International Journal of Immunopathology & Pharmacology

Editorial

International Journal of Immunopathology and Pharmacology
1–10

DOI: 10.1177/0394632015584724
iji.sagepub.com
SAGE

Mucociliary clearance techniques for treating non-cystic fibrosis bronchiectasis: Is there evidence?

D Snijders,[1] B Fernandez Dominguez,[2] S Calgaro,[1] I Bertozzi,[1] A Escribano Montaner,[2] G Perilongo[1] and A Barbato[1]

Abstract

Non-cystic fibrosis bronchiectasis (nCFb) is an acquired condition of variable etiology. An impaired mucociliary clearance seems to be one of the mechanisms behind nCFb, and treatment involves antibiotics, mucoactive agents, and airway clearance techniques (ACTs). Traditional ACTs have four components: postural drainage, percussion, vibration of the chest wall, and coughing. Reviewing the international medical literature on the use of ACTs for patients with nCFb from 1989 to the present day, we retrieved 93 articles, of which 35 met our selection criteria for this analysis. We reviewed active cycle of breathing techniques (ACBT), forced expiration techniques (FET), autogenic drainage, postural drainage, oscillating positive expiratory pressure (OPep), high frequency chest wall oscillation (HFCWO), and exercise or pulmonary rehabilitation. Overall, ACTs appear to be safe for individuals (adults and children) with stable bronchiectasis; where there may be improvements in sputum expectoration, selected measures of lung function, and health-related quality of life. Unfortunately, there is a lack of RCTs in nCFb patients, especially in children. Moreover, none of the studies describes long-term effects of ACTs. It should be noted that a single intervention might not reflect the longer-term outcome and there is no evidence to recommend or contest any type of ACTs in nCFb management. Multicenter RCTs are necessary to evaluate the different techniques of ACTs especially in children with nCFb.

Keywords

airway clearance techniques, chest physiotherapy, non-CF bronchiectasis

Date received: 17 June 2014; accepted: 18 February 2015

Bronchiectasis is a progressive condition characterized by early focal destruction of elastic tissue, damage of muscle layers and eventually destruction of the supportive cartilage and airway dilatation as shown on computed tomography (CT) scan in association with clinical symptoms of cough and sputum production.[1] Bronchiectasis can be focal or diffuse and permanent or reversible. Usually they are caused by recurrent or chronic infections or inflammations, anatomic airway obstruction, or underlying congenital disease that predisposes to bronchiectasis. The pathophysiology of bronchiectasis causes a vicious circle of airway infection and inflammation, impairing mucociliary clearance by alteration of the cilia.[2]

Cystic fibrosis (CF) is the most common cause of bronchiectasis in children and is extensively studied. The global prevalence of non-CF bronchiectasis (nCFb) is not well described in the literature; but includes a variety of disease processes, most of which includes a combination of bronchial obstruction and infection.[1]

[1]Department of Women's and Children's Health, University of Padova, Italy
[2]Pediatric Service, Hospital Clínico Universitario, Valencia, Spain

Corresponding author:
Deborah Snijders, Pediatric Endoscopy Unit, Department of Women's and Children's Health, University of Padova, via Giustiniani 3, 35138 Padova, Italy.
Email: olanda76@gmail.com

Treatment methods, which improve mucus clearance, are considered essential in optimizing respiratory function and reducing the progression of lung disease. For this reason, oral or inhaled drugs[3] and chest physiotherapy are used, alone or in association, to remove secretions from the lower airways.[1,4]

Normal airway clearance is accomplished by the mucociliary clearance system and cough. The first depends on the methacronal wave generated by beating cilia and by the mucus layer, the physical properties of which can influence the methacronal wave. Coughing, the most efficient reserve mechanism in the central airways, relies on a high linear airflow velocity generated by ample flow and airway narrowing with a two-phase, air-liquid flow regime. The failure of one of the mechanisms may lead to sputum retention in the airways, leading to local infection and/or inflammation.[5]

Traditional airway clearance techniques (ACTs) have four components: postural drainage, percussion, vibration of the chest wall, and coughing.

Due to the lack of literature on ACTs in patients with non-CF bronchiectasis, their indication is often extrapolated from other research such as CF and chronic obstructive pulmonary disease (COPD). Although understandable, such extrapolation should be performed with caution and the physiologic differences in the conditions considered carefully. Expert clinical opinion recommends that ACTs are important in nCFb to enhance mucociliary clearance, improve ventilation, manage breathlessness, and reduce cough frequency.

There are various ACTs utilized in clinical practice that range from positioning, gravity-assisted drainage, manual techniques, various breathing strategies, directed coughing, positive expiratory pressure (PEP) devices, airway oscillating devices, and mechanical tools that are applied to the external chest wall. The ACTs may be used as an isolated technique or in combination.[5]

In the last 25 years (1989–2014), 93 randomized controlled trials (RCTs), uncontrolled observational studies, or case reports, reporting efficacy data of ACTs on children aged 0–18 years or on adults with nCFb were described in the international literature: PubMed Medical Subject Headings (MeSH): 'active cycle of breathing techniques' (ACBT), 'forced expiration techniques' (FET), 'autogenic drainage' (AD), 'postural drainage' (PD), 'oscillating positive expiratory pressure' (OPep), 'high frequency chest wall oscillation' (HFCWO), 'exercise', 'pulmonary rehabilitation', and 'humidification', each of them combined to 'bronchiectasis').

However efficacy between different techniques of ACTs have been compared, there is no published evidence to indicate which ACTs should be implicated in nCFb and which patients may benefit from the different ACT devices. However, it is widely believed that a routine airway clearance regimen is an important component of the management of nCFb in order to improve mucociliary clearance and reduce cough frequency.[1]

In this review we have evaluated 93 articles, 58 of which were rejected on the strength of our analytical criteria, while 35 on nCFb were considered eligible for this review (Figure 1).

ACBT is frequently utilized in nCF bronchiectatic patients.[1,5–15] It can be used in conjunction with manual techniques (e.g. chest clapping and shaking) and postural drainage. The studies on the efficacy of ACBT in patients with nCFb (Table 1) show that ACBT improves lung sounds, sputum expectoration, and reduces perceived breathlessness. ABCT have a more acute efficacy in adults in comparison with OPep devices as show in four RCTs.[9,10,13,15] No trials on children have been reported in nCFb.

FET or 'huffing' is considered an alternative to coughing for the removal of lung secretions and airways clearance. It is supposed to reduce transpulmonary pressure compared with cough, avoiding airway compression and closure. The four articles in this review[7,15–17] show that FET is an effective ACT mainly when preceded by inhalation therapy; however, no control studies with other ACTs in nCFb have been reported (Table 2).

AD is an ACT that employs controlled expiratory airflow during tidal breathing to mobilize secretions in the peripheral airways and distribute them centrally, in order to facilitate its elimination. Its efficacy has been briefly studied in CF patients, but only one article on AD has been published in patients with nCFb.[15]

PD has been reported in patients with nCFb in five RCTs,[8,9,10,14,18] especially in combination with ACBT, increases sputum yield (Table 3).

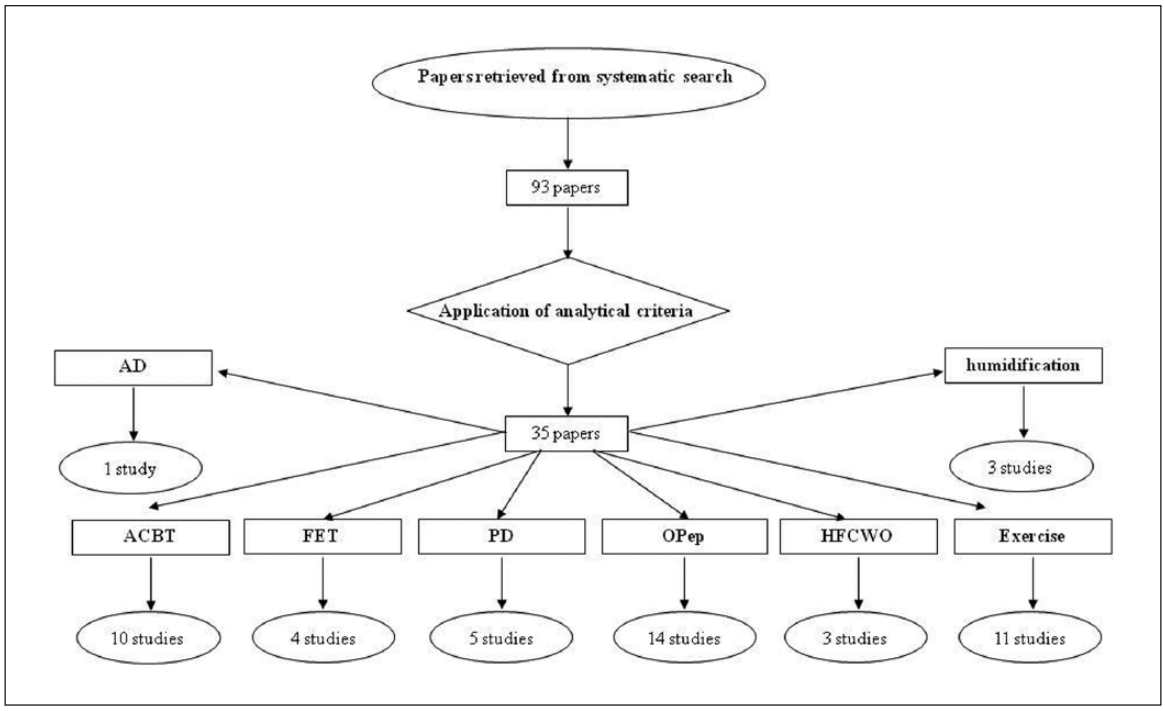

Figure 1. Flow chart of literature review on nCFb and ACTs. Results of the systematic literature search on pediatric nCFb in the English-language medical literature from 1989 to 2014. ACT: airway clearance techniques; ACTB: active cycle of breathing techniques; AD: autogenic drainage; FET: forced expiration techniques; HFCWO: high frequency chest wall oscillation; nCF: non-cystic fibrosis bronchiectasis; OPep: oscillating positive expiratory pressure; PD: postural drainage.

OPep techniques increase clearance of pulmonary secretions, improve exercise capacity, and reduce cough severity (Table 4). In literature on nCFb, these devices consist in Acapella®, Flutter®, and UNIKO®, and habitually are preferred over regular ACTs such as ACBT and PD.[7,10,13,15,18–27]

HFCWO refers to the application of positive pressure air pulses to the chest wall usually by means of inflatable vest. There are few published studies (Table 5) available to evaluate its indications and benefits in patients with nCFb,[28–30] but its use shows a trend in reduction of sputum expectoration and an improvement in symptoms and quality of life.

Reduced exercise tolerance may be a problem for children with non-CF bronchiectasis. On the other hand, physical training has been shown to improve exercise tolerance and reduce symptoms of breathlessness in many patient populations including CF and COPD (Table 6). There is little information regarding the benefits of physical training in bronchiectasis: however it is probable that the benefits of physical training in bronchiectasis are at least comparable to benefits demonstrated in other respiratory conditions.[20,31–40]

Humidification is used as an adjunct to chest physiotherapy (Table 7), showing even just humidificated air improves effects of ACT in patients with nCFb, increasing sputum yield and improving mucociliary clearance and lung function.[16,17,41]

From a recent survey in Italy among children with PCD (primary ciliary dyskinesia), PEP techniques are the most frequently prescribed ACTs; variable from normal PEP devices to OPeps.

Overall, ACTs appear to be safe for individuals (adults and children) with stable bronchiectasis, where there may be improvements in sputum expectoration, selected measures of lung function, and health-related quality of life.

Unfortunately, there is a lack of RCTs in nCFb patients, especially in children. Moreover, none of the studies describes long-term effects of ACTs. It should be noted that a single intervention might not reflect the longer-term outcome and there is no evidence to recommend or contest any type of ACTs in nCFb management. Multicenter RCTs are necessary to evaluate the different techniques of ACTs, to improve indication and be able to select best ACTs for every patient, especially in children with nCFb.

Table 1. Studies on the effect of ACBTs on nCFb.

Active cycle of breathing techniques				
Year	Method	Patients	Intervention	Results
2012 (Marques[6])	Single interventional study	23 (adults)	One cycle of ABCT, median duration of 24 min	• Minimal statistical change in lung sounds was observed after a single session of ACBT • Perceived breathlessness was significantly reduced post intervention • No significant changes were observed in either lung function or oxygen saturation
2012 (Guimarães[7])	RCT crossover	10 (adults)	Flutter VRP1® vs. ELTGOL vs .control with a 1-week wash-out period	• A significant decrease in RV, FRC, and TLC • A significant higher sputum production during ELTGOL • The ELTGOL and Flutter VRP1® acutely reduced lung hyperinflation, but only the ELTGOL increased the removal of pulmonary secretions
2008 (Mutalithas[8])	Controlled clinical trial	10 out of 53 (adults)	Two weeks of ACTs (combination of AD, PD, or cough techniques in combination with ABCT)	• Reduction of cough symptoms and health-related quality of life issues after ACTs
2007 (Eaton[9])	RCT crossover	36 (adults)	Flutter® vs. ACBT vs. ACBT-PD	• Time of intervention was similar between ACTs • All three techniques were well accepted and tolerated • ACBT-PD proved superior in terms of acute efficacy
2005 (Patterson[10])	RCT crossover	20 (adults)	Single cycle ABCT vs. single cycle of Acapella®	• ACBT does not cause obstruction • Sputum expectoration similar between the two interventions • ACBT less effective in airway clearance
2005 (Kellet[11])	RCT crossover	24 (adults)	Four single schedules in random order: (1) Active cycle breathing technique (ACBT) alone; (2) Nebulized terbutaline followed by ACBT after 10 min; (3) Nebulized terbutaline followed after 10 min by nebulized IS (0.9%) then ACBT; (4) Nebulized terbutaline followed after 10 min by nebulized HS (7%) then ACBT	• ABCT is more effective when combined with terbutaline, IS, or HS
2004 (Patterson[12])	RCT crossover	20 (adults)	ACBT (incorporating PD and vibration) vs. TIRE	• Significant higher sputum expectoration with ACBT
2002 (Thompson[13])	RCT crossover	17 (adults)	4 weeks Flutter vs. 4 weeks ACBT	• No significant differences between ACTs in median weekly sputum weights • No significant changes in health status, ventilatory function, and BORG scale • Patients preferred the Flutter to ACBT for routine use
1999 (Cecins[14])	RCT crossover	6 out of 19 (adults)	2-day crossover: ACBT with head-down tilt vs. ACBT alone	• No significant differences for the number of productive coughs and weight of sputum expectorated during treatment • No significant changes in SAO2 and FEV1 • Preference for ACBT alone, but with head-down tilt seems more effective
2011 (Herrero[15])	RCT crossover	7 (adults)	ELTGOL vs. AD vs. temporary PEP (Uniko®)	• AD obtained the major short-time sputum production • AD was the favorite technique

Author's name and reference number in brackets under the year.
ACT: airway clearance techniques; ACTB: active cycle of breathing techniques; ACBT-PD: ACBT plus postural draining; AD: autogenic drainage; ELTGOL: l'expiration lente totale glotte overte en decubitus lateral; FRC: functional residual capacity; HS: hypertonic saline; IS: isotonic saline; PD: postural drainage; Pep: positive expiratory pressure; RCT: randomized controlled trial; RV: residual volume; TIRE: test of incremental respiratory endurance; TLC: total lung capacity.

Table 2. Studies on the effect of forced expiration techniques in children and adults with nCFb.

Forced expiration technique (FET)				
Year	Method	Patients	Intervention	Results
1994 (Hasani[16])	RCT crossover	19 (adults)	1 day FET vs. 1 day Cough vs. 1 day Control intervention	• No change in pulmonary function • FET and cough increased clearance of the lung and amount of sputum produced expectorated
1992 (Conway[17])	RCT crossover	7 (adults)	Chest physiotherapy with and without previous humidification.	• Significant increase in total weight of sputum and airway clearance
2012 (Guimarães[7])	RCT crossover	10 (adults)	Flutter VRP1® vs. ELTGOL vs. control with a 1-week wash-out period	• A significant decrease in RV, FRC, and TLC • A significant higher sputum production during ELTGOL • The ELTGOL and Flutter VRP1® acutely reduced lung hyperinflation, but only the ELTGOL increased the removal of pulmonary secretions
2011 (Herrero[15])	RCT crossover	7 (adults)	ELTGOL vs. AD vs. temporary PEP (Uniko®)	• ELTGOL showed a higher sputum production at 24 h • ELTGOL was effective at long-term

Author's name and reference number in brackets under the year.
ACTB: active cycle of breathing techniques; AD: autogenic drainage; ELTGOL: l'expiration lente totale glotte overte en decubitus lateral; FRC: functional residual capacity; Pep: positive expiratory pressure; PD: postural drainage; RCT: randomized controlled trial; RV: residual volume; TLC: total lung capacity.

Table 3. Studies on the effect of postural drainage in children and adults with nCFb.

Postural drainage (PD)				
Year	Method	Patients	Intervention	Results
2008 (Mutalithas[8])	RCT	53 (adults)	Two weeks of ACTs (combination of AD, PD, or cough techniques plus ABCT)	• Reduction of cough symptoms and health-related quality of life issues after ACTs
2007 (Eaton[9])	RCT crossover	36 (adults)	Flutter® vs. ACBT vs. ACBT-PD	• Time of intervention was similar between ACTs • All three techniques were well accepted and tolerated; patient preferred Flutter ® • ACBT-PD proved superior in terms of acute efficacy
2004 (Patterson[10])	RCT crossover	20 (adults)	ACBT (plus PD and vibration) vs. TIRE	• Significant higher sputum expectoration with ACBT
1999 (Cecins[14])	RCT crossover	6 out of 19 (adults)	2-day crossover: ACBT with head-down tilt vs. ACBT alone	• ACBT with head-down tilt was considered more effective • Horizontal position was better tolerated
1995 (Ambrosino[18])	RCT	14 (adults)	OPep vs. PD combined with chest percussion	• No differences in tolerance or amount of sputum produced

Author's name and reference number in brackets under the year.
ACT: airway clearance techniques; ACTB: active cycle of breathing techniques; ACBT-PD: ACBT plus postural draining; AD: autogenic drainage; OPep: oscillating positive expiratory pressure; PD: postural drainage; RCT: randomized controlled trial; TIRE: test of incremental respiratory endurance.

Table 4. Studies on the effect of oscillating positive expiratory pressure in children and adults with nCFb.

Oscillating PEP techniques

Year	Method	Patients	Intervention	Results
2012 (Figueiredo[19])	RCT crossover	8 (adults)	Flutter Valve TM vs. sham Flutter (placebo)	• Flutter ValveTM cleared more secretions than the Sham Flutter intervention • Flutter ValveTM increases sputum removal during treatment and diminishes total and peripheral airway resistance in hypersecretive patients with bronchiectasis
2012 (Guimarães[7])	RCT crossover	10 (adults)	Flutter VRP1® vs. ELTGOL vs. control with a 1-week wash-out period	• A significant decrease in RV, FRC, and TLC • A significant higher sputum production during ELTGOL • The ELTGOL and Flutter VRP1® acutely reduced lung hyperinflation, but only the ELTGOL increased the removal of pulmonary secretions
2012 (Mandal[20])	RCT	27 (adults)	8 weeks Acapella® vs. Acapella® + PR	• PR in addition to regular chest physiotherapy with Acapella® led to significant improvement in exercise capacity and health-related quality of life • No significant improvement PFT or inflammatory markers
2011 (Tambascio[21])	RCT crossover	18 (adults)	4 weeks Flutter® vs. 4 weeks PEP exercise	• The use of the Flutter®VRP1 alters the respiratory secretion transport properties
2010 (Naraparaju[22])	RCT crossover	30 (adults)	Acapella® vs. threshold inspiratory muscle trainer	• A statistically significant difference was found in the sputum volume expectorated after treatment with the Acapella® • Patients preferred Acapella® in terms of usefulness of clearing secretions
2009 (Ramos[23])	Controlled clinical trial	5 (adults)	Flutter® with PEP: 15 vs. 25 cmH2O	• Flutter® decreases sputum viscosity independently by different PEP
2009 (Murray[24])	RCT crossover	20 (adults)	3 months Acapella Choice® vs. 3 months No ACT	• Acappela Chioce®, significantly improved perceived cough severity, increased 24-h sputum volume; improved exercise capacity and SGRQ score • No effect on sputum microbiology, FEV1, FVC, FEF25–75%, MIP, MEP, or exacerbation frequency in respect to no ACT
2007 (Patterson[25]) (A)	RCT crossover	20 (adults)	Acapella ® vs. usual ACTs	• Increase in sputum expectoration with Acapella® device • Time of intervention was longer with Acapella® vs usual ACTs • There were no significant differences in lung function
2005 (Patterson[10])	RCT crossover	20 (adults)	Single cycle ABCT vs. single cycle of Acapella ®	• ACBT does not cause obstruction • Sputum expectoration similar between the two interventions • ACBT less effective in airway clearance
2004 (Valente[26])	Pilot, single cohort.	8 (adults + adolescents)	A Flutter Valve TM vs. Sham Flutter (placebo) vs. PEP intervention	• The ciliary or cough transport and adhesive force of sputum in a small sample of patients with bronchiectasis are not modified by the use of FlutterVRP1 in a single session

Table 4. (Continued)

Oscillating PEP techniques				
Year	Method	Patients	Intervention	Results
2002 (Thompson[13])	RCT crossover	17 (adults)	4 weeks Flutter® vs. 4 weeks ACBT	• No significant differences between ACTs in median weekly sputum weights • No significant changes in Health status, ventilatory function, and BORG scale • Patients preferred the Flutter® to ACBT for routine use
1995 (Ambrosino[18])	RCT	14 (adults)	OPep vs. PD combined with chest percussion	• No differences in tolerance or amount of sputum produced
2013 (Venturelli[27])	RCT	20 out of 98 (adults)	Temporary PEP (UNIKO®) vs. control group	• No significant changes for the oxygenation index • Dynamic lung volumes and respiratory muscle strength significantly improved. Inspiratory capacity was significantly increased
2011 (Herrero[15])	RCT crossover	7 (adults)	ELTGOL vs. AD vs. temporary PEP (Uniko®)	• Uniko® showed a higher sputum production at 24 h • Uniko® was more effective in the long term

Author's name and reference number in brackets under the year.
ACT: airway clearance techniques; ACTB: active cycle of breathing techniques; ACBT-PD: ACBT plus postural draining; AD: autogenic drainage; ELTGOL: l'expiration lente totale glotte ouverte en decubitus lateral; FEF25-75: forced expiratory flow at 25–75% of FVC; FRC: functional residual capacity; FVC: forced vital capacity; MEP: maximum expiratory; MIP: maximum inspiratory pressure; OPep: oscillating positive expiratory pressure; PD: postural drainage; Pep: positive expiratory pressure; PFT: pulmonary function tests; PR: pulmonary rehabilitation; RCT: randomized controlled trial; RV: residual volume; SGRQ: St George's Respiratory Questionnaire; TIRE: test of incremental respiratory endurance; TLC: total lung capacity.

Table 5. Studies on the effect of high frequency chest wall oscillation in children and adults with nCFb.

HFCWO				
Year	Method	Patients	Intervention	Results
2011 (Chakravorty[28])	RCT crossover	22 (adults)	4 weeks HFCWO device vs. 4 weeks conventional ACTs	• A trend in reduction of sputum expectoration with HFCWO • Improvement in quality of life and clinical symptoms
2013 (Nicolini[29])	RCT	30 (adults)	Vest® vs. traditional ACTs (Pep bottle, Pep mask, ELTGOL, vibratory Pep)	• The HFCWO technique provides an improvement both in pulmonary function and quality of life • A significant improvement in some biochemical tests and PFTs as well as in the quality of life compared to control • A significant improvement in blood inflammation parameter C and inflammation markers in sputum
2013 (Gokdemir[30])	RCT crossover	24 (children)	5 day Vest vs. 5 day conventional PR	• PFT values of patients increased significantly after both interventions. There was no significant difference in PFT values between the two groups • HFCWO was found more comfortable by the patients

Author's name and reference number in brackets under the year.

Table 6. Studies on the effect of exercise in children and adults with nCFb.

Exercise				
Year	Method	Patients	Intervention	Results
2012 (Mandal[20])	RCT	27 (adults)	8 weeks Acappella® vs Acapella® + PR	• PR in addition to regular chest physiotherapy with Acapella® led to significant improvement in exercise capacity and health related quality of life. • No significant improvement PFT or inflammatory markers.
2012 (Van Zeller[31])	Retrospective study	41 (adults)	12 weeks PR	• Significant improvement in FVC and RV after PR. • Patients with severe obstruction showed a statistically significant decrease in RV
2011 (Lavery[32])	RCT	64 (adults)	Standardized education + usual cares vs usual care alone.	• Improvement in the control group
2011 (Liaw[33])	RCT	26 (adults)	8 weeks of Inspiratory muscle training vs no intervention.	• Improvement in respiratory muscle strength. • No effect in respiratory function or QOL.
2010 (Jenkins[34])	Retrospective study	349 (adults)	6MWT prior and after a PRP.	• Greater Increase in 6MWT after PRP.
2011 (Ong[35])	Retrospective review	95 (adults)	6 to 8 weeks of PR	• Significant improvements in 6MWT (and CRQ total score • Effect similar to COPD patients
2010 (Lee[36])	RCT	64 (adults)	8 weeks of PRP vs control.	• PRP modifies diary symptoms.
2005 (Newall[37])	RCT	32 (adults)	8 weeks PRP + sham IMT vs PRP + targeted-IMT vs no intervention.	• Improvements in endurance exercise capacity, in both the intervention group. • No significant changes in health status or sputum production.
2014 (Lee[38])	RCT	85 (adults)	Exercise vs control	• Short term improvement in exercise capacity, dyspnea and fatigue • Reduction of exacerbations over 12 months.
2012 (Santamato[39])	Case report	3 (adults)	Exercise and PD with percussion and vibration	• Improvements in both exercise capacity and health status • Reduction of acute bronchial exacerbations

Author's name and reference number in brackets under the year.

Table 7. Studies on the effect of humidification children and adults with nCFb.

Humidification				
Year	Method	Patients	Intervention	Results
2009 (Rea[41])	RCT	45 out of 108 (adults)	Humidification vs. usual therapy over 12 months	• Significant improvements in exacerbation days, time to first exacerbation, lung function, and QOL compared to non-intervention group
2008 (Hasani[16])	Interventional study	10 (adults)	Humidification therapy	• A significant improvement in lung mucociliary clearance
1992 (Conway[17])	RCT crossover	7 (adults)	CPT + humidification vs. chest physiotherapy alone	• Significant increase in total weight of sputum and airway clearance in humidification group

Author's name and reference number in brackets under the year.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

This review has been funded by the Italian Health Ministry (RF-VEN-2008-1201767).

Reference

1. McShane PJ, Naureckas ET, Tino G, et al. (2013) Non-cystic fibrosis bronchiectasis. *American Journal of Respiratory and Critical Care Medicine* 188: 647–656.
2. Chalmers JD and Hill AT (2013) Mechanisms of immune dysfunction and bacterial persistence in non-cystic fibrosis bronchiectasis. *Molecular Immunology* 55: 27–34.

3. Snijders D, Calgaro S, Bertozzi I, et al. (2013) Inhaled mucoactive drugs for treating non-cystic fibrosis bronchiectasis in children. *International Journal of Immunopathology and Pharmacology* 26: 529–534.
4. Pasteur MC, Bilton D and Hill AT (2010) British Thoracic Society Bronchiectasis non-CF Guideline Group. British Thoracic Society guideline for non-CF bronchiectasis. *Thorax* 65: i1–58.
5. Volsko TA (2013) Airway clearance therapy: Finding the evidence. *Respiratory Care* 58: 1669–1678.
6. Marques A, Bruton A, Barney A, et al. (2012) Are crackles an appropriate outcome measure for airway clearance therapy? *Respiratory Care* 57: 1468–1475.
7. Guimarães FS, Moço VJ, Menezes SL, et al. (2012) Effects of ELTGOL and Flutter VRP1® on the dynamic and static pulmonary volumes and on the secretion clearance of patients with bronchiectasis. *Revista Brasileira de Fisioterapia* 16: 108–113.
8. Mutalithas K, Watkin G, Willig B, et al. (2008) Improvement in health status following bronchopulmonary hygiene physical therapy in patients with bronchiectasis. *Respiratory Medicine* 102: 1140–1144.
9. Eaton T, Young P, Zeng I, et al. (2007) A randomized evaluation of the acute efficacy, acceptability and tolerability of flutter and active cycle of breathing with and without postural drainage in non-cystic fibrosis bronchiectasis. *Chronic Respiratory Disease* 4: 23–30.
10. Patterson JE, Bradley JM, Hewitt O, et al. (2005) Airway clearance in bronchiectasis: A randomized crossover trial of active cycle of breathing techniques versus Acapella®. *Respiration* 72: 239–242.
11. Kellett F, Redfern J and Niven RM (2005) Evaluation of nebulised hypertonic saline (7%) as an adjunct to physiotherapy in patients with stable bronchiectasis. *Respiratory Medicine* 99: 27–31.
12. Patterson JE, Bradley JM and Elborn JS (2004) Airway clearance in bronchiectasis: A randomized crossover trial of active cycle of breathing techniques (incorporating postural drainage and vibration) versus test of incremental respiratory endurance). *Chronic Respiratory Disease* 1: 127–130.
13. Thompson CS, Harrison S, Ashley J, et al. (2002) Randomised crossover study of the Flutter device and the active cycle of breathing technique in non-cystic fibrosis bronchiectasis. *Thorax* 57: 446–448.
14. Cecins NM, Jenkins SC, Pengelley J, et al. (1999) The active cycle of breathing techniques–to tip or not to tip? *Respiratory Medicine* 93: 660–665.
15. Herrero B, Polverino E, Martí D, et al. (2011) Efficacy of airway clearance therapy with different autonomy degrees in nonCF-BE: Randomized cross-over trial. *European Respiratory Journal* 38 (S5): 2977.
16. Hasani A, Pavia D, Agnew JE, et al. (1994) Regional lung clearance during cough and forced expiration technique (FET): Effects of flow and viscoelasticity. *Thorax* 49: 557–561.
17. Conway JH, Fleming JS, Perring S, et al. (1992) Humidification as an adjunct to chest physiotherapy in aiding tracheo-bronchial clearance in patients with bronchiectasis. *Respiratory Medicine* 86: 109–114.
18. Ambrosino N, Callegari G, Galloni C, et al. (1995) Clinical evaluation of oscillating positive expiratory pressure for enhancing expectoration in diseases other than cystic fibrosis. *Monaldi Archives for Chest Disease* 50: 269–275.
19. Figueiredo PH, Zin WA and Guimarães FS (2012) Flutter valve improves respiratory mechanics and sputum production in patients with bronchiectasis. *Physiotherapy Research International* 17: 12–20.
20. Mandal P, Sidhu MK, Kope L, et al. (2012) A pilot study of pulmonary rehabilitation and chest physiotherapy versus chest physiotherapy alone in bronchiectasis. *Respiratory Medicine* 106: 1647–1654.
21. Tambascio J, de Souza LT, Lisboa RM, et al. (2011) The influence of Flutter®VRP1 components on mucus transport of patients with bronchiectasis. *Respiratory Medicine* 105: 1316–1321.
22. Naraparaju S, Vaishali K, Venkatesan P, et al. (2010) A comparison of the Acapella and a threshold inspiratory muscle trainer for sputum clearance in bronchiectasis: A pilot study. *Physiotherapy Theory and Practice* 26: 353–357.
23. Ramos EM, Ramos D, Iyomasa DM, et al. (2009) Influence that oscillating positive expiratory pressure using predetermined expiratory pressures has on the viscosity and transportability of sputum in patients with bronchiectasis. *Jornal Brasileiro de Pneumologia* 35: 1190–1197.
24. Murray MP, Pentland JL and Hill AT (2009) A randomised crossover trial of chest physiotherapy in non-cystic fibrosis bronchiectasis. *European Respiratory Journal* 34: 1086–1092.
25. Patterson JE, Hewitt O, Kent L, et al. (2007) Acapella versus 'usual airway clearance' during acute exacerbation in bronchiectasis: A randomized crossover trial. *Chronic Respiratory Disease* 2007; 4:67-74.
26. Valente AM, Gastaldi AC, Cravo SC, et al. (2004) The effect of two techniques on the characteristics and transport of sputum in patients with bronchiectasis: A pilot study. *Physiotherapy* 90: 158–164.
27. Venturelli E, Crisafulli E, DeBiase A, et al. (2013) Efficacy of temporary positive expiratory pressure (TPEP) in patients with lung diseases and chronic mucus hypersecretion. The UNIKO® project: A multicentre randomized controlled trial. *Clinical Rehabilitation* 27: 336–46.
28. Chakravorty I, Chahal K and Austin G (2011) A pilot study of the impact of high-frequency chest wall oscillation in chronic obstructive pulmonary disease patients with mucus hypersecretion. *International Journal of Chronic Obstructive Pulmonary Disease* 6: 693–699.

29. Nicolini A, Cardini F, Landucci N, et al. (2013) Effectiveness of treatment with high-frequency chest wall oscillation in patients with bronchiectasis. *BMC Pulmonary Medicine* 13: 21.
30. Gokdemir Y, Karadag-Saygi E, Erdem E, et al. (2014) Comparison of conventional pulmonary rehabilitation and high-frequency chest wall oscillation in primary ciliary dyskinesia. *Pediatric Pulmonology* 49: 611–616.
31. van Zeller M, Mota PC, Amorim A, et al. (2012) Pulmonary rehabilitation in patients with bronchiectasis: pulmonary function, arterial blood gases, and the 6-minute walk test. *Journal of Cardiopulmonary Rehabilitation and Prevention* 32: 278–283.
32. Lavery KA, O'Neill B, Parker M, et al. (2011) Expert patient self-management program versus usual care in bronchiectasis: a randomized controlled trial. *Archives of Physical Medicine and Rehabilitation* 92: 1194–1201.
33. Liaw MY, Wang YH, Tsai YC, et al. (2011) Inspiratory muscle training in bronchiectasis patients: A prospective randomized controlled study. *Clinical Rehabilitation* 25: 524–536.
34. Jenkins S and Cecins NM (2010) Six-minute walk test in pulmonary rehabilitation: Do all patients need a practice test? *Respirology* 15: 1192–1196.
35. Ong HK, Lee AL, Hill CJ, et al. (2011) Effects of pulmonary rehabilitation in bronchiectasis: A retrospective study. *Chronic Respiratory Disease* 8: 21–30.
36. Lee AL, Cecins N, Hill CJ, et al. (2010) The effects of pulmonary rehabilitation in patients with non-cystic fibrosis bronchiectasis: Protocol for a randomised controlled trial. *BMC Pulmonary Medicine* 10: 5.
37. Newall C, Stockley RA and Hill SL (2005) Exercise training and inspiratory muscle training in patients with bronchiectasis. *Thorax* 60: 943–948.
38. Lee AL, Hill CJ, Cecins N, et al. (2014) The short and long term effects of exercise training in non-cystic fibrosis bronchiectasis: A randomised controlled trial. *Respiratory Research* 15: 44.
39. Santamato A, Ranieri M, Panza F, et al. (2012) Pulmonary rehabilitation for patients with bronchiectasis: Case reports. *European Journal of Physical and Rehabilitation Medicine* 48: 293–298.
40. Morgan M and Singh S (1997) *Practical Pulmonary Rehabilitation*. 1st edn. London: Chapman and Hall Medical.
41. Rea H, McAuley S, Jayaram L, et al. (2010) The clinical utility of long-term humidification therapy in chronic airway disease. *Respiratory Medicine* 104: 525–533.