



A randomised crossover trial of chest physiotherapy in non-cystic fibrosis bronchiectasis

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ABSTRACT: Regular chest physiotherapy is advocated in non-cystic fibrosis bronchiectasis despite little evidence supporting its routine use. This study aimed to establish the efficacy of regular chest physiotherapy in non-cystic fibrosis bronchiectasis compared with no regular chest physiotherapy.

20 patients not practising regular chest physiotherapy were enrolled in a randomised crossover trial of 3 months of twice daily chest physiotherapy using an oscillatory positive expiratory pressure device compared with 3 months of no chest physiotherapy. The primary end-point was the Leicester Cough Questionnaire (LCQ). Additional outcomes included 24-h sputum volume, forced expiratory volume in 1 s (FEV₁), forced vital capacity (FVC), forced expiratory flow at 25–75% of FVC (FEF_{25–75%}), maximum inspiratory pressure (MIP), maximum expiratory pressure (MEP), exercise capacity, sputum microbiology and St George's Respiratory Questionnaire (SGRQ). The treatment effect was estimated using the differences of the pairs of observations from each patient.

There was a significant improvement in all domains and total LCQ score with regular chest physiotherapy (median (interquartile range) total score improvement 1.3 (-0.17–3.25) units; $p=0.002$). 24-h sputum volume increased significantly with regular chest physiotherapy (2 (0–6) mL; $p=0.02$), as did exercise capacity (40 (15–80) m; $p=0.001$) and SGRQ total score (7.77 (-0.99–14.5) unit improvement; $p=0.004$). No significant differences were seen in sputum bacteriology, FEV₁, FVC, FEF_{25–75%}, MIP or MEP.

Regular chest physiotherapy in non-cystic fibrosis bronchiectasis has small, but significant benefits.

KEYWORDS: Bronchiectasis, physiotherapy

In bronchiectasis there is abnormal permanent dilatation of the airways, and the normal mucociliary clearance mechanism is impaired [1, 2]. There are excessive bronchopulmonary secretions and patients have a persistent cough, frequent infective exacerbations and a poor health-related quality of life (HRQoL) [3, 4].

Chest physiotherapy aims to mobilise secretions and facilitate effective expectoration, providing control of cough and improving airway clearance. It is widely advocated as a mainstay of management for this chronic disease [5]. However, to date, there are no randomised controlled trials of chest physiotherapy exclusively in patients with non-cystic fibrosis bronchiectasis [6].

Several different techniques or regimens exist for airway clearance, such as postural drainage, autogenic drainage, the active cycle of breathing

technique, positive expiratory pressure (PEP), oscillatory PEP devices and high-frequency chest wall percussion. Previous small studies in non-cystic fibrosis bronchiectasis have compared various techniques and found no single method to be superior; however, patient preference for technique has varied [7, 8].

The aim of this randomised crossover study was to establish the efficacy of routine chest physiotherapy in non-cystic fibrosis bronchiectasis, comparing the effect of twice daily physiotherapy using an oscillatory PEP device with no chest physiotherapy in patients not previously practising regular chest physiotherapy.

METHODS

This was a randomised crossover trial of 3 months of twice daily chest physiotherapy

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followed by a 1-month washout period compared with 3 months of no chest physiotherapy in adults with non-cystic fibrosis bronchiectasis not routinely practising chest physiotherapy from October 2007 to December 2008 (Clinical Trial Registration NCT00816309). Randomisation was determined by computer generation and the study was approved by the Lothian Research Ethics Committee (Edinburgh, UK). The primary outcome was patient perceived cough severity measured using the Leicester Cough Questionnaire (LCQ) [9]. Secondary outcomes included 24-h sputum volume, forced expiratory volume in 1 s (FEV₁), forced vital capacity (FVC), forced expiratory flow at 25–75% of FVC (FEF_{25–75%}), maximum inspiratory pressure (MIP), maximum expiratory pressure (MEP), exercise capacity, sputum microbiology and St George's Respiratory Questionnaire (SGRQ) [10].

Patients

Patients were recruited from the bronchiectasis clinic, Royal Infirmary of Edinburgh. Inclusion criteria were: 1) a radiological diagnosis of bronchiectasis using a high-resolution computed tomography (HRCT) chest scan according to the features described by NAIDICH *et al.* [11]; 2) chronic sputum expectoration; 3) not carrying out regular chest physiotherapy (for the purposes of this study this was defined as less than two occasions per week); and 4) clinically stable disease (defined as no requirement for antibiotics in the 4 weeks preceding study entry). Exclusion criteria were: current smokers; ex-smokers of ≤ 2 yrs or ex-smokers with a history of ≥ 10 pack-yrs of smoking and emphysema on HRCT; primary diagnosis of asthma; cystic fibrosis (as defined by the presence of transmembrane conductance regulator sequence variants present on genotyping); and active sarcoidosis or active tuberculosis.

Physiotherapy

Chest physiotherapy was carried out using the oscillatory PEP device Acapella Choice® (Smiths Medical ASD Inc., Weston, MA, USA). Each patient was trained by the chest physiotherapist (J.L. Pentland) to complete three sets of the following cycle for each treatment session: 10 breaths (each inhaling to three quarters of the maximum inspiratory capacity then a 3-s breath hold followed by exhalation to functional residual capacity) followed by two to three forced expiratory techniques (huffs) or coughs. The frequency/resistance dial (range 1–5) was set at three for all participants. This setting was the maximum tolerated by all participants. Patients completed two treatment sessions each day (morning and evening, typical duration 20–30 min). Compliance and occurrence of any adverse effects (specifically, any haemoptysis or increased use of short-acting bronchodilator therapy) were assessed using a diary card which was reviewed monthly during the treatment phase. Technique was reviewed by the chest physiotherapist at monthly intervals during the treatment phase and the devices were retained by the physiotherapist during the nontreatment phase.

Other interventions

Exacerbations requiring antibiotic therapy

An exacerbation was defined as a clinical deterioration with all of the following: increasing cough, increasing sputum volume and worsening sputum purulence [12]. All patients who experienced an exacerbation during the study were reviewed

by the study doctor and received a 14-day course of antibiotics (prescribed according to sputum bacteriology culture and sensitivities). No additional chest physiotherapy was advised. All were reviewed following completion of antibiotics to ensure recovery.

Routine therapy

Any changes made to the patient's usual respiratory medication during the study period were noted.

End-points

The study design and assessment time-points are shown in figure 1.

Cough severity and HRQoL

The LCQ and the SGRQ were completed. Both questionnaires have been validated to reflect impaired HRQoL in bronchiectasis [13, 14]. The LCQ is a 19 item self-completed quality of life measure of the impact of cough severity [9]. It has three domains: physical (eight items), psychological (seven items) and social (four items). The total severity score ranges from 3 to 21, with a lower score indicating a more severe cough. The minimal clinically important difference (MCID) for change is 1.3 units [15]. The SGRQ is a 50 item self-administered HRQoL questionnaire consisting of three components: symptoms (eight items), activity (16 items) and impacts (26 items). The total score ranges from 0–100, with a higher score indicating a poorer HRQoL. The MCID for the SGRQ is 4 units [14].

Sputum analysis

The total volume of sputum expectorated over a 24-h period was collected in a sterile transparent graduated container. Qualitative and quantitative bacteriology was performed on a separate early morning sample [16].

Pulmonary function tests

The following pulmonary function tests were performed: FEV₁, FVC, FEF_{25–75%}, MIP and MEP [17, 18]. The highest of three technically satisfactory measurements (within 10%) was recorded for each.

Incremental shuttle walk test

An externally paced, 10-m incremental field walking test was performed [19].

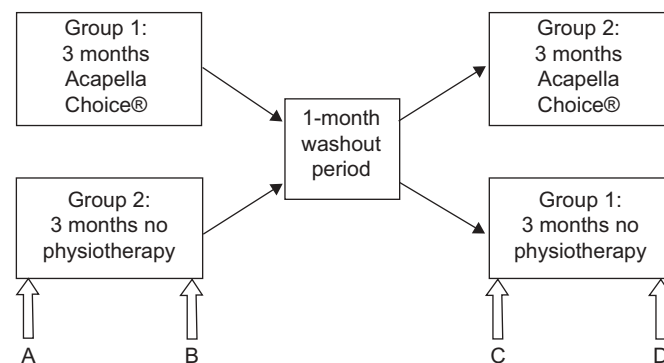


FIGURE 1. Study protocol. Assessments were performed at the start and end of each treatment period. A, B, C and D represent the assessment time-points. Acapella Choice®: Smiths Medical ASD Inc., Weston, MA, USA.

Statistical analysis

Statistical analysis was performed using SPSS for Windows, Version 17 (SPSS Inc., Chicago, IL, USA). The primary aim was to detect an improvement in LCQ score. Using the original validation of the LCQ, with 20 patients, a 5% level of significance (two tailed), a common SD of 0.94 and a power of 80% would detect a mean difference in LCQ score of 0.63 [9]. Using the validation of the LCQ in non-cystic fibrosis bronchiectasis, with 20 patients, a 5% level of significance (two tailed), a common SD of 1.1 and a power of 80% would detect a mean difference in LCQ score of 0.73 [13]. Data was analysed according to the method of JONES and KENWARD [20]. The treatment effect was estimated using the differences of the matched pairs of observations from each patient and are presented as median (interquartile range). Treatment differences between regular chest physiotherapy and no chest physiotherapy were compared using the Wilcoxon test. A two-tailed p-value of <0.05 was considered significant.

RESULTS

Patients

In total, 20 outpatients were recruited. The baseline demographics and patient characteristics are detailed in table 1.

Study entry and post-washout

The baseline characteristics for the end-points at entry to each phase of the study are detailed in table 2. There was no significant difference in total LCQ score, 24-h sputum volume,

FEV₁, FVC, FEF_{25–75%}, MIP, MEP, exercise capacity, sputum microbiology and SGRQ score (table 2) between entry to the first arm of the study (fig. 1, point A) and at the end of the washout period (fig. 1, point C), prior to entry to the second arm of the study.

Completion and adverse events

All patients completed the study and no adverse effects with the oscillatory PEP device occurred. There were 12 exacerbations affecting 11 patients during the study period (table 3). No other interventions or changes to patients' care were required throughout the duration of the study.

Treatment differences

There was a significant improvement in all domains of the LCQ and total score (table 3, fig. 2).

24-h sputum volume significantly increased with regular chest physiotherapy compared with no chest physiotherapy (fig. 3). The total SGRQ score improved significantly with regular chest physiotherapy but the only significant improvement seen in the individual domains of the SGRQ score was in the activity domain (fig. 4). Exercise capacity also improved significantly with regular chest physiotherapy (fig. 5) but there were no significant differences seen in sputum bacteriology, FEV₁, FVC, FEF_{25–75%}, MIP or MEP, or exacerbation frequency (table 3).

DISCUSSION

This randomised crossover trial found that twice daily chest physiotherapy in patients with non-cystic fibrosis bronchiectasis not normally practising regular physiotherapy, significantly improved perceived cough severity, increased 24-h sputum volume, improved exercise capacity and SGRQ score, but had no effect on sputum microbiology, FEV₁, FVC, FEF_{25–75%}, MIP, MEP or exacerbation frequency.

Clearance of bronchopulmonary secretions is impaired in patients with bronchiectasis [2]. MAZZAOCCO *et al.* [21] first explored the potential benefits of chest physiotherapy in bronchiectasis patients over 20 yrs ago, but despite further studies investigating various physiotherapy techniques to aid clearance, there have been no randomised controlled studies exploring the efficacy of regular chest physiotherapy. The primary outcome measured was selected to reflect one of the major goals of management of chronic disease: an improvement in HRQoL. Specifically, we wished to assess the impact of the predominant symptom of bronchiectasis, cough severity.

Our study population had clinically significant bronchiectasis. They had an average of 2 (1.5–3) exacerbations in the preceding 12 months, over two-thirds were chronically colonised with pathogenic organisms in their sputum and, radiologically, 4 (3–4.75) lobes were affected with bronchiectasis on computed tomography chest scan and 75% had varicose or cystic dilatation in at least one lobe. Despite this, they did not carry out regular chest physiotherapy prior to the study.

Our study was conducted with twice daily chest physiotherapy over 3 months as an outpatient. We selected the Acapella Choice® device as the airway clearance technique both for ease of use and based on patient preference from previous studies [8, 22]. Currently, there is no clear evidence for the optimum frequency or duration of airway clearance.

TABLE 1 Patient characteristics

Study participants [#]	20
Male	12 (60)
Age yrs	73 (72–77)
Ex-smokers	8 (40)
Chronic cardiac disease	3 (15)
Neurological disease	1 (5)
Chronic renal impairment	1 (5)
Diabetes mellitus	0
Inhaled corticosteroid therapy	12 (60)
Systemic corticosteroid therapy	0
Long-term antibiotic therapy	2 (10)
Infective exacerbations requiring antibiotic treatment in preceding 12 months	2 (1.5–3)
Lobes affected with bronchiectasis on HRCT	4 (3–4.75)
Varicose or cystic dilatation affecting ≥ 1 lobe	15 (75)
Chronically colonised with pathogenic organisms in sputum when stable	14 (70)
<i>Pseudomonas aeruginosa</i>	6 (42.9)
<i>Haemophilus influenzae</i>	5 (35.7)
<i>Staphylococcus aureus</i>	2 (14.3)
<i>Moraxella catarrhalis</i>	1 (7.1)
Aetiology of bronchiectasis	
Post-infective	10 (50)
Idiopathic	8 (40)
Inactive allergic bronchopulmonary aspergillosis	1 (5)
Inflammatory bowel disease	1 (5)

Data are presented as n, n (%) or median (interquartile range). HRCT: high-resolution computed tomography. [#]: all outpatients.

TABLE 2 Patient characteristics at entry to each study phase

Characteristic	Start of study [#]	End of washout period [†]	p-value
Total LCQ score [‡]	16.3 (14.1–17.9)	15.9 (13.8–19.4)	0.5
24-hr sputum volume mL	5 (1.25–15)	5 (1–13.1)	0.3
FEV ₁ L	1.68 (1.25–2.31)	1.72 (1.19–2.10)	0.8
FEV ₁ % pred	75.7 (48.3–98.1)	68.4 (53–107.1)	
FVC L	2.64 (1.9–3.65)	2.82 (1.75–3.5)	0.6
FVC % pred	79.5 (68.2–95.4)	81.6 (66.1–95.4)	
FEV ₁ /FVC	0.63 (0.57–0.77)	0.62 (0.56–0.82)	0.7
FEV ₁ /FVC % pred	87.1 (77.6–104.4)	97.0 (76.1–120)	
FEF _{25–75%} L·s ⁻¹	0.95 (0.64–1.54)	1.09 (0.54–1.84)	0.96
FEF _{25–75%} % pred	47.5 (21.9–64.8)	44.8 (24.8–96.4)	
MIP cmH ₂ O	43.5 (33.2–72.5)	48 (32.5–61.5)	0.2
MIP % pred	58.5 (37.2–77.2)	51.7 (31.1–63)	
MEP cmH ₂ O	68.5 (58.5–95.2)	67 (51–109)	0.3
MEP % pred	60.9 (41.9–83.4)	51.3 (38.3–55.7)	
Exercise capacity m	220 (120–405)	210 (137.5–357.5)	1.0
Sputum bacterial load cfu·mL ⁻¹	3.8×10^6 (3.9×10^5 – 3.8×10^7)	1.1×10^6 (1×10^3 – 1.1×10^9)	0.6
Total SGRQ score [§]	41.1 (24.6–44.8)	40.4 (18.0–52.5)	0.6

Data are presented as median (interquartile range), unless otherwise stated. LCQ: Leicester Cough Questionnaire; FEV₁: forced expiratory volume in 1 s; % pred: % predicted; FVC: forced vital capacity; FEF_{25–75%}: forced expiratory flow at 25–75% of FVC; MIP: maximum inspiratory pressure; MEP: maximum expiratory pressure; SGRQ: St George's Respiratory Questionnaire. [#]: see point A on figure 1; [†]: see point C on figure 1; [‡]: the total severity score ranges from 3–21, a lower score indicates a more severe cough; [§]: the total score ranges from 0–100, a higher score indicates a poorer health-related quality of life.

However, it is recognised that airway clearance regimens need to be effective without affecting other activities of daily living. We selected a twice daily physiotherapy regimen to account for this and also because previous studies assessing different physiotherapy techniques for non-cystic fibrosis bronchiectasis have achieved compliance with this frequency [8, 23]. Further studies are needed to specifically address the optimal frequency and duration of physiotherapy.

Several adjuncts to physiotherapy currently exist including: 1) bronchodilator therapy which may minimise bronchial

hyperreactivity and improve airway clearance; 2) inhaled hyperosmolar agents (nebulised hypertonic saline has been shown to yield greater sputum weights and inhaled mannitol has been shown in small studies to aid mucociliary clearance [24, 25]); and 3) pulmonary rehabilitation and inspiratory muscle training has previously been shown to improve exercise tolerance [26]. However, inhaled mucolytics (recombinant human DNase), although of benefit in cystic fibrosis, are not recommended in non-cystic fibrosis bronchiectasis because they have a significant negative impact on FEV₁ [27]. Our study did not employ any such adjuncts. Further studies are

TABLE 3 Treatment differences

Outcome	Twice daily physiotherapy	No regular physiotherapy	p-value
Total LCQ score improvement	1.3 (-0.17–3.25)	0 (-1.5–0.5)	0.002
24-h sputum volume mL	2 (0–6)	-1 (-5–0)	0.02
FEV ₁ L	-0.01 (-0.06–0.08)	-0.01 (-0.1–0.11)	0.7
FVC L	-0.01 (-0.09–0.28)	0.06 (-0.08–0.21)	0.9
FEF _{25–75%} L·s ⁻¹	-0.02 (-0.17–0.16)	0.04 (-0.1–0.34)	0.6
MIP cmH ₂ O	-1 (-9–7)	5.5 (-10–12.5)	0.7
MEP cmH ₂ O	5 (-11–25)	8.5 (-3.7–19.7)	0.7
Exercise capacity m	40 (15–80)	0 (-10–20)	0.001
Sputum bacterial load cfu·mL ⁻¹	-1×10^3 (-2.78×10^6 – -1.74×10^7)	1×10^3 (-6.5×10^7 – -6.4×10^6)	0.72
Total SGRQ score improvement	7.8 (-0.99–14.5)	-0.7 (-2.3–0.05)	0.005
Exacerbations n	5	7	0.48

Data are presented as median (interquartile range), unless otherwise stated. LCQ: Leicester Cough Questionnaire; FEV₁: forced expiratory volume in 1 s; FVC: forced vital capacity; FEF_{25–75%}: forced expiratory flow at 25–75% of FVC; MIP: maximum inspiratory pressure; MEP: maximum expiratory pressure; SGRQ: St George's Respiratory Questionnaire.

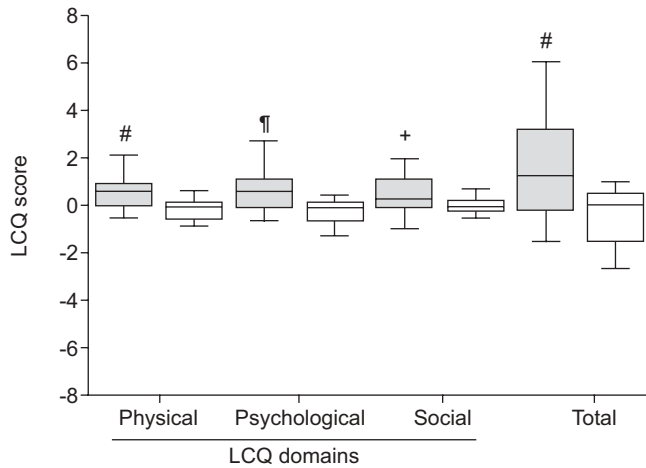


FIGURE 2. Change in Leicester Cough Questionnaire (LCQ) individual domain and total scores with physiotherapy (■) and with no physiotherapy (□). The horizontal lines represent the median and interquartile ranges for each group and the whiskers represent the maximum and minimum. #: $p=0.002$; †: $p<0.0001$; ‡: $p=0.02$.

needed to assess efficacy of such techniques in addition to regular chest physiotherapy.

This study did not have a sham arm and, instead, we compared twice daily chest physiotherapy using an oscillatory PEP device with no chest physiotherapy. This design was intentional as any type of sham would involve some form of airway clearance. A limitation of this study design, however, is the potential for a placebo effect. The crossover design was used to offer all patients a period of regular chest physiotherapy during the study. There was no carry over effect with the 1-month washout phase.

One of the main goals of long-term management of chronic respiratory disease is to improve HRQoL and with regular,

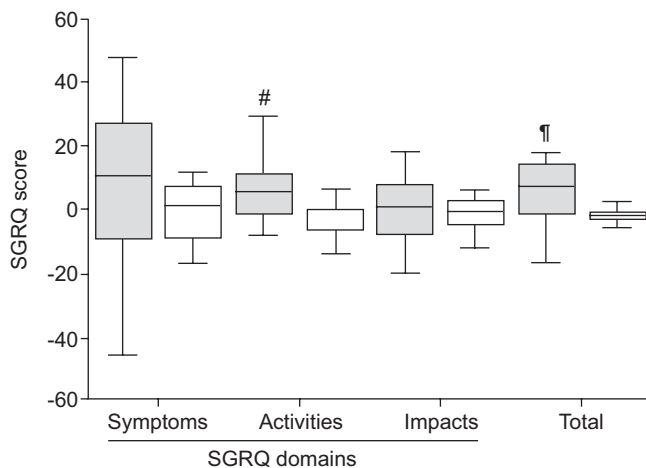


FIGURE 4. Change in St George's Respiratory Questionnaire (SGRQ) individual domain and total scores with physiotherapy (■) and with no physiotherapy (□). The horizontal lines represent the median and interquartile ranges for each group and the whiskers represent the maximum and minimum. #: $p=0.02$; †: $p=0.005$.

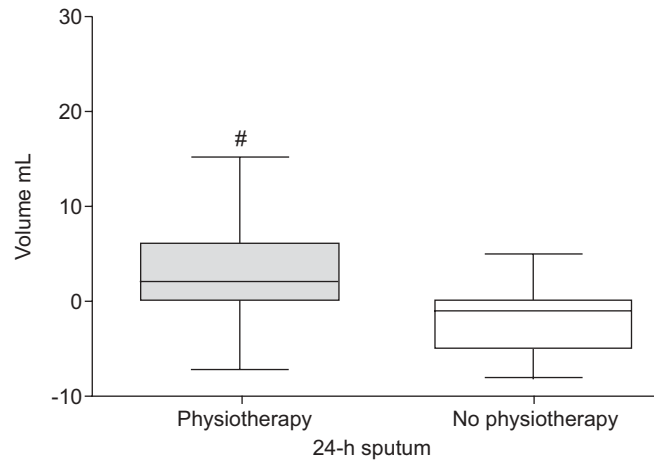


FIGURE 3. Change in 24-h sputum volume with physiotherapy and with no physiotherapy. The horizontal lines represent the median and interquartile ranges and the whiskers represent the maximum and minimum. #: $p=0.02$.

controlled airway clearance, patient perception of cough severity improved with an increase in score seen in all domains of the LCQ. Since the completion of this study, a 1.3 unit difference in the total LCQ score has been established as a clinically significant change and we observed a median increase of 1.3 units following 3 months of twice daily chest physiotherapy [15]. An open label study by MUTALITHAS *et al.* [28] found a mean improvement of 3.1 units in total LCQ score with bronchopulmonary hygiene physical therapy. Importantly, although our study was not powered to detect a change in SGRQ score, we observed that this too improved, with the total score improving beyond its established minimal clinically significant change of 4 units (median improvement of 7.8 units) [14].

A major rationale for chest physiotherapy is to loosen secretions and enhance expectoration. According to previous work by CECINS *et al.* [29], our study was sufficiently powered to detect a 15% change in 24-h sputum volume and we found that with

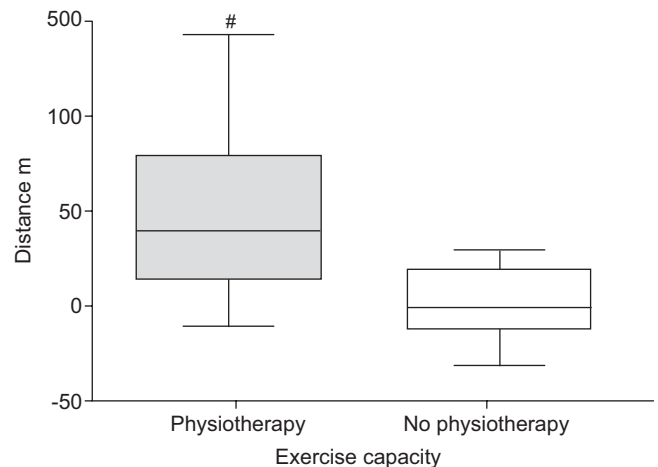


FIGURE 5. Change in exercise capacity with physiotherapy and with no physiotherapy. The horizontal lines represent the median and interquartile ranges for each group and the whiskers represent the maximum and minimum. #: $p=0.001$.

twice daily chest physiotherapy the mean volume of sputum expectorated over 24 h increased by 2 (0–6) mL. Although the value of 24-h sputum collections in clinically stable outpatients may be limited by patient compliance and confounded by factors such as swallowed secretions, it is a highly pertinent, noninvasive marker and has been selected as a relevant outcome measure in previous studies assessing other potential long-term therapeutic strategies in bronchiectasis, including inhaled steroids and long-term antibiotics [30–33].

We also observed an increase in the distance achieved during the incremental shuttle walk test following 3 months of twice daily chest physiotherapy. Based on a previous study by NEWALL *et al.* [26], our patient sample size was powerful enough to detect a significant effect on exercise capacity. This perhaps emphasises the improvement in the activities domain of the SGRQ and that with greater control of cough and clearance of mucus from the airways, exercise capacity also improves.

The benefits observed with regular chest physiotherapy were small however, and we did not find any improvements in the remaining study end-points. Despite increased sputum expectoration, we observed no change in sputum bacterial load or any improvement in FEV₁, FVC, FEF_{25–75%}, MIP, MEP or exacerbation frequency. One previous study of airway clearance techniques in bronchiectasis comparing the Flutter device with the active cycle of breathing technique found a significant improvement in FEV₁ (0.08 L, 95% CI 0.01–0.15 using the Flutter device); however, this improvement in FEV₁ was not thought to be clinically significant [8]. Our patient cohort had a mean age of 73 (72–77) yrs and with increasing age there is less airway reversibility, perhaps further limiting the opportunity for any benefit from chest physiotherapy on FEV₁ or FVC. In addition, we found no improvements in the assessment of small airways or inspiratory and expiratory pressures. However, this may be due to the intrinsic variability of such measurements. A previous study by NEWALL *et al.* [26] in non-cystic fibrosis bronchiectasis patients found MEP to be impaired but MIP were within normal range. Our study population was, however, older which may explain the difference. Despite the lack of improvements in these measures, exercise capacity significantly increased.

In conclusion, this randomised crossover study found that regular chest physiotherapy in non-cystic fibrosis bronchiectasis has significant benefits compared with no chest physiotherapy. Despite the differences being small, achieving an improvement in functional ability and HRQoL is highly relevant to the management of this long-term illness. Larger studies are needed to explore potential benefits on other outcome measures.

CLINICAL TRIALS

This study is a registered on the Clinical Trials Database at Clinicaltrials.gov (NCT00816309). It is also registered on the National Research Registry (N0519192394).

SUPPORT STATEMENT

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STATEMENT OF INTEREST

None declared.

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