | Study design                  | Treatment                                                                 | Outcomes                                                                 | Significant results |
|--------------------|------------------------|-------------------------------|---------------------------------------------------------------------------|---------------------------------------------------------------------------|---------------------|
| Thompson 2002 [12] | 17 (70%)               | Crossover 4 weeks (no wash out) | Twice per day until no further sputum to expectorate                     | Spirometric parameters, sputum weight, Borg dyspnea, CRQ                  | ↑ FEV1, after Flutter |
|                    |                        |                               | Information sheets FET after both techniques                              |                                                                          | 65% of patients preferred Flutter device                             |
|                    |                        |                               | PD in 2 positions chosen by therapist as needed                            |                                                                          |                     |
|                    |                        |                               | Flutter device ACBT TEE, BC, HUFF                                          |                                                                          |                     |
| Patterson 2005 [13]| 20 (64%)               | Crossover 2 days (no wash out) | 1 time per day - lasting up to 30 min Medication at least 1 hour before therapy | Spirometric parameters, sputum weight, Borg dyspnea, Dyspnea (VAS)         | 70% of patients preferred Flutter device                             |
|                    |                        |                               | PD in 2 positions chosen by therapist as necessary                        |                                                                          |                     |
|                    |                        |                               | Acapella+PD Individual Acapella setting                                    |                                                                          |                     |
|                    |                        |                               | ACBT+PD TEE, BC, HUFF PD gravity assisted in 2 positions chosen by therapist |                                                                          |                     |
| Eaton 2007 [14]    | 36 (57.8%)             | Crossover 3 days (2 days wash out) | 1 time per day - lasting up to 30 min Information sheets Flutter devices | Spirometric parameters, sputum weight and volume, timing of sessions, Likert scale | ↑ sputum weight and volume after ACBT+PD |
|                    |                        |                               | ACBT TEE, BC, HUFF                                                         |                                                                          | 44% of patients preferred Flutter device                             |
|                    |                        |                               | PD gravity assisted in 2 positions chosen by therapist                    |                                                                          |                     |
|                    |                        |                               | Individual Acapella setting                                                |                                                                          |                     |
|                    |                        |                               | TEE, BC, HUFF                                                              |                                                                          |                     |
|                    |                        |                               | Borg dyspnea, CRQ                                                          |                                                                          |                     |
| Tsang 2003 [15]    | 15 (41%)               | RCT 1 week                    | 3 times per day - lasting 15 min                                          | Spirometric parameters, Heart rate, O2 saturation, Bronchial encumbrance (VAS) |                     |
|                    |                        |                               | BC5 deep inspirations with relaxed                                         |                                                                          |                     |
|                    |                        |                               | BC+PD2 positions with gravity                                              |                                                                          |                     |
|                    |                        |                               | BC+flutter device Patient in sitting position                              |                                                                          |                     |
|                    |                        |                               | Normal inspiration with active exhalation through the device               |                                                                          |                     |
| Patterson 2007 [16]| 20 Acute exacerbation (65%) | RCT 14 days                  | 2 times per day - lasting up to 30 min Acapella Individual Acapella setting | Spirometric parameters, O2 saturation, sputum weight and volume, dyspnea (VAS), timing of sessions, Borg dyspnea | ↑ Acceptability of sessions with Acapella |
|                    |                        |                               | Usual (ACBT) Usual technique review with therapist                        |                                                                          |                     |
| Murray 2009 [17]   | 20 (75%)               | Crossover Acapella           | No chest therapies                                                        | Spirometric parameters, LCO, sputum volume                                | ↑ LCO, sputum volume and ISWT after Acapella |
|                    |                        |                               | 3 months 2 times per day lasting 20-30 min                                |                                                                          |                     |
|                    |                        |                               | (1 month breath hold, active exhalation 2-3 HUFF or cough                |                                                                          |                     |
|                    |                        |                               | Device set at position 310 inspirations up to ¾ MIC,                      |                                                                          |                     |
|                    |                        |                               | 10 inspirations per 3 min with relaxed gravity                            |                                                                          |                     |
| Guimarães 2012 [18]| 10 (53%)               | Crossover 3 days (1 week wash out) | 100 x 2 mcg salbutamol 1 time per day ELTGOL Not assisted by therapist     | Spirometric parameters, Sputum volume                                    | ↓ RV, FRC, TLC after ELTGOL and after flutter compared to control group |
|                    |                        |                               | 7.5 min each lateral position                                             |                                                                          | ↑ sputum volume after ELTGOL                                        |
|                    |                        |                               | Flutter Patient in sitting position, inspiration up to TLC and relaxed expiration |                                                                          | ↓ IC/TLC after flutter                                               |

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alone (control group). Both active treatment groups were associated with a significant increase in the amount of sputum, and a reduction of symptoms and scores related to health status in comparison to the control group. Direct comparison between the two active treatment groups demonstrated the superior efficacy of HFCWO in reducing inflammatory parameters, and in improving forced vital capacity (FVC) and FEV1 [26].

In another study, intrapulmonary percussive ventilation (IPV) was compared with conventional therapy: PD and forced expiration technique (FET). In both groups there was no significant change in oxygen saturation, whereas a reduction of respiratory rate, an improvement in dyspnea and an increased amount of sputum were observed in the group treated with IPV [27].

Furthermore, four crossover studies (Table 3) analyzed the direct mechanical effects of O-PEP on mucus and airway resistance. Valente [28] investigated the effect of oscillating waves comparing the flutter with a “sham flutter” obtained by removing the metal ball and partially blocking the holes to maintain the PEP effect. There were no significant changes in the displacement velocity and mucosal adhesion after 20 and 40 minutes of treatment. Other recent studies have used sham flutter as a method of comparison, with different results from the former study. Tambascio highlighted that mechanical oscillations were able to modify mucus rheology by reducing adhesive strength (p<0.05) [29]. Figueiredo observed that the use of vibrations decreased bronchial tree resistances, particularly distal resistances, improving ventilation distribution (p<0.05) in patients with hypersecretive bronchiectasis [30]. Ramos has showed that

| Reference | No. of patients (FEV1) | Study design | Treatment | Outcomes | Significant results |
|-----------|------------------------|--------------|-----------|----------|---------------------|
| Munoz 2018 [19] | 44 (60%) | RCT1 year | 2 times per day lasting 15 min for each lung affected (1 lung = 15 min; 2 lungs = 30 min) ELTGOL Not assisted by therapist | Sputum volume after 24h and after 1-3-6-9-12 months, Inflammatory markers, number of exacerbations, time to the first exacerbation, LCQ and SGRQ at 6-12 months, Sputum typesetting, FEV1, PEVI Exercise capacity, Treatment adherence Side effects | ↑ sputum volume after ELTGOL at all times ↓ number of exacerbations after ELTGOL ↑ LCQ after ELTGOL at all times ↓ SGRQ after ELTGOL at all times ↑ Treatment adherence with ELTGOL |
| Abdelhalim 2015 [20] | 30 acute exacerbation (55%) | RCT14 days PD gravity assisted | 2 times per day - lasting 15-20 min ACBT+PDTEE+BC+HUFF | LCQ, mMRC, Spirometric parameters, Blood gas analysis, sputum volume | ↑ LCQ e ↑PaO2 after ACBT ↑ Blood gas analysis and sputum volume after CPT |
| Syed 2009 [21] | 35 (ns) | Crossover 2 days (12 hours wash out) | 4 times per day - lasting up to 30 min CPT+PD Diaphragmatic breathing, clapping | Spirometric parameters, Spirometric parameters, sputum weight and volume, comfort (VAS) | ↑ comfort after ACBT |

↑, increase; ↓, decrease; no negative meaning or worsening; FET, forced expiration technique; ACBT, active cycle of breathing technique; BC, breathing control; TEE, thoracic expansion exercise; HUFF, forced expiration with open glottis; PD, postural drainage; RTC, randomised controlled trial; CRQ, chronic respiratory questionnaire; FEV1, forced expiration volume at first second; VAS, visual analogic scale; MIC, maximum inspiratory capacity; CPT, chest physiotherapy; LCQ, Leicester cough questionnaire; mMRC, modified Medical Research Council dyspnea scale; PaO2, oxygen partial pressure; MEP, maximum inspiratory pressure; MEIP, maximum expiratory pressure; ISWT, incremental shuttle walking test; SGRQ, Saint George respiratory questionnaire; ELTGOL, expiration leinte totale glotte ouverte en infralateral; TLC, total lung capacity; RV, residual volume; FRC, functional residual capacity; IC, inspiratory capacity; ns, not specified. *This technique is often poorly described. When not specified positioning may be referred to change in regional lung ventilation or may be only turning. Please refer to authors.
manual percussion and forced expiration with open glottis (HUFF) might be effective in improving the drainage of viscous-elastic secretions, but only after application times longer than 60-90 min [31].

**Interventions aiding airway clearance**

In current clinical practice, humidification and saline (isotonic

### Table 2. Studies evaluating the use of techniques other than usual PEP (IMT, T-PEP, HFCWO, IPV).

| Reference          | No. of patients (FEV₁) | Study design | Treatment                                                                 | Outcomes                                                                 | Significant result                              |
|--------------------|------------------------|--------------|---------------------------------------------------------------------------|--------------------------------------------------------------------------|-------------------------------------------------|
| Naraparaju 2010 [22] | 30 (44.5%)             | Crossover 2 days (no wash out) | 1 time per day Medication at least 1 hour before treatment Acapella10 inspirations up to ¾ MIC, 2-3 sec breath hold, active exhalation through device HUFF or cough every 5 breaths | Sputum volume, timing of session, patient preference | † Sputum volume after Acapella                   |
| Venturelli 2012 [23]    | 98 (56%) only 20 out of 98 were NCFB | RCT 10 days | 2 times per day Training with therapist Manually assisted techniques + T-PEP 20 min + 15 min T-PEP | Spirometric parameters, MIP, MEP, PaO₂/FiO₂, sputum volume, Sputum density and purulence, bronchial encumbrance (VAS) | † FEV₁, FVC, CV after T-PEP, † IC after T-PEP |
| Herrero 2016 [24]       | 29 (63%)               | Crossover 3 weeks (1 week wash out) | 3 times per week - lasting 40 min AD Breathing from lower through higher lung volume levels with open glottis. Not assisted | Spirometric parameters, O₂ saturation, Heart rate, Sputum weight after 40 min and 24 hours, LCQ, Likert scale to T-PEP | † Sputum weight during wash out compared to basal values, † sputum weight during session with AD and ELTGOL compared with T-PEP |
| D’Abrosca 2017 [25]     | 162 (51%)             | Retrospective 10 days | 2 times per day – lasting 15 min Sitting position (+2 times per day exercise training upper and lower limbs) PEP Deep inspiration, active exhalation FET or HUFF or cough every 2 min | Spirometric parameters, Blood gas analysis (except CO₂) after both techniques compared to basal values | † FVC, FEV₁, PEF, blood gas analysis with emphysema and/or long-time oxygen therapy, † usual FiO₂ after T-PEP, † usual FiO₂ after PEP, † PaO₂/FiO₂ after PEP |

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or hypertonic) administration are used to modify mucus characteristics and improve airway clearance.

**Humidification**

In 1992, Conway [32] published a study evaluating airway clearance by radio-marking aerosol after a session of cold humidification with sterile water. Significant results were found for sputum weight (p<0.05) and radio-marking clearance (p<0.05).

More recently, several studies have evaluated the effects of warm air humidification in subjects with bronchiectasis (Table 4). In the first observational study, 14 patients were enrolled for 7 days of home-warming humidification lasting 3 h a day, with a high-flow system that supplied water vapor air at 37°C at a flow of 20 to 25 l/min through a special nasal-cannula. The study measured tracheobronchial clearance through the retention of a radioactive tracer monitored at 6 and 24 hours, and assessed pulmonary function. After the treatment, an increase in mucosal clearance was observed (p=0.007) [33].

In 2012, Rea and colleagues [34] evaluated the effects of one-year-treatment using the same high-flow system from the former study. They recruited 108 patients, including 73 patients with COPD and 45 with bronchiectasis. The treatment group performed active humidification using high flow nasal cannula (HFNC) 2 h per day, the control group received usual care according to Australian-Asian guidelines [35]. There were no statistically significant differences between the two groups in the exacerbation rate, number of admissions, distance walked during 6 minutes walking test (6MWT) and inflammatory markers; whereas statistically significant differences were found in the total days of exacerbations, number of subjects who did not show exacerbations, FEV₁ and FVC at 6 and 12 months, antibiotic therapy consumption, and SGRQ scores.

**Inhalation of nebulized saline solution**

In the study published by Kellett and coll. four interventions with different humidification techniques and timing were compared. Saline solutions, isotonic solution (IS) and hypertonic solution (HS), have proved to be significantly more effective in increasing sputum amount, reducing viscosity, and facilitating expectoration compared to ACBT alone. HS was significantly more efficient than IS regarding the weight of produced sputum, viscosity and ease of sputum production [36].

Subsequently, the same authors conducted a crossover study that lasted 9 months comparing the use of IS at 0.9% to HS at 7%. A significant improvement in FEV₁ (p<0.01) and FVC (p<0.01) in the

Table 2. Continued from previous page.

| Reference        | No. of patients (FEV₁) | Study design | Treatment                                                                 | Outcomes                                                                 | Significant result                                                                 |
|------------------|------------------------|--------------|---------------------------------------------------------------------------|--------------------------------------------------------------------------|-----------------------------------------------------------------------------------|
| Nicolini 2013 [26] | 30 (60%)               | RCT2 weeks   | 2 times per day HFCWO 30 min 1-15 Hz Patient in sitting position          | Spirometric parameters, MIP, MEP, Sputum cellularity Sputum volume        | ↑ sputum volume, BCSS, CAT, mMRC after CPT compared to control group               |
|                  |                        |              | CPT 45 min ELTIGOL PEP mask, PEP bottle, Acapella                        | Blood gas analysis Sputum availability                                   |                                                                                   |
|                  |                        |              | Control no chest therapy                                                 |                                                                          |                                                                                   |
| Paneroni 2011 [27] | 22 (53%)               | Crossover    | 1 time per day - lasting 30 min Cough after treatment session            | O₂ saturation, heart rate, respiratory rate, sputum volume and weight,   | ↑ Respiratory rate, dyspnea and discomfort (VAS)                                  |
|                  |                        | 2 days       | Patient in sitting position, 2 phases low pressure high frequency, 1 phase high pressure low frequency | bronchial encumbrance (VAS), discomfort and dyspnea (VAS)                |                                                                                   |
|                  |                        | (no wash out)| CPT PD in 3 position with FET, percussion and clapping set in a cycle    |                                                                          |                                                                                   |

*T, increase, improvement; ↓, only decrease, no negative meaning or worsening; ns, not specified; RCT, randomised controlled trial; NCFB, non-cystic fibrosis bronchiectasis; IMT, inspiratory muscle training; T-PEP, temporary PEP (called also UNIKO); HFCWO, High frequency chest wall oscillation; IPV, intrapulmonary percussive ventilation; HUFF, forced expiration with open glottis; CPT, chest physiotherapy; PD, postural drainage; FET, forced expiration technique; ELTIGOL, expiration lente totale glotte ouverte en decubitus lateral; VAS, visual analogic scale; BCSS, breathlessness, cough and sputum scale; CAT, COPD assessment test; mMRC, modified Medical Research Council dyspnea scale; O₂, Quality of Life; AD, autogenic drainage; MIC, maximum inspiratory capacity; MIP, maximum inspiratory pressure; MEP, maximum expiratory pressure; RV, residual volume; TLC, total lung capacity; FRC, functional residual capacity; FEV₁, forced expiration volume at first second; PEF, peak expiratory flow; CO₂, carbon dioxide; PaO₂, oxygen partial pressure; PaO₂/FiO₂, derived arterial oxygen tension to inspiratory oxygen fraction ratio; FET, forced expiration flow at 50% of vital capacity.

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hypertonic treatment phase compared with the isotonic control phase was observed. Significant differences were found for SGRQ global score and in domains of symptoms and impacts (p<0.05), but not for domain activity. A retrospective analysis found a lower use of antibiotics (p<0.05) and number of exacerbations (p<0.05) in the active phases of the study compared to the period prior to the study [37]. An RCT compared the use of HS at 6% with the use of IS at 0.9% twice per day for a period of 12 months. A daily diary was used to record patient adherence, changes in medical therapy, and symptoms (differences in sputum color or volume, hemoptysis, coughing, dyspnea, lethargy, fever or nasal secretions). There was no statistically significant difference at 3, 6, and 12 months between the two groups [38].

Physical exercise

Some studies have investigated the role and effectiveness of specific muscle training programs and/or respiratory muscle training in bronchiectasis patients (Table 5).

Newall examined the effects of a non-specific training program, with and without the combination of IMT, on exercise tolerance and QoL versus control group only involved in educational meetings. A significant increase in ISWT in both sham (PR-SHAM) and intervention (PR-IMT) groups (96.7 m and 124.5 m respectively) compared to baseline was observed after 8 weeks without significant differences between the two groups. Significant improvement in the strength of respiratory muscles was observed, with an increase in maximal inspiratory pressure (MIP) in both groups who performed training, without significant differences between the two groups (p=0.22). There was no improvement in the peak maximal oxygen uptake (VO₂ max) in any of the three groups. At three months follow-up evaluation, improvement in exercise capacity was maintained only in the PR-IMT group compared to PR-SHAM group (p=0.01). Also, SGRQ significantly improved in the PR-IMT group compared to the control group (p=0.05). Conversely, in the PR-SHAM group there was no significant improvement in QoL despite the improvement in exercise capacity. Finally, no significant changes in the sputum volume were observed in any of the participants [39].

To confirm that the same chest rehabilitation programs used in COPD patients are effective also in patients with bronchiectasis, Ong [40] retrospectively compared the effects of the same outpatient retraining program performed in patients with bronchiectasis and in patients with COPD. At the end of an eight-week rehabilitation program, a significant improvement in the 6MWT (53-meter average increase) and in the CRQ (average change of 14.0 units) was observed in the bronchiectasis group. This positive effect was also significantly higher than the baseline at one year (20.5-meter average increase for 6MWT increase and 12.1 points at CRQ) and did not differ from those found in the COPD patients’ group. Another retrospective study [41] showed significant improvement in vital capacity (VC) and a significant reduction in RV in 41 patients with bronchiectasis (7 with Cystic Fibrosis) after a 12-week training program, although the increase in the 6MWT did not show significant variations. The authors demonstrated that physical exercise was not contraindicated, and developed functional benefits,

### Table 3. Physiological studies about effects of manual or mechanical oscillation.

| Reference         | No. of patients (FEV₁) | Study design | Treatment                                                                 | Outcomes                                                                 | Significant result                          |
|-------------------|------------------------|--------------|---------------------------------------------------------------------------|---------------------------------------------------------------------------|---------------------------------------------|
| Valente 2004 [28] | 8 (63%)                | Crossover 3 days (no wash out) | 1 time per day Flutters – lasting 40 min Sharm flutter PEP set at 6-8 cm H₂O | Coughs                                                                 | Sputum viscosity and stickiness with oscillations | No changes in sputum rheology |
| Tambascio 2011 [29] | 18 (60%)              | Crossover 4 weeks (1 week wash out) | 1 time per day – lasting 30 min Patient in sitting position Therapist overlook Flutters | Sputum viscosity and stickiness                                               | Sputum viscosity after flutter              |
| Figueiredo 2012 [30] | 8 (65%)               | Crossover 2 days (1 week wash out) | 1 time per day – lasting 15 min Flutters Patient in sitting position, inspirations to TLC and relaxed exhalation | Sharm flutters                                                             | Respiratory mechanics with oscillometer      |
| Ramos 2015 [31]  | 22 (n.s.%)             | Cross over 4 days (no wash out) | 1 time per day in a set cycle: 20 min cough before treatment + 10 min rest + 3 cycle of treatment lasting 30 min (20 min +10 min rest) PD + cough Cough Patient performs all cough steps | Sputum typesetting, viscosity and elasticity | ↑ % dry and wet sputum after 60 min of PD+ clapping |

↑, increase, improvement; ↓, only decrease, no negative meaning or worsening; n.s., not specified; PEP, positive expiratory pressure; HUFF, forced expiration with open glottis; PD, postural drainage; ELT/GO, expiration lente totale glotte ouverte en decubitus lateral; FEV₁, forced expiration volume at first second; TLC, total lung capacity.
also in severely obstructed patients (mean FEV₁ 44% of predicted). They suggested a lack of improvement in the 6MWT due to the fact that enrolled subjects had a high baseline exercise tolerance (mean distance covered 425 m). Other comments from the same study were that the design of training programs for bronchiectasis patients should differ from those for patients with COPD in terms of intensity, frequency and duration of sessions.

A high-intensity training program (workload achieving a heart rate of 70-80% of the maximum reached at 6MWT and a Borg dyspnea score of 3-5) was implemented in another retrospective study. A significant improvement in the 6MWT, QoL and dyspnea reduction [42] was observed.

Two further studies have compared training programs in addition to ACTs [43,44]. In the study published by Mandal et al. [43], 30 patients with clinical stability and purulent or mucopurulent expectoration who performed regular airway clearance sessions were randomized into two groups: a control group performing bronchial airway clearance twice a day, and a treatment group, which added a three weekly training session. At the end of the study, there was a significant improvement in the treatment group: ISWT

### Table 4. Studies evaluating the use of adjuncts to physiotherapy (humidification or saline nebulization).

| Reference | No. of patients (FEV₁) | Study design | Treatment | Outcomes | Significant result |
|-----------|------------------------|--------------|-----------|----------|-------------------|
| Conway 1992 [32] | 7 (46% on average, broad range) | Crossover 2 days (1 week wash out) | Technetium 99 radioaerosol + 10 min rest Humidification 30 min sterile water nebulization with System 22 Misty Ox Nebulizing Humidifier PD and FET lasting 20 min | Radiolabel clearance, FEV₁, sputum weight after humidification | †Radiolabel clearance and sputum weight clearance |
| Hasan 2008 [33] | 14 (51%) | Prospective observational 7 days | Domiciliary humidification 3 hours per day with MR880 humidifier with nasal flow system 20-25 L/min Temperature 37ºC | Radiolabel clearance, FEVI, FVC, Penetration index, Alveolar deposition, AUC | †Radiolabel clearance and AUC with humidification |
| Rea 2010 [34] | 108 mixed group NCFB and COPD (60%) | RCT 12 months | Humidification 2 hours per day at least with MR880 humidifier with optiflow system | Control | FEV₁, FVC, Exacerbation rate, hospitalization rate, SGRQ, 6MWT, inflammatory markers |
| Kellett 2005 [36] | 24 (ns) Sputum <10 ml per day | Crossover 4 weeks (1 week wash out) | 1 session alone lasting 5 min nebulization+10-20 min treatment ACBT only 2 side lying positions, maximum 10 min each 10 min break between different steps Terbutaline Terbutaline Terbutaline + ACBT +IS 0.9% + HS 7% +ACBT +ACBT | Spirometric parameters, sputum weight, sputum viscosity, ease of expectoration (VAS) | †sputum weight, sputum viscosity and ease of expectoration with HS e IS compared to ACBT only |
| Kellett 2011 [37] | 32 (66.4%) | Crossover 8 months (1 month wash out) | 5 times per week lasting 30 min per day HS 4 ml 7% | IS (placebo) 4 mL 0.9% | Spirometric parameters, SGRQ, antibiotic usage, exacerbation rate, sputum viscosity, ease of expectoration (VAS) |
| Nicholson 2012 [38] | 48 (82.8%) | RCT 12 months | 2 times per day Daily diary 100 g salbutamol with spacer Stop usual ACT HS5 mL 6% | IS (placebo) 5 mL 0.9% | Spirometric parameters, SGRQ, LCQ, exacerbation rate, sputum viscosity |

↑, increase; improvement; ↓, only decrease; no negative meaning or worsening; ns, not specified; RTC, randomised controlled trial; FEV₁, forced expiration volume at first second; FVC, forced vital capacity; IS, Isotonic Saline solution; HS, Hypertonic Saline solution; PD, postural drainage; FET, forced expiration technique; ACBT, active cycle of breathing technique; VAS, visual analogic scale; AUC, area under tracheobronchial retention curve; SGRQ, Saint George respiratory questionnaire; LCQ, Leicester cough questionnaire; COPD, chronic obstructive pulmonary disease; NCFB, non-fibrosis cystic bronchiectasis; 6MWT, 6 minutes walking test.
and endurance walk test (EWT) increased 56.7m (p=0.03) and 193.3m (p=0.01) respectively. Furthermore, QoL questionnaires were improved: LCQ increased by 2.6 units (p<0.001) and SGRQ by 8 units (p<0.001) in the training group. No improvement was observed in the control group that only performed bronchial airway clearance sessions with Acapella. Even at 20 weeks, 3 months after

Table 5. Studies evaluating pulmonary rehabilitation programs (aerobic exercise training, lower and upper limb strength training, inspiratory muscle training).

| Reference          | No. of patients (FEV1) | Study design | Treatment                                                                 | Outcomes                              | Significant result |
|--------------------|------------------------|--------------|---------------------------------------------------------------------------|---------------------------------------|--------------------|
| Newall 2005 [39]   | 32 (62%)               | RCT 8 weeks  | Educational program 2 times per week assisted sessions lasting 15 min cycle<br>ergometer + 15 min treadmill<br> + 15 min stairs (training set at 80% maximum heart rate)<br> + 1 time per week home session 45 min walking<br> PR+Sham device 15 min 2 times per week<br> Threshold device set at 7 cm H2O<br> PR+IMT device 15 min 2 times per week<br> Threshold device set at 30% MIP<br> Progression set at +5% every week up to 60% MIP | Control<br> MIP, MEP, VO2 peak<br> Endurance exercise test (treadmill), ISWT, SGRQ, Sputum volume | †MIP, endurance test, ISWT in PR groups compared to control<br> †SGRQ after PR+IMT<br> After 3 months improvement in endurance exercise capacity was maintained only in the PR+IMT group |
| Ong 2011 [40]      | 111 (60%)              | Retrospective 8 weeks<br> Follow up 12 months | 4 times per week (2 assisted sessions, 2 at home) lasting 60-90 min: 15 min cycle ergometer (intensity according Borg) + 15 min treadmill (70% 6MWT, progression according Borg) + 15 min strengthening/functional exercises<br> NCFB COPD | 6MWT<br> CRQ | †6MWT and CRQ in both groups<br> After 1 year, improvements were maintained |
| Van Zeller 2012 [41]| 41 (44.6%)             | Retrospective 12 weeks<br> Follow up 12 months | 3 times per week lasting 30 min: cycle ergometer (target load 60% maximum work rate or tolerance) + upper limbs and quadriceps training | Spirometric parameters, blood gas analysis, 6MWD | †RV and †FEV1 in patients with FEV<50%<br> †RV and †FVC in patients with idiopathic etiology |
| Zanini 2015 [42]   | 108 (76%)              | Retrospective 3 weeks | 5 times per week lasting 2-3 hours: 30-40 min cycle ergometer or treadmill (initial load 60-70% maximum heart rate in 6MWT) + upper limb training+ educational activities/airway clearance techniques, positioning and IMT if necessary | Spirometric parameters, DBI/TDI, 6MWT, EQ-VAS | †TDI<br> †6MWT especially in male patients with low FEV1 and exacerbation rate >2/year<br> †EQ-VAS especially in male patients with low FEV1. |
| Mandal 2012 [43]   | 27 (74%)               | RCT 8 weeks<br> 3 months follow up | 2 times per day Acapella set at 3 lasting 20-30 min<br> 10 inspirations up to 3/6 MRC, 2-3 sec breath hold, relaxed exhalation 2-3 HUFF or cough<br> Training 3 times per week (2 assisted sessions + 1 session at home) lasting 30-40 min: treadmill, ski machine, cycle ergometer<br> (10 min each) target load 85% VO2max + 3 x 10 upper and lower limb exercise (from 60% to 80% of IRM) | Spirometric parameters, ISWT, EWT, LCQ, SGRQ, MIP, MEP; inflammatory markers<br> Control<br> No exercise | †ISWT, EWT, LCQ in training group<br> †SGRQ in training group |

To be continued on next page.
the end of training, the improvement was only present in the intervention group, with an increase in the ISWT (80mt, p=0.04), EWT (247.5mt, p=0.003), LCQ score (4.4 units, p<0.001), and SGRQ score (4 units, p<0.001).

The second study [44] which compared the effects of a training program in addition to usual ACT, evaluated the short and long term effects on the capacity to sustain exercise, QoL, and the incidence of exacerbations. The study involved 85 clinically stable bronchiectasis patients with dyspnea ≥ 1 according to the modified Medical Research Council scale (mMRC) and a history of two or more exacerbations per year which required antibiotic therapy in the two years previous the study. At the end of the 8-week treatment, the improvement in the distance walked on ISWT (average difference of 62 m) and 6MWT (mean difference of 41 m) was higher in the treatment group than in the control group. This effect was lost at 6 and 12-month follow-up. In the exercise group, there

**Table 6.** Main result for outcome.

| Outcome | Main results | Notes |
|---------|--------------|-------|
| Number of exacerbations/hospital admission | ACTs may decrease number of exacerbations | Very few studies have considered this outcome |
| | High flow systems and saline nebulization (HS better than IS) | |
| | PR may decrease number of exacerbations | |
| Health related quality of life | ACTs may improve QoL, dyspnea and fatigue | |
| | High flow system and saline nebulization (HS better than IS) | |
| | PR may reduce dyspnea and fatigue and enhance ability to sustain exercise. IMT alone can’t improve QoL but can help to extend benefits of PR | |
| Symptoms | Sputum volume increases with ACTs, no evidence among different techniques | |
| | Sputum volume increase with humidification and saline nebulization | |
| Respiratory function | ACTs, humidification and saline nebulization may improve same selected parameters | |
| | PR may improve respiratory function in selected patients | |
| Safety and tolerability of treatments | No adverse effects were described | |
| | All treatments were well-tolerated | |

ACTs, airway clearance technique; HS, hypertonic saline solution; IS, isotonic saline solution; PR, pulmonary rehabilitation; FEV1, forced expiration volume at first second; IS, isotonic saline solution; HS, hypertonic saline solution; LCQ, quality of life; IMT, inspiratory muscle training.
was also a reduction in dyspnea (p=0.009) and muscle fatigue (p=0.01), but no significant improvement in CRQ, LCQ and psychological conditions [hospital anxiety depression scale (HADS)]. Among the long-term results, a significant reduction in the number of exacerbations was observed at 12 months in the treatment group compared to the control group (p=0.012).

A single study, Liaw et al. [45] evaluated the feasibility and effectiveness of a respiratory muscle training program. At the end of the study, only a significant MIP improvement (mean -25.3 versus -16.4 cmH2O, p=0.005) and maximal expiratory pressure (MEP) (mean +30.8 versus +20.8 cmH2O p=0.038) were observed in the treatment group.

Discussion

Bronchial airway clearance

ACTs are physiotherapy interventions designed to facilitate the removal of tracheo-bronchial and lung secretions. In clinical practice, a large number of single or combined techniques based on different intervention strategies are used: positioning, pulmonary volume and expiratory flow changes, application of positive expiratory pressure, vibration, airway oscillations and chest wall oscillations [46,47].

Although some guidelines recommend the use of chest physiotherapy [7,9] and there is consensus in the literature over the associated improvements in symptoms and QoL [48-50], its effectiveness has not been clearly demonstrated in patients with bronchiectasis.

The difficulty in determining its efficacy is related to disease heterogeneity, linked to individual variability in daily sputum volume, the magnitude of ventilatory limitation and degree of obstruction, and the severity of respiratory symptoms [1,7,8,46].

The majority of the published studies show several methodological limitations that can affect their results. Most studies had a small sample size and a crossover design [12,16-18,22,27-30]. Only three studies compared an airway clearance technique with a placebo (sham therapy) [19,29,30] and only three studies had a control group that did not perform any treatment, other than medical therapy [17,18,26].

One of the major difficulties in evaluating the effectiveness of ACTs lies in selecting appropriate outcome measures that accurately reflect therapeutic effects, such as improved mucus transport, or secondary effects of mucus removal as frequency and the duration of exacerbations, hospitalization days, changes in respiratory function and QoL. Secretion removal is often evaluated by measuring the volume of sputum produced. This evaluation may be highly influenced by factors as inhibition of the patient expectoration, secretions swallowing, etc. In the studies we have analyzed, the sputum was significantly increased in the following treatments: ACBT + PD compared to Flutter [14] Flutter versus sham-Flutter [29], Acpella compared to no treatment [17] or IMT [22], ELTGOL compared to placebo [19], and HFCWO compared to conventional or no treatment [26]. Spirometric parameters are frequently used as short-term outcome, although there are some limitations in using them. The presence of secretions may have different effects depending on the level of obstruction. Secretions may worsen obstruction by reducing the expiratory flow in the small airways, whereas complete airway obstruction can lead to a reduction in lung volumes. FEV1 was seldom significantly modified [12,23,26] despite all studies having considered spirometric measures. The study of Guimarães et al. suggested a correlation between sputum quantity and a static volume improvement [18]. Nevertheless, this data was applicable only to the bronchiectasis phenotype with detectable dynamic hyperinflation. It is therefore difficult to find changes in these parameters if a small number of patients are analyzed. Finally, the effect of airways clearance programs on QoL has been analyzed in two studies [17,19] which demonstrated an improvement in cough, an improvement in the psychological /social impact, an improvement of exercise tolerance and a reduction of exacerbation rate. The distinguishing feature of the study performed by Munoz [19] relative to other randomized clinical trials was the longer duration of intervention.

This should open a debate as to what is the most clinically relevant endpoint to measure the effectiveness of airway clearance (Table 6).

Interventions aiding airway clearance

Conway and Hasani [32,33] observed an improvement in mucociliary clearance after using sterile water nebulization and warm humidification with a high flow system. Regarding the long-term use (12 months), a single study [34] reported a statistically significant improvement on the exacerbation rate, and lung function at 6 to 12 months. There was a decrease in antibiotic therapy. Also an improvement of QoL measured by SGRQ in all domains, except for activity was observed. The results of this study, however, have to be considered with caution, since the patients population included 73 COPD and 45 bronchiectasis subjects without separated analysis performed.

Concerning saline nebulization, we found a statistically significant improvement in sputum volume, in ease and viscosity of sputum clearing with HS (7%) compared to IS [36]. Moreover, with HS (7%) improved FEV1, and FVC, QoL (except for domain activity), and lower use of antibiotic therapy and number of exacerbations were observed [37].

Very different results, however, were reported by Nicolson [38] who demonstrated no significant improvement in QoL, respiratory function, number of exacerbations or changes of sputum colonization by comparing the use of IS and HS at 6% for 12 months with two nebulizations per day.

Physical exercise

In bronchiectasis as in other respiratory conditions, especially in the most advanced stages, the combination of bronchial obstruction and pulmonary hyperinflation may worsen dyspnea and result in reduced tolerance to physical exercise and QoL [5,51,52]. All studies in which physical exercise training was performed have clearly demonstrated short-term improvements in the ability to sustain exercise, with reduced dyspnea and fatigue [39-44,53]. This effect was comparable to those reported in COPD patients treated with similar programs [7].

Studies showing also long-term results have observed different results. Improvement in the ability to sustain physical exercise was maintained at the 3 month-follow-up in the studies of Mandal [43] and Newall [39], and at one year follow-up in Ong’s study [40]. However, this effect was not maintained after 6 and 12 months in Lee’s study [44].

Long term results regarding QoL are also different: in the
Newall’s study [39] the improvement in QoL measured with SGRQ at the end of treatment persisted at 3 months; otherwise, QoL in Ong’s study [40] (measured with the CRQ) and Mandal’s study [43] (measured with LCQ and SGRQ) showed improvement at the end of the program, and the benefits were maintained at 20 weeks and 12 months, respectively. In the study performed by Lee [44], even if physical exercise reduced dyspnea and fatigue, no changes were observed in LCQ and HADS. These findings suggest that this type of intervention should include maintenance programs useful in modifying patient lifestyles for long-term benefits. Moreover, an important emerging issue in the long-term follow-up, as demonstrated by Lee’s study [44], is a lower incidence of exacerbations in subjects participating in a full pulmonary rehabilitation program compared to the group who only performed airway clearance.

The training of respiratory muscles in patients with bronchiectasis is feasible and seems to improve the strength of respiratory muscles as already demonstrated in COPD subjects. Nevertheless, if it is performed without the addition of a physical exercise program, is incapable to improve short term respiratory function and QoL [44]. It has been shown that a respiratory muscle training associated with lower limb muscle training can affect the distance maintenance obtained with a physical exercise program and improve the QoL [39].

Exercise may play a role in favoring mucus expectoration [54], but such observations were not confirmed in the study of Newall [39]. The author found no significant changes in sputum volume in subjects who performed high intensity exercise, nor in the group who added lower limb muscle training to a respiratory muscles training program. Unfortunately, other studies comparing bronchial airway clearance programs with the addition of peripheral muscle training did not insert sputum amount between the outcome measures. Therefore, this observation cannot be confirmed nor denied.

It is unclear whether individual bronchial airway clearance programs may play a role in improving the ability to enhance physical exercise, and reduce dyspnea and fatigue [46,48]. Some studies did not find any improvement in dyspnea scales (VAS or Borg) after an airway clearance session [12,13,16], whereas other studies have showed improvements in ISWT [17], mMRC [20,26] and breathlessness, cough and sputum scale (BCSS) [26]. The paucity of information is obviously due to the fact that the ability to perform physical exercise is not a primary outcome in airway clearance programs.

So far, studies on training programs in patients with bronchiectasis are few and far from homogeneous in design and management. Patients have not been selected in relation to clinical severity clusters, type, intensity, frequency. Furthermore, the duration of individual sessions has been variable and outcomes not always comparable. New studies are therefore desirable to provide clearer guidance on the essential components and the most effective ways of conducting specific training programs for patients with bronchiectasis.

Limitations

This review has some limitations. First, quality and weigh of the various studies have not been evaluated. Second, the heterogeneity across the selected studies may have affected the results of the review. However, the high number of records may give further hints on the effects of the various interventions.

Conclusions

Bronchiectasis represent the result of confluent factors involving infectious, genetic, autoimmune, evolutive and allergic components. Etiology, clinical manifestations and prognosis may be very heterogeneous [8]. This scenario makes it difficult to individualize the best outcome in terms of physiologic and or clinical benefit for non-cystic fibrosis bronchiectasis patients. ACTs seem effective in increasing sputum volume although no benefit in QoL or exacerbation rate have been shown. There were no differences in effectiveness between several techniques used. From our point of view, ACTs should also be accompanied by global rehabilitation interventions involving educational aspects in the management of the disease. Proper management of medical therapy and early recognition of exacerbations, linked to endurance training programs should be included. PR has been associated with short term benefits in exercise capacity, dyspnea and fatigue. Exercise training might improve QoL and exacerbation rate, but long-term data are not available. No adverse effects were described. All treatments were well-tolerated.

As emphasized by the European Multicentre Bronchiectasis Audit and Research Collaboration (EMBARC), physiotherapy and respiratory rehabilitation are the major topics of research in the field of bronchiectasis. Further studies are needed to optimize compliance, access to bronchial airway clearance and physical exercise training [55].

In particular, future studies should include significant clinical outcomes as the number of exacerbations, access to medical assistance, and improvements in QoL. Patients selection should also be oriented towards a better stratification and should take associated comorbidities into account.

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