

**“LAPORAN TUGAS MODUL KARDIOPULMONAL”**



**Disusun Oleh :**

**Nama : Ilham Wally**

**NIM : 1810301058**

**Kelas : 6 A**

**PROGRAM STUDI S1 FISIOTERAPI**

**FAKULTAS ILMU KESEHATAN**

**UNIVERSITAS 'AISYIYAH YOGYAKARTA**

## **RESUME JURNAL ASMA :**

### **Effects of Aerobic Training versus Breathing**

#### **Exercises on Asthma Control: A Randomized Trial**

Tahun : 2020

### **INTRODUCTION**

Latihan aerobik dan latihan pernapasan merupakan intervensi yang meningkatkan pengendalian asma. Namun, hasil dari 2 intervensi ini belum dapat dibandingkan. Tujuan dari penelitian ini untuk membandingkan efek latihan aerobik versus latihan pernapasan pada kontrol klinis (hasil utama), kualitas hidup, kapasitas olahraga, dan peradangan saluran napas pada pasien rawat jalan dengan asma sedang hingga berat.

### **METODE**

Peserta pada penelitian ini sebanyak 54 pasien rawat jalan dengan asma persisten sedang hingga berat (berusia 30-65 tahun). Kriteria inklusi : kedua jenis kelamin, orang dengan indeks massa tubuh (BMI)  $<35 \text{ kg} / \text{m}^2$ , tidak banyak bergerak ( $<60$  menit aktivitas fisik / minggu selama waktu senggang), dalam perawatan medis selama minimal 6 bulan, dan stabil secara klinis (yaitu, tidak ada krisis atau perubahan pengobatan selama  $\geq 30$  hari). Kriteria eksklusi : riwayat tembakau  $> 10$  bungkus / tahun; penyakit paru-paru lain atau hipertensi yang tidak terkontrol; serta diabetes dan gangguan muskuloskeletal yang memengaruhi kemampuan pasien untuk melakukan latihan.

Desain studi pada penelitian ini yaitu peserta dibagi menjadi dua kelompok secara acak, kelompok 1 Aerobic training 25 peserta (AG,  $n = 25$ ), kelompok 2 Breathing group 29 peserta (BG,  $n = 29$ ).

Pada aerobic grup diberikan program latihan dengan treadmill dalam ruangan, dan setiap sesi berlangsung selama 40 menit, terdiri dari 5 menit pemanasan, 30 menit latihan aerobik, dan 5

menit pendinginan. Pelatihan aerobik dimulai pada 60% HR sesuai dengan rumus Karvonen :  
 $HR_{\text{training}} = HR_{\text{rest}} + 0.6 (HR_{\text{maximal}} - HR_{\text{rest}})$ .

Pada Breathing grup diberikan latihan breathing, latihan dibagi menjadi 3 fase progresif. Fase pertama bertujuan untuk meningkatkan kontrol pernapasan diafragma; fase kedua bertujuan untuk meningkatkan kontrol pernapasan dengan mengubah durasi inspirasi dan ekspirasi (1: 1 menjadi 1: 4) sesuai dengan kapasitas dan kenyamanan pasien. Fase ketiga menggabungkan latihan dari fase 1 dan 2.

Kedua intervensi tersebut berlangsung selama 24 sesi (2 / minggu, 40 menit / sesi). Kontrol klinis asma (Asthma Control Questionnaire [ACQ]), kualitas hidup (Asma Quality of Life Questionnaire), asthma symptom-free days (ASFD), radang saluran napas, kapasitas olahraga, tekanan psikologis (Hospital Anxiety and Depression Scale), daily life physical activity (DLPA), dan fungsi paru dievaluasi sebelum, segera setelah, dan 3 bulan setelah intervensi.

## **HASIL**

Kedua intervensi menyajikan hasil yang serupa mengenai skor ACQ, tekanan psikologis, ASFD, DLPA, dan peradangan saluran napas ( $P > .05$ ). Namun, peserta di AG 2,6 kali lebih mungkin untuk mengalami perbaikan klinis pada follow up 3 bulan dibandingkan peserta di BG ( $P = .02$ ). Sebagian besar peserta di AG juga menunjukkan pengurangan jumlah hari tanpa penggunaan obat penyelamat dibandingkan dengan BG (34% vs 8%;  $P = .04$ ).

## **DISKUSI**

Pelatihan aerobik dapat meningkatkan pengendalian asma baik dengan meningkatkan kapasitas aerobik dan / atau dengan mengurangi hiperresponsivitas bronkial (BHR) karena keduanya terkait dengan pengendalian asma yang lebih baik. Latihan pernapasan juga bisa menurunkan BHR.

Efek latihan pernapasan pada gejala asma tampaknya bergantung pada tekniknya. Cooper et al membandingkan 2 teknik pernapasan dan menyarankan bahwa hanya teknik Buteyko yang dapat

mengurangi gejala asma. Ritz et al mengamati peningkatan yang signifikan setelah latihan pernapasan yang dipandu oleh kapnometri, sedangkan Manocha et al tidak menunjukkan adanya perbaikan gejala asma pada pasien yang melakukan latihan pernapasan yoga.

#### Keterbatasan

Pertama, kami mengembangkan latihan pernapasan Pranayama tertentu, dan hasil kami tidak dapat dibandingkan dengan penelitian lain yang telah menggunakan yoga atau kelompok latihan pernapasan Pranayama lainnya. Kedua, ISWT bukanlah standar emas untuk menilai kapasitas olah raga dan tidak pernah terbukti sensitif dalam mengevaluasi pelatihan olah raga pada subyek dengan asma. Ketiga, kesimpulan dari penelitian ini tampaknya hanya berguna untuk subjek dengan asma sedang hingga berat tanpa penyakit penyerta lainnya.

#### **KESIMPULAN**

Pasien rawat jalan dengan asma sedang hingga berat yang mengikuti pelatihan aerobik atau program latihan pernapasan menunjukkan hasil yang sama dalam pengendalian asma, kualitas hidup, gejala asma, tekanan psikologis, aktivitas fisik, dan peradangan saluran napas. Namun, sebagian besar peserta di AG menunjukkan perbaikan dalam pengendalian asma dan pengurangan penggunaan obat.

## **RESUME JURNAL CYSTIC FIBROSIS :**

### **Effects of exercise and airway clearance (positive expiratory pressure) on mucus clearance in cystic fibrosis: a randomized crossover trial**

Tahun : 2019

#### **INTRODUCTION**

Olahraga meningkatkan pembersihan lendir pada orang tanpa penyakit paru-paru dan mereka yang menderita bronkitis kronis. Tidak ada penelitian yang menyelidiki olahraga saja untuk pembersihan lendir pada cystic fibrosis (CF). Tujuan dari penelitian ini adalah untuk membandingkan efek latihan treadmill terhadap istirahat pernapasan dan pembersihan saluran napas dengan terapi tekanan ekspirasi positif (PEP) pada pembersihan lendir pada orang dewasa dengan CF.

#### **METODE**

Peserta pada penelitian ini sebanyak 15 orang dengan kriteria inklusi : berusia  $\geq 17$  tahun, memiliki diagnosis CF yang dikonfirmasi (pengujian genetik dan / atau tes keringat positif sebelumnya) dan dokter yang merawat mereka menganggap mereka stabil secara klinis. Kriteria eksklusi : menerima transplantasi paru-paru, terinfeksi dengan kompleks Burkholderia cepacia, hamil atau telah melebihi batasan dosis dari paparan radiasi tambahan untuk manajemen klinis normal.

Desain studi pada penelitian ini yaitu Sebuah uji silang acak dilakukan, terdiri dari empat kunjungan. Pada kunjungan 1, penilaian fungsi paru dan kapasitas latihan dilakukan sebelum pengacakan. Urutan intervensi (satu intervensi per kunjungan 2, 3 dan 4). Ketiga intervensi tersebut adalah sebagai berikut: 1) latihan treadmill beban konstan; 2) PEP plus FET (mulai sekarang disebut sebagai terapi PEP); dan 3) pernapasan istirahat (kontrol). Setiap intervensi dilakukan selama 20 menit. Untuk menstandarkan prosedur, kunjungan 2, 3 dan 4 dijadwalkan

pada waktu yang sama di sore hari, dipisahkan oleh setidaknya 48 jam dan dalam periode 2 minggu (selama pengobatan, pembersihan jalan napas, dan rejimen olahraga tidak berubah).

Untuk intervensi latihan, peserta berlatih di treadmill selama 20 menit dengan kecepatan kerja konstan yang setara dengan 60% dari konsumsi oksigen puncak ( $V'O_2$ peak) yang dicapai dalam uji treadmill puncak tambahan pada kunjungan 1. Intervensi terapi PEP terdiri dari pernapasan melalui perangkat PEP selama 15 napas, diikuti dengan pernapasan dalam dan rileks, huffing dan coughing, menurut FET. Siklus ini diulang sebanyak enam kali.

## **HASIL**

Latihan treadmill meningkatkan pembersihan lendir seluruh paru dibandingkan dengan resting breathing (perbedaan rata-rata 3%, 95% CI 2-4); namun, exercise saja kurang efektif dibandingkan terapi PEP (perbedaan rata-rata -7%, 95% CI -6- -8). Ketika membandingkan latihan treadmill dengan terapi PEP, tidak ada perbedaan yang signifikan dalam pembersihan lendir dari daerah paru-paru antara dan perifer, tetapi pembersihan yang jauh lebih sedikit dari daerah paru-paru pusat (kemungkinan mencerminkan huffing dan coughing yang hanya ada pada terapi PEP).

## **DISKUSI**

Penelitian ini telah menunjukkan bahwa satu kali latihan treadmill meningkatkan pembersihan lendir paru secara keseluruhan dibandingkan dengan tanpa intervensi; namun, exercise saja kurang efektif dibandingkan dengan teknik pembersihan jalan napas yang sudah mapan dari terapi PEP, yang meliputi huffing dan coughing. Dalam kaitannya dengan efek dari dua intervensi pada daerah paru-paru yang berbeda, tidak ada perbedaan dalam jumlah lendir yang dikeluarkan dari daerah perifer dan perantara, namun secara signifikan lebih sedikit lendir yang dibersihkan dari daerah pusat hanya dengan exercise. Perbedaan ini kemungkinan besar disebabkan oleh huffing dan coughing pada komponen FET terapi PEP. Oleh karena itu, dalam praktik klinis, FET direkomendasikan untuk disertakan dengan exercise jika tujuannya adalah untuk meningkatkan pembersihan lendir paru sentral dan keseluruhan. Studi jangka panjang yang

menyelidiki exercise (dengan huffing dan coughing) sebagai teknik pembersihan jalan napas mandiri diperlukan untuk menentukan apakah itu efektif teknik pembersihan jalan napas yang sudah mapan pada hasil yang penting secara klinis, seperti frekuensi eksaserbasi, kualitas hidup dan kapasitas latihan, yang mana berhubungan dengan morbiditas dan mortalitas pada CF.

## **KESIMPULAN**

Latihan treadmill secara signifikan meningkatkan pembersihan lendir dari seluruh paru dibandingkan tanpa intervensi, latihan treadmill secara signifikan kurang efektif dibandingkan dengan terapi PEP. Tidak ada perbedaan yang signifikan, bagaimanapun, dalam jumlah lendir yang dikeluarkan dari daerah paru-paru antara dan perifer ketika membandingkan latihan treadmill dan terapi PEP.

## **RESUME JURNAL PNEUMONIA :**

### **Inpatient Rehabilitation Improves Functional Capacity, Peripheral Muscle Strength and Quality of Life in Patients with Community-acquired Pneumonia:**

#### **A Randomised Trial**

Tahun : 2016

#### **INTRODUCTION**

Efek latihan aerobik dan ketahanan terhadap kapasitas fungsional, kekuatan otot perifer, dan kualitas hidup memerlukan penyelidikan menyeluruh selama rawat inap. Mengingat tingginya prevalensi dan biaya pengobatan pneumonia, dampak sosialnya, dan kelangkaan bukti yang mendukung fisioterapi pernapasan standar untuk pasien tersebut, penting untuk menyelidiki apakah program pelatihan fisik dapat mengarah pada pemulihan yang lebih baik dari kapasitas fungsional saat keluar dari rumah sakit.

Tujuan penelitian ini untuk mengetahui apakah program rehabilitasi berbasis latihan rawat inap meningkatkan hasil fungsional, gejala, kualitas hidup dan lama tinggal di rumah sakit lebih dari rejimen fisioterapi pernapasan pada pasien pneumonia.

#### **METODE**

Peserta pada penelitian ini sebanyak 49 orang dengan kriteria inklusi : berusia > 18, dirawat di rumah sakit selama <48 jam, dan memiliki kesadaran yang memadai dan ambulasi independen. Kriteria eksklusi : tidak mau berpartisipasi, mengalami gangguan kognitif, mengalami gangguan osteoartikuler, dan penyakit pernapasan akut atau kronis lainnya.

Penelitian ini dilakukan secara acak, peserta dibagi menjadi dua kelompok, kelompok eksperimental sebanyak 32 orang (n=32), kelompok kontrol sebanyak 17 orang (n=17).



Intervensi pada kelompok kontrol :

1. Breathing exercise :
  - Diafragma breathing : 10 kali repetisi, 3 set, rest 1 menit
  - Inspirasi dan ekspirasi maksimum : 10 kali repetisi, 3 set, rest 1 menit
2. Teknik pembuangan sekresi  
perkusi dan vibrocompression dengan posisi berbaring selama 10 menit di setiap sisi, kemudian diinstruksikan huffing dan coughing.
3. Jalan kaki diatur sendiri dengan durasi selama 10 menit.
4. Semua dilakukan 50 menit setiap hari selama 8 hari

Intervensi pada kelompok eksperimen :

1. Pemanasan, 5 menit gerak aktif pada ekstremitas atas dan bawah
2. Stretching, 5 menit tiap gerakan ditahan selama 30 detik, target pada otot pectoralis mayor, latissimus dorsi, trapezius, quadriceps femoris dan hamstring.
3. Latihan kekuatan otot, selama 25 menit, I = 70% 1RM, Repetisi = 8 kali, Set = 3, Rest = 1 menit. Target pada otot bicep brachii, deltoid, hamstring dan quadriceps.
4. Latihan Aerobic, berjalan dengan track 10 meter dengan waktu 15 menit.
5. Semua dilakukan 50 menit setiap hari selama 8 hari.

## **HASIL**

Ada peningkatan yang lebih besar pada kelompok eksperimen daripada pada kelompok kontrol pada tes Aktivitas Kehidupan Sehari-hari Glittre (rata-rata perbedaan antar kelompok 39 detik, 95% CI 20 sampai 59) dan tes jalan kaki tambahan (rata-rata perbedaan antar kelompok 130 m, 95% CI 77 hingga 182). Ada juga peningkatan yang secara signifikan lebih besar dalam kualitas hidup, dispnea dan kekuatan otot perifer pada kelompok eksperimen dibandingkan pada kelompok kontrol. Tidak ada perbedaan antara kelompok dalam fungsi paru-paru, protein C-reaktif atau lama tinggal di rumah sakit.

## **DISKUSI**

Penelitian ini mengidentifikasi peningkatan yang signifikan dalam kapasitas fungsional, kekuatan otot perifer, dispnea dan kualitas hidup dengan rehabilitasi olahraga rawat inap yang bertentangan dengan intervensi pernapasan. Dipercaya bahwa manfaat ini, bersama dengan bukti lain tentang manfaat senam rawat inap pada populasi ini, cukup untuk merekomendasikan penggunaan program rehabilitasi rawat inap - terutama di mana perawatan rutin saat ini untuk pasien ini adalah teknik fisioterapi pernapasan, karena yang terakhir tidak memiliki bukti kuat untuk mendukung penggunaannya pada populasi ini. Mengingat efek tak terduga dari rehabilitasi latihan rawat inap pada eksaserbasi PPOK, bagaimanapun, penelitian lebih lanjut harus menyelidiki efek intervensi orang dengan pneumonia yang didapat dari komunitas setelah keluar dari rumah sakit.

Batasan dari penelitian ini adalah bahwa para peneliti yang mengevaluasi tes Glittre Activities of Daily Living, ISWT, kualitas hidup, dispnea, kekuatan otot tepi dan spirometri sama dengan mereka yang melakukan intervensi terapeutik. Namun, evaluasi tersebut distandarisasi dengan pedoman tertulis untuk meminimalkan potensi bias dari penilai yang tidak buta. Selain itu, penilai tidak mengetahui beberapa hasil studi utama seperti CRP, lama rawat inap, dan hasil (kematian atau keluar dari rumah sakit).

## **KESIMPULAN**

Peningkatan hasil fungsional setelah program rehabilitasi rawat inap lebih besar daripada peningkatan setelah fisioterapi pernapasan standar. Program latihan olah raga memberikan manfaat yang lebih besar pada kapasitas fungsional, kekuatan otot perifer, dispnea dan kualitas hidup.

## 1. JURNAL ASMA :

## Original Article

## Effects of Aerobic Training versus Breathing Exercises on Asthma Control: A Randomized Trial

Karen B. Evaristo, MSc<sup>a</sup>, Felipe Augusto Rodrigues Mendes, PhD<sup>a,b</sup>, Milene G. Saccomani, PhD<sup>a</sup>, Alberto Cukier, PhD<sup>c</sup>, Regina M. Carvalho-Pinto, PhD<sup>c</sup>, Marcos R. Rodrigues, MSc<sup>d</sup>, Danilo F. Santaella, PhD<sup>d</sup>, Beatriz M. Saraiva-Romanholo, PhD<sup>e,f</sup>, Milton A. Martins, PhD<sup>d</sup>, and Celso R.F. Carvalho, PhD<sup>a</sup> São Paulo, Brazil

**BACKGROUND:** Aerobic training and breathing exercises are interventions that improve asthma control. However, the outcomes of these 2 interventions have not been compared.

**OBJECTIVE:** To compare the effects of aerobic training versus breathing exercises on clinical control (primary outcome), quality of life, exercise capacity, and airway inflammation in outpatients with moderate-to-severe asthma.

**METHODS:** Fifty-four asthmatics were randomized into either the aerobic training group (AG, n [ 29) or the breathing exercise group (BG, n [ 25). Both interventions lasted for 24 sessions (2/week, 40 minutes/session). Asthma clinical control (Asthma Control Questionnaire [ACQ]), quality of life (Asthma Quality of Life Questionnaire), asthma symptom-free days (ASFD), airway inflammation, exercise capacity, psychological distress (Hospital Anxiety and Depression Scale), daily-life physical activity (DLPA), and pulmonary function were evaluated before, immediately after, and 3 months after the intervention.

**RESULTS:** Both interventions presented similar results regarding the ACQ score, psychological distress, ASFD, DLPA, and airway inflammation ( $P > .05$ ). However, participants in the AG were 2.6 times more likely to experience clinical improvement at the 3-month follow-up than participants in the

BG ( $P [ .02$ ). A greater proportion of participants in the AG also presented a reduction in the number of days without rescue medication use compared with BG (34% vs 8%;  $P [ .04$ ).

**CONCLUSIONS:** Outpatients with moderate-to-severe asthma who participated in aerobic training or breathing exercise programs presented similar results in asthma control, quality of life, asthma symptoms, psychological distress, physical activity, and airway inflammation. However, a greater proportion of participants in the AG presented improvement in asthma control and reduced use of rescue medication. 2020 American Academy of Allergy, Asthma & Immunology (J Allergy Clin Immunol Pract 2020;:--)

**Key words:** Pulmonary rehabilitation; Persistent asthma; Symptoms; Clinical control; Quality of life; Airway inflammation; Asthma guidelines

Asthma is a chronic disease defined as reversible airflow obstruction, inflammation, and hyperresponsiveness to different stimuli and characterized by wheezing, breathlessness, chest tightness, and coughing.<sup>1</sup> These symptoms reduce patients' quality of life and restrict daily-life physical activity (DLPA).<sup>2</sup> Subjects with asthma also present higher levels of anxiety and

<sup>a</sup>Department of Physical Therapy, School of Medicine, University of São Paulo, São Paulo, Brazil

<sup>b</sup>Department of Physical Therapy, Universidade Ibirapuera, São Paulo, Brazil

<sup>c</sup>Department of Pulmonary Division (InCor), School of Medicine, University of São Paulo, São Paulo, Brazil

<sup>d</sup>Department of Sports, School of Medicine, University of São Paulo, São Paulo, Brazil

<sup>e</sup>Department of Medicine, School of Medicine, University of São Paulo, São Paulo, Brazil

<sup>f</sup>Department of Physical Therapy, University City of Sao Paulo (UNICID), São Paulo, Brazil

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Corresponding author: Celso R.F. Carvalho, PhD, Department of Medicine, School of Medicine, University of Sao Paulo, Av. Dr. Arnaldo 455, Room 1210, Postal Code 01246-903, São Paulo, Brazil. E-mail: [cscarval@usp.br](mailto:cscarval@usp.br). 2213-2198

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## Abbreviations used

ACQ- Asthma Control Questionnaire  
 AG- Aerobic training group  
 AQLQ- Asthma Quality of Life Questionnaire  
 BG- Breathing group  
 BHR- Bronchial hyperresponsiveness  
 CI- Confidence interval  
 DLPA- Daily-life physical activity  
 HADS- Hospital Anxiety and Depression Scale  
 HR- Heart rate  
 HRQoL- Health-related quality of life  
 SWT- Incremental shuttle walking test  
 LMM- Linear mixed model  
 MCID- Minimal clinically important difference  
 NNT- Number needed to treat  
 RCT- Randomized controlled trial  
 RR- Relative risk

depression, which may reduce adherence to medication<sup>3</sup> and clinical control.<sup>4</sup> Such control is essential to avoid a patient's impairment and reduce the risk of exacerbation and is centered on the amount of medication (controllers and relievers) required to avoid symptoms.

Aerobic<sup>5</sup> training and breathing<sup>6</sup> exercises are non-pharmacological interventions that improve asthma control and have been considered important adjuvants for medical treatment.<sup>1</sup> Both exercises have been widely used and are low cost, easy to apply, and safe. Aerobic training reduces corticosteroid consumption,<sup>7</sup> psychosocial distress,<sup>8</sup> and dyspnea and asthma symptoms<sup>5</sup> in addition to improving health-related quality of life (HRQoL),<sup>9-11</sup> aerobic capacity,<sup>5</sup> and clinical control.<sup>9,10</sup> There is evidence that breathing exercises also provide benefits, such as improvement in HRQoL<sup>12-14</sup> and reduction of anxiety and depression,<sup>12,13</sup> asthma symptoms,<sup>12,15</sup> the use of relief medication,<sup>16</sup> episodes of exacerbation, and airway hyper-responsiveness.<sup>17</sup> However, the benefits of these 2 types of exercises as interventions for asthma control have not yet been compared. In the present study, we aimed to compare the effects of aerobic training and breathing exercises on clinical control (primary outcome) and airway inflammation (secondary outcome) in outpatients with persistent moderate-to-severe asthma.

## METHODS

More details on the patient inclusion criteria, study design, randomization, interventions, outcome assessments, and statistical analysis are available in the Methods section of the Online Repository at [www.jaci-inpractice.org](http://www.jaci-inpractice.org).

### Patients

Fifty-four outpatients with moderate-to-severe persistent asthma (aged 30-65 years) were recruited from the University Hospital during a regular medical visit. All volunteers gave their written informed consent. Asthma was diagnosed according to the Global Initiative for Asthma.<sup>1</sup>

### Study design

The study was a prospective and randomized controlled trial (RCT) with 2 arms that compared nonpharmacological interventions (breathing exercises vs aerobic training) and was conducted between 2 medical consultations to avoid changes in

medication during the interventions. All patients were advised to maintain their medications during the study.

**Randomization.** The eligible participants were randomly allocated to one of the following groups: aerobic training (AG, n = 25) or breathing (BG, n = 29). A simple randomization sequence was computer-generated by an investigator who was not directly involved with the recruitment, assessment, or treatment of the patients. Each patient's allocation was concealed using sequential numbering that was sealed and placed in opaque envelopes. The randomization process was performed after the baseline measurements.

### Interventions

**Educational program.** This program consisted of two 2-hour classes/week for 2 weeks.<sup>8</sup> Presentations and group discussions included information on asthma pathophysiology, medication skills, self-monitoring techniques, and environmental control.<sup>1</sup>

**Aerobic training program.** The program was performed with an indoor treadmill (Imbramed Export Plus, Brazil), and every session lasted 40 minutes, consisting of 5 minutes of warm-up, 30 minutes of aerobic training, and 5 minutes of cool-down. Aerobic training was initiated at 60% of heart rate (HR) recovery obtained by the Karvonen equation:  $HR_{training} = \frac{1}{4} (HR_{max} - HR_{rest}) + HR_{rest}$ .

**Breathing exercise program.** This program was based on the Pranayama Yoga breathing technique, which was developed by 2 senior yoga instructors (MRR and DFS). Breathing exercises aimed to stimulate nasal and diaphragmatic breathing, to increase expiratory time, to slow respiratory flow, and to regulate breathing rhythm.<sup>18</sup>

**Outcome assessments.** The primary outcome was clinical improvement of the Asthma Control Questionnaire 6 (ACQ6) scores.<sup>19</sup> Asthma symptoms and exacerbation were evaluated using a daily diary of symptoms as previously reported.<sup>8,10</sup> Sputum was collected and processed using a standard method.<sup>20</sup> Maximal exercise capacity was assessed by the incremental shuttle walking test (ISWT).<sup>21</sup> The Asthma Quality of Life Questionnaire (AQLQ)<sup>22</sup> and Hospital Anxiety and Depression Scale (HADS)<sup>23</sup> were used to estimate the quality of life and psychological distress. DLPA was quantified using an accelerometer (Power Walker SW 610, Japan),<sup>24</sup> and the spirometry test was performed following the American Thoracic Society/European Respiratory Society protocol<sup>25</sup> (Sensor-medics Vmax 229, Yorba Linda, Calif). All outcomes were evaluated before and after the interventions. The ACQ, AQLQ, and HADS were also evaluated in a 3-month postintervention follow-up.

### Statistical analysis

A sample size of 48 patients was calculated based on the minimal clinically important difference (MCID) in the ACQ score between the groups (0.5-0.72, mean standard deviation)<sup>9</sup> and considering a power of 80% and a 5% level of significance. The sample size was increased to 54 patients considering a 20% dropout rate. Analyses were preceded by multiple imputation analyses based on 100 imputed versions obtained via predictive mean matching. A linear mixed model (LMM) was used to test the significance of the effect of group, time, and their interaction over the course of the study. For all measures, a group-by-time interaction effect was tested using a full-factorial model. In all models, the subjects were considered random effects to account for within-subject correlations over time.

Group was used as a fixed factor, and time was used as a repeated measure. Post hoc comparisons were performed to determine the significance of the differences of the means and the Bonferroni method was used to adjust the P value obtained from the multiple comparisons.<sup>26</sup> Asthma symptom-free days (count data) were analyzed with a generalized linear model (generalized estimation equations) with the adequacy of the data determined by the negative binomial distribution. The threshold for statistical significance was set at 5%, and the Satterthwaite approximation was used to compute the degrees of freedom in the denominator of the LMM. The relative risk (RR) and number needed to treat (NNT) were used to evaluate the clinically important differences in the outcomes of the participants in the AG and BG. Data were analyzed using the Statistical Package for the Social Sciences (SPSS) (IBM, New York, NY).

## RESULTS

More details on the patients and baseline characteristics, the HADS, the induced sputum, and the DLPA are available in the

Results section of the Online Repository at [www.jaci-inpractice.org](http://www.jaci-inpractice.org).

### Patients and baseline characteristics

A flow diagram of the study is presented in [Figure 1](#). Both groups had similar demographic and clinical characteristics at baseline ([Table I](#)). No study-related adverse events were observed during or after the interventions. Ten patients in the AG (35%) and 6 patients (24%) in the BG reported asthma exacerbation during the study (nonstudy-related adverse events), and there was no significant difference between the groups ( $P = .31$ ,  $\chi^2$ ).

### Primary outcome

**Clinical asthma control.** The results show a significant effect for the "Treatment Time" interaction ( $P = .004$ ) and a main effect for "Time" ( $P = .001$ ). The main effect for group was not significant ( $P = .5$ ). Specifically, the "Treatment Time" interaction was explored to check the group differences over time and the time differences within groups. No significant differences were observed between the groups after the

TABLE I. Baseline demographic and clinical characteristics in the breathing exercise and aerobic training groups

	Breathing exercise group (n [ 25)	Aerobic training group (n [ 29)	P value
Anthropometric data			
Sex, F/M	17/8	22/7	.41*
Age (y), mean (SD)	50.6(9.2)	49.8(9.7)	.95†
BMI (kg/m <sup>2</sup> ), mean (SD)	27.5(4.7)	28.4(3.2)	.63†
Bronchodilator responders, n (%)	3(12)	9(31)	.10*
Budesonide dosage (mg/day), mean (SD)	774(278)	869(330)	.92†
Lung function			
FEV1 (L), mean (SD)	1.87(0.5)	1.88(0.6)	.39†
% of predicted, mean (SD)	70.2(16.6)	72.7(18.4)	.44†
FVC (L)	2.7(0.8)	2.6(1.0)	.67†
% of predicted, mean (SD)	84.7(18.8)	83.9(19.7)	.88†
FEV1/FVC, mean (SD)	0.67(0.2)	0.71(0.08)	.99†
Clinical control			
ACQ7 score, mean (SD)	2.11(0.92)	2.31(1.22)	.20†
Control level			
Uncontrolled, n (%)	21(72)	17(68)	.94*
Partially controlled, n (%)	7(24)	7(28)	
Controlled, n (%)	1(4)	1(4)	
Monthly symptom-free days, mean (SD)	6(7.58)	8(8.76)	.50†
No. of days/months of rescue medication use, mean (SD)	14.4(10.7)	10.8(11.4)	.26
Health-related quality of life			
AQLQ total score, mean (SD)	4.06(1.14)	3.63(1.47)	.28†
Cellularity in sputum			
Total number (10 <sup>5</sup> mL <sup>-1</sup> )	9.4(7.5)	9.3(6.9)	.21†
Differential cell counting (%)			
Neutrophils, median (95% CI)	48.0(38.3-57.4)	54.7(38.6-61.4)	.94†
Eosinophils, median (95% CI)	2.1(0.3-3.7)	1.2(0.1-2.6)	.60†
Macrophages, median (95% CI)	43.9(34.7-53.1)	35.7(24.0-47.4)	.08†
Lymphocytes, median (95% CI)	0.0(0.1-0.6)	0.0(0.1-1.0)	.50†
Maximal exercise capacity			
Distance ISWT (m), mean (SD)	341.8(96.1)	360.4(103.9)	.52†

intervention (adjusted mean difference, 0.1; 95% confidence interval [CI], 0.59 to 0.38; P  $\frac{1}{4}$  .68) or after 3 months of follow-up (adjusted mean difference, 0.38; 95% CI, 0.86 to 0.11; P  $\frac{1}{4}$  .13) (Figure 2). The AG presented a decrease in the ACQ6 score from 2.0 (95% CI, 1.6-2.3) at the baseline to 1.3 (95% CI, 0.9-1.6) after the intervention and to 1.2 (95% CI, 0.8-1.5) at the 3-month follow-up (P < .001 for both after the intervention and at the 3-month follow-up vs the baseline). The BG presented no significant change in the ACQ6 score comparing the baseline score of 1.7 (95% CI, 1.2-2.0) with 1.5 (95% CI, 1.0-1.8; P  $\frac{1}{4}$  .71 vs baseline) after the intervention and 1.7 (95% CI, 1.4-2.2; P  $\frac{1}{4}$  1.00 vs baseline) at the 3-month follow-up. Fifty-eight percent of participants from the AG (n  $\frac{1}{4}$  17) and 32% in the BG (n  $\frac{1}{4}$  8) showed a clinically significant improvement in the ACQ6 score (0.5 points) after intervention (RR, 1.8; 95% CI, 1.4-1.1; P  $\frac{1}{4}$  .06), and the NNT was 4. After 3 months of follow-up, 52% (n  $\frac{1}{4}$  15) of the participants from the AG and 20% (n  $\frac{1}{4}$  5) from the BG maintained

their improvement (RR, 2.6; 95% CI, 1.2-10; P  $\frac{1}{4}$  .02), and the NNT was 4.

### Secondary outcomes

**Asthma symptoms.** The results show a main effect for "Time" (P  $\frac{1}{4}$  .003), and there was no difference between the groups (P  $\frac{1}{4}$  .69) or for the interaction (P  $\frac{1}{4}$  .25). The number of days with rescue medication use was reduced by 34% in the AG from 14.3 (95% CI, 10.1-18.3) to 9.5 days (95% CI, 5.6-13.4) after intervention and by 6% in the BG from 12.2 (95% CI, 7.6-16.6 days) to 11.5 days (95% CI, 6.8-16.4 days) (Figure 3). After the intervention, 34% (n  $\frac{1}{4}$  10) of the participants from the AG and 8% (n  $\frac{1}{4}$  2) from the BG showed a reduction in the number of days with rescue medication use of more than 5 days (RR, 4.3; 95% CI, 1.04-17.8; P  $\frac{1}{4}$  .04), and the NNT was 4.

**Health-related quality of life.** The "Treatment Time" interaction was not statistically significant for the total score, nor

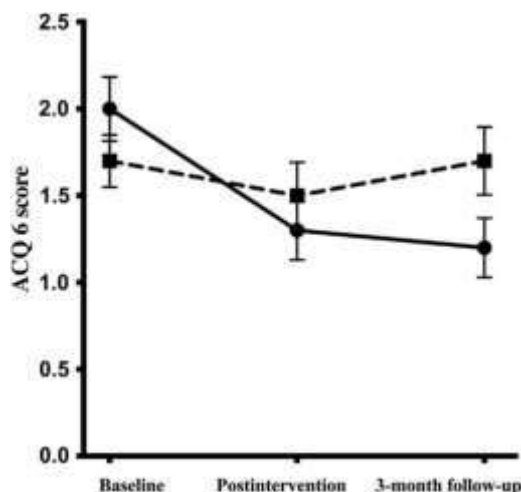


FIGURE 2. Effects of aerobic training (solid line) and breathing exercises (dashed line) on the Asthma Control Questionnaire 6 (ACQ6) score after intervention and after the 3-month follow-up. Data are presented as the least-squares means and standard error.

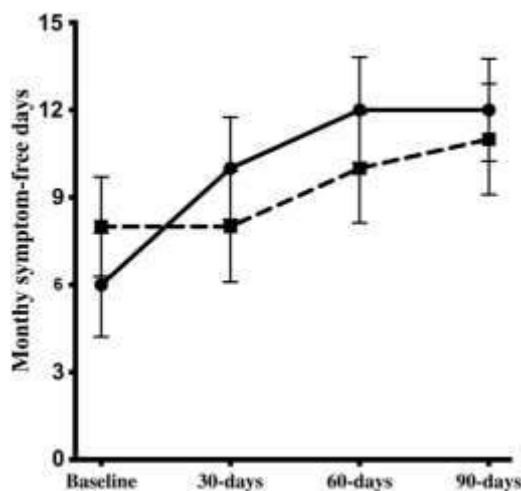


FIGURE 3. Effects of aerobic training (solid line) and breathing exercises (dashed line) on the monthly symptom-free days at 30, 60, and 90 days during the intervention. Data are presented as the least-squares means and standard error.

was the main effect for “Group” (Table II). In contrast, a main effect was observed for “Time” for all results, including the do-mains (symptom, activity limitation, environmental stimulus, emotional domains domain) (Table II). The activity limitation domain had a significant effect for the “Treatment Time” interaction in favor BG ( $P = .018$ ; Table II). After the intervention, 62% ( $n = 18$ ) of the participants from the AG and 44% ( $n = 11$ ) from the BG showed a clinically significant improvement in the total AQLQ score (0.5 points) after the intervention (RR, 1.6; 95% CI, 0.86-2.6;  $P = .18$ ), and the NNT was 6. After 3 months of follow-up, 62% ( $n = 18$ ) of the participants from the AG and 36% ( $n = 9$ ) from the BG maintained their improvement (RR, 1.6; 95% CI, 0.99-3.6;  $P = .15$ ), and the NNT was 4.

Induced sputum cellularity. There was no effect for “Time” ( $P = .118$ ), Group ( $P = .924$ ), or the “Treatment Time” interaction ( $P = .086$ ). The adjusted mean difference in the eosinophils between the AG and the BG was 0.67% (95% CI, 2.9%-1.5%) after the intervention.

Incremental shuttle walking test. The results show significant interaction ( $P = .042$ ) and time ( $P < .01$ ) effects; however, there was no significant group effect ( $P = .98$ ). The adjusted mean difference in the walking distance between the AG and the BG was 17 m after the intervention. The AG had a mean improvement in the ISWT distance of 90.2 (95% CI, 65.0-115.5), and the BG had a mean improvement of 73.0 (95% CI, 36.9-109.2) (Figure 4).

Hospital Anxiety and Depression Scale. The results show a main effect for “Time” ( $P < .001$ ), and there was no difference between the “Groups” or for the “Treatment Time” interaction for the HADS anxiety and depression symptoms (Table II).

Daily-life physical activity. After interventions, no main effect was observed either for “Time,” “Group,” or for the “Treatment Time” interaction ( $P > .05$ ).

#### Magnitude of the interventions

Figure 5 shows the effect size (baseline to postintervention) for each outcome in both groups. Effect size was evaluated between baseline and postintervention. Patients in the BG had small-to-moderate effect sizes for all outcomes, whereas patients in the AG had moderate-to-large effect sizes (Figure 5). The asthma symptom-free days and the ISWT had lower and higher effects, respectively. Finally, the ACQ6 had the largest discrepancy in the effect between groups (Figure 5).

#### DISCUSSION

Our results demonstrate that aerobic training and breathing exercise resulted in a similar effect in asthma control evaluated by the ACQ score; however, when the improvement in asthma control was evaluated individually, aerobic training induced a longer-lasting benefit than breathing exercises and a greater reduction in rescue medication use. There were no differences between groups for the other outcomes, such as HRQoL, asthma symptom-free days, psychological distress, and DLPA and airway inflammation.

#### Primary outcome

Previous RCTs have shown that breathing exercises<sup>30,31</sup> and aerobic training<sup>10,32</sup> are appropriate adjuvant therapies to improve asthma control. However, the effect of breathing exercises on asthma control assessed by the ACQ score was evaluated in only 2 RCTs, and its benefits remain controversial.<sup>13,14</sup> Bruton et al,<sup>14</sup> in a recent and well-designed study, showed that physiotherapy mainly focusing on breathing exercises does not improve asthma control assessed by the ACQ score. The effect of exercise training on the ACQ score was evaluated in 4 RCTs,<sup>10,11,32,33</sup> and 3 trials demonstrated that exercise training improved the ACQ score.<sup>10,32,33</sup> Our results showed that there were no differences in the ACQ score between the AG and BG; however, the AG participants were 2.6 times more likely to experience clinical improvement than the BG participants at the 3-month follow-up. Our results suggest that at the group level,



TABLE II. Comparison of healthy-related quality of life and psychosocial symptoms between aerobic and breathing training

Outcome	Groups	Time period			P values		
		Baseline	After	Follow-up	"Group 3 Time"	"Time"	"Group"
AQLQ							
Activity limitation	AG	3.5 (1.1)	4.6 (1.0)	4.2 (1.3)	.018	.001	.600
	BG	4.0 (1.0)	4.1 (1.2)	4.8 (1.7)			
Symptoms	AG	4.3 (1.4)	5.0 (1.3)	5.3 (1.5)	.241	.001	.154
	BG	4.2 (1.3)	4.6 (1.5)	4.5 (1.5)			
Emotional function	AG	4.0 (1.5)	4.6 (1.7)	4.9 (1.2)	.614	<.001	.481
	BG	4.2 (1.4)	4.5 (1.6)	4.9 (1.3)			
Environmental stimuli	AG	3.5 (1.7)	4.4 (1.4)	4.9 (1.9)	.181	.038	.666
	BG	4.2 (1.6)	4.6 (1.5)	4.3 (1.4)			
AQLQ							
HAD anxiety	AG	3.9 (1.1)	4.7 (1.0)	4.7 (1.0)	.468	<.001	.909
	BG	4.2 (1.0)	4.5 (1.3)	4.6 (1.2)			
HAD depression	AG	8.7 (3.9)	7.7 (3.6)	7.1 (3.4)	.443	<.001	.948
	BG	8.6 (4.6)	7.2 (4.4)	7.3 (3.9)			
HAD depression	AG	7.2 (3.8)	5.7 (4.3)	5.7 (3.5)	.877	<.001	.383
	BG	8.3 (4.4)	6.2 (3.9)	6.4 (4.8)			

AQLQ, Asthma Quality of Life Questionnaire; HAD, Hospital Anxiety and Depression.

Health-related quality of life and psychological distress at baseline, after intervention, and 3-month follow-up for aerobic training (AG) and breathing exercise (BG) groups. Data are presented as mean (standard deviation). P values from the main effects linear mixed models.

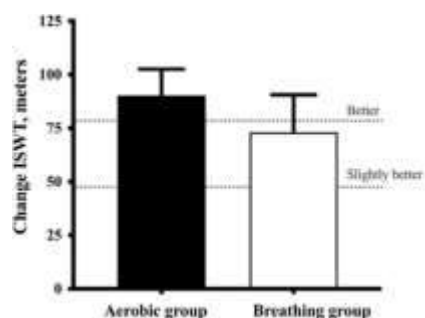


FIGURE 4. Effects of aerobic training (black bar) and breathing exercises (white bar) on the incremental shuttle walk test (ISWT) after the intervention (in meters). Data are presented as the mean change and standard error. Dotted lines represent a significant improvement of >78.7 m and a slight improvement of >47.5 m.<sup>28</sup>

both aerobic training and breathing exercises induced a similar decrease in ACQ score; however, when the improvement in asthma control was evaluated individually, aerobic training induced a longer-lasting benefit than breathing exercises. These results suggest that further studies are required to comprehend which intervention results in a better response and long-term effect.

We hypothesize that aerobic training improves asthma control either by increasing aerobic capacity<sup>5</sup> and/or by reducing bronchial hyperresponsiveness (BHR)<sup>10</sup> because both are associated with better asthma control.<sup>8,34</sup> Breathing exercise could also reduce BHR, as reported by Manocha et al.<sup>17</sup> Breathing exercises are performed using different breathing patterns, and these changes in lung volume seem to relax the smooth muscle in the airway and improve the BHR. For instance, in asthma animal

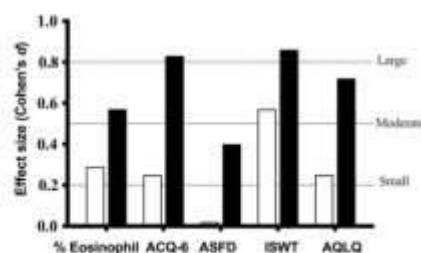


FIGURE 5. Effect size in the breathing exercises (white bars) and aerobic training (black bars) after intervention for eosinophil percentage. The dotted lines represent small (<0.2), medium (>0.2 and <0.5), and large (>0.8) effects.<sup>29</sup> The effect size was evaluated between baseline and postintervention. ACQ6, Asthma Control Questionnaire 6; AQLQ, Asthma Quality of Life Questionnaire; ASFD, asthma symptom-free days; ISWT, incremental shuttle walk test.

models, the airway resistance is reduced when the animals are ventilated with a greater tidal volume and lower breathing frequency in comparison with those animals ventilated with a smaller tidal volume and higher breathing frequency.<sup>35</sup> However, this hypothesis remains to be confirmed in humans after a breathing exercise program. In fact, 2 other studies did not show any effect of breathing exercises on BHR.<sup>13,16</sup>

### Secondary outcomes

Asthma symptom-free days were similar between the AG and BG groups over the course of the study. The effect of exercise training on asthma symptom-free days in adults was assessed in 6 RCTs,<sup>8,10,36-39</sup> and 5 trials demonstrated that exercise training improved symptom-free days.<sup>8,36-39</sup> The effect of breathing exercises on asthma symptoms seems to depend on the technique.



Cooper et al<sup>30</sup> compared 2 breathing techniques and suggested that only the Buteyko technique produced a reduction in asthma symptoms. Ritz et al<sup>40</sup> observed a significant improvement after breathing exercises guided by capnometry, whereas Manocha et al<sup>17</sup> did not show any improvement in asthma symptoms in patients who performed yoga breathing exercises. Our results also demonstrate that a greater proportion of participants in the aerobic training group presented a reduction in the number of days without the use of rescue medication compared with those in the breathing exercises (34% vs 8%, respectively). Our results are supported by previous studies demonstrating that aerobic training reduced the consumption of rescue medication.<sup>41</sup>

Contrary to our results, Slader et al<sup>16</sup> observed that breathing exercises reduced the number of days of rescue medication use by 86%. A possible explanation for this difference between our findings and those of Slader et al<sup>16</sup> is that in our study, the reduction was reported spontaneously, whereas in the study by Slader et al,<sup>16</sup> the participants were instructed to use breathing exercises before using rescue medication whenever they presented asthma symptoms.

Aerobic training and breathing exercises showed similar results in the total HRQoL. Previous studies have demonstrated that aerobic training<sup>8,10,32</sup> and breathing exercises<sup>13-15</sup> both have a positive impact on the HRQoL in asthmatic patients. Recently, Bruton et al<sup>14</sup> performed a very well-designed study with a large sample size and demonstrated that the HRQoL was the only outcome that had a significant effect after breathing exercise, even after 6 months of the intervention. The authors also demonstrated that 64% of patients in a face-to-face group exceeded the MCID for AQLQ score. Our results showed that 65% in the AG and 42% in the BG had significant clinical improvements with an average AQLQ score improvement of 0.8 and 0.6, respectively. These results may suggest that, on average, participants in both groups had clinically relevant improvements in quality of life during the study period.

The effects of nonpharmacological interventions on airway and systemic inflammation are still not well understood. There is evidence suggesting that aerobic training reduces airway eosinophil numbers<sup>38</sup> and inflammatory blood cytokine levels in adult asthmatics<sup>10,32</sup>; however, no effect was observed on blood eosinophilia in asthmatic children.<sup>42</sup> Thomas et al<sup>13</sup> evaluated the effects of breathing exercises on airway inflammation and did not show benefits. Our results showed no effects on sputum eosinophils in either group. However, it is important to note that the patients in our study presented normal mean values for sputum eosinophils.

Our results demonstrated that aerobic group had greater improvement in the ISWT than the breathing group over the course of the study. The AG had an improvement in ISWT distance greater than the limit for "better" (>78.7 m), whereas the BG improved to the limit for "slightly better" (>47.5 m).<sup>28</sup> Therefore, on average, both groups exceeded the MCID after the intervention.<sup>43</sup> This increase in exercise capacity after a breathing exercise program has never been previously shown. A possible explanation for this finding may rely on the fact that breathing exercises can improve a patient's ventilatory control and confidence in performing physical activities. We also observed that the DLPA did not differ significantly after the intervention between groups. However, patients in both groups increased their capacity by approximately 2000 steps after the interventions, reaching 10,000 steps, which is the recommended number for the general population to be considered physically active and to obtain health benefits.<sup>44</sup>

No difference between groups was observed in anxiety and depression symptoms. Only the depression domain exceeded the MCID of 1.5 points for both groups. In addition, previous studies with asthmatic subjects have demonstrated improvement in psychosocial symptoms in participants engaging in either aerobic training<sup>8,10</sup> or breathing exercise programmes<sup>13,15</sup> compared with the symptoms of controls. Finally, we compared the impacts of the interventions and observed that patients participating in aerobic training seemed to obtain a greater effect (from moderate to large) than patients in the breathing exercise program (from none to moderate). The present study is the first to compare these 2 interventions, and the results must be interpreted with caution. However, the comparison of the effect sizes shows the intervention's magnitude and provides a piece of complementary information that may help a clinician advise patients based on evidence.

### Limitations

Our study has limitations. First, we developed a specific Pra-nayama breathing exercise, and our results cannot be compared with those of other studies that have used yoga or other groups of Pranayama breathing exercises. However, the sequence of exercises was developed by 2 senior yoga instructors (with >15 years of experience). In addition, our program aimed to stimulate nasal and diaphragmatic breathing, to increase expiratory time and to slow respiratory flow, as is recommended by other breathing exercises techniques, such as the Buteyko and Papworth techniques.<sup>12,15,30</sup> In addition, the sequence of exercises has been properly described.<sup>18</sup> Second, ISWT is not the gold standard to assess exercise capacity and has never been demonstrated to be sensitive in evaluating exercise training in subjects with asthma. However, this maximal incremental and standardized test was developed for patients with obstructive lung diseases, and the walked distance during the test has a good linear correlation with peak VO<sub>2</sub>.<sup>45</sup> Third, the conclusions of this study seem to be useful only for subjects with moderate-to-severe asthma without other comorbidities. On the other hand, the literature has shown that most excluded patients (elderly individuals, obese individuals, and those with cardiovascular disease) can also benefit from either exercise training or breathing exercise. Finally, although the results of some outcomes showed greater improvement than the MCID, these results need to be interpreted with caution because of the absence of a usual care or sham group. On the other hand, the effect size analysis suggests that these results may have clinical relevance.

### CONCLUSION

Outpatients with moderate-to-severe asthma who participated either in aerobic training or breathing exercise programs presented similar results regarding asthma control, HRQoL, asthma symptom-free days, psychological distress, DLPA, and airway inflammation. However, a greater proportion of participants in the aerobic training presented a longer-lasting clinical control and reduced use of rescue medication than the breathing exercises. These results are relevant in clinical practice to support the benefits from nonpharmacological interventions.

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# Effects of exercise and airway clearance ( positive expiratory pressure) on mucus clearance in cystic fibrosis: a randomised crossover trial

Tiffany J. Dwyer<sup>1,2</sup>, Evangelia Daviskas<sup>2</sup>, Rahizan Zainuldin<sup>1,3,4</sup>,  
Jordan Verschuer<sup>5</sup>, Stefan Eberl<sup>5</sup>, Peter T.P. Bye<sup>2,6</sup> and Jennifer A. Alison<sup>1,7</sup>

Affiliations: <sup>1</sup>Discipline of Physiotherapy, Faculty of Health Sciences, University of Sydney, Sydney, Australia. <sup>2</sup>Dept of Respiratory and Sleep Medicine, Royal Prince Alfred Hospital, Sydney, Australia. <sup>3</sup>Rehabilitation Dept, Ng Teng Fong General Hospital, Jurong Campus, NUHS Group, Singapore. <sup>4</sup>Physiotherapy, Health and Social Sciences Cluster, Singapore Institute of Technology, Singapore. <sup>5</sup>Dept of PET and Nuclear Medicine, Royal Prince Alfred Hospital, Sydney, Australia. <sup>6</sup>Central Clinical School, Sydney Medical School, University of Sydney, Sydney, Australia. <sup>7</sup>Sydney Local Health District, Sydney, Australia.

Correspondence: Tiffany J. Dwyer, Discipline of Physiotherapy, University of Sydney, PO Box 170, Lidcombe NSW 1825, Australia. E-mail: tiffany.dwyer@sydney.edu.au

**ABSTRACT** Exercise improves mucus clearance in people without lung disease and those with chronic bronchitis. No study has investigated exercise alone for mucus clearance in cystic fibrosis (CF). The aim of this study was to compare the effects of treadmill exercise to resting breathing and airway clearance with positive expiratory pressure (PEP) therapy on mucus clearance in adults with CF.

This 3-day randomised, controlled, crossover trial included 14 adults with mild to severe CF lung disease (forced expiratory volume in 1 s % predicted 31–113%). Interventions were 20 min of resting breathing (control), treadmill exercise at 60% of the participant's peak oxygen consumption or PEP therapy (including huffing and coughing). Mucus clearance was measured using the radioaerosol technique and gamma camera imaging.

Treadmill exercise improved whole lung mucus clearance compared to resting breathing (mean difference 3%, 95% CI 2–4); however, exercise alone was less effective than PEP therapy (mean difference -7%, 95% CI -6– -8). When comparing treadmill exercise to PEP therapy, there were no significant differences in mucus clearance from the intermediate and peripheral lung regions, but significantly less clearance from the central lung region (likely reflecting the huffing and coughing that was only in PEP therapy).

It is recommended that huffing and coughing are included to maximise mucus clearance with exercise.

## Introduction

People with cystic fibrosis (CF) produce large amounts of thick mucus that is not cleared normally from the lungs, resulting in mucus retention and chronic lung damage [1]. Treatments to improve mucus clearance, including airway clearance therapies, remain a cornerstone of the standards of care and the respiratory management of CF lung disease [2–5]. These time-consuming therapies are required daily and adults with CF report performing an average of 108 min of treatment each day, with the majority of time taken up with airway clearance and exercise [6]. Exercise may aid secretion clearance in patients with CF [7–9]; however, there is no conclusive evidence to show if exercise can act as a substitute for established airway clearance treatments. Treatment time and burden for patients with CF would be reduced if exercise could replace airway clearance time whilst still reaping the known benefits of exercise training [10].

The most widely accepted technique to measure mucus clearance is to assess bronchial mucus transport, using a radioaerosol technique and imaging with a gamma camera [11, 12]. Mucus clearance measured in this way is not confounded by sputum that is swallowed or saliva mixed with expectorated sputum. Individual physiological studies using this measurement procedure have investigated the effects of exercise and airway clearance techniques on mucus clearance compared to no intervention. Exercise has been shown to significantly increase mucus clearance in people without lung disease [13] and in adults with chronic bronchitis [14]. Several airway clearance techniques have been shown to significantly increase mucus clearance in adults with CF, including “conventional chest physiotherapy” ( postural drainage combined with percussion and vibration) [15, 16]; the forced expiratory technique (FET), which is relaxed breathing and huffing [17, 18]; and positive expiratory pressure (PEP) therapy [17, 18]. No specific airway clearance technique has been shown to be significantly more effective than other techniques [15–19]. Participants, however, report higher preference for techniques that can be done independently, e.g. with the use of PEP devices, compared to techniques performed on the patient by a healthcare professional or carer, e.g. percussion and vibration [20].

To date, no study has measured the effect of exercise alone on mucus clearance in adults with CF, nor compared exercise alone to an established airway clearance technique. For this study we have chosen to use PEP therapy as the airway clearance technique, because it has demonstrated both good efficacy and patient preference [20]. Therefore, the aim of this study was to determine the effect of treadmill exercise, compared to resting breathing (control) and PEP therapy, on mucus clearance and subjective responses in adults with CF. We hypothesised that treadmill exercise would be more effective than no intervention (control) and that treadmill exercise would be similarly effective to PEP therapy.

## Materials and methods

### Study design

A randomised, crossover trial was conducted, comprising four visits (figure 1). Participants were recruited from the Adult CF Clinic at Royal Prince Alfred Hospital, Sydney, Australia, and via an advertisement in the Cystic Fibrosis New South Wales newsletter. On visit 1, lung function and exercise capacity assessments were made prior to randomisation. Intervention order (one intervention per visit 2, 3 and 4) was determined by computer-generated randomisation, performed by a person not involved in the interventions and stored in sealed, sequentially numbered opaque envelopes. The three interventions were as follows: 1) constant-load treadmill exercise; 2) PEP plus FET (from now on referred to as PEP therapy); and 3) resting breathing (control). Each intervention was performed for 20 min.

In order to standardise procedures, visits 2, 3 and 4 were scheduled at the same time in the afternoon, separated by at least 48 h and within a 2-week period (during which medication, airway clearance and exercise regimens were unchanged). Participants were asked to withhold routine mucolytic therapy and not to perform any airway clearance or exercise until after completing all procedures on a trial day. Participants withheld  $\beta$ -agonist medication for at least 8 h before any study visit, unless they had a history of exercise-induced bronchoconstriction. Those participants took 200  $\mu$ g of salbutamol via a metered dose inhaler and spacer 30 min before the peak treadmill test on visit 1 and the interventions on visits 2, 3 and

Outcomes were measured before the interventions, immediately after the interventions and during a 60-min period following the interventions. All outcome measures were later analysed by an assessor blinded to the intervention.

This trial was registered with the Australian and New Zealand Clinical Trials Registry (#ACTRN12608000287336). Research procedures were approved by the Sydney South West Area Health Service Ethics Committee (RPAH Zone; protocol X08-0030) and participants provided written informed consent prior to data collection.

### Participants

Patients were eligible for inclusion if they were 17 years, had a confirmed diagnosis of CF (genetic testing and/or previous positive sweat test) and their treating physician deemed them to be clinically stable [21].

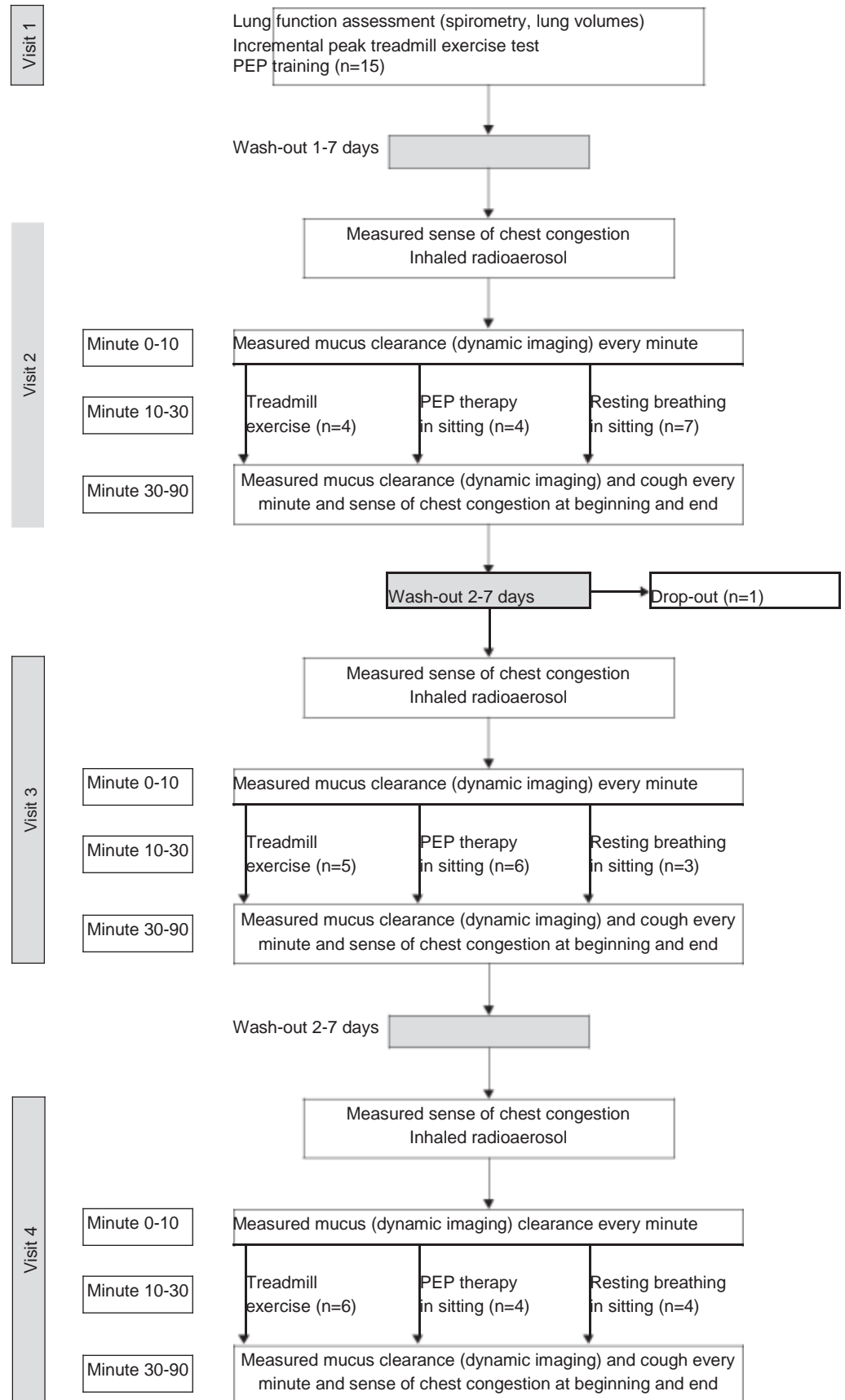


FIGURE 1 Design and flow of participants through the trial. PEP therapy: positive expiratory pressure therapy (including forced expiratory technique).



Patients were excluded if they had received a lung transplant, were infected with *Burkholderia cepacia* complex, were pregnant or had exceeded the dose constraints from radiation exposure additional to normal clinical management, according to the Australian Radiation Protection and Nuclear Safety Agency code of practice for exposing humans to ionising radiation for research purposes [22]. Characteristics of participants (height, weight, spirometry, lung volumes and treadmill peak exercise capacity) were measured on visit 1 to describe the sample and individually prescribe the treadmill exercise intervention.

### Interventions

For the exercise intervention, participants exercised on the treadmill for 20 min at a constant work rate equivalent to 60% of the peak oxygen consumption ( $V'O_{2peak}$ ) achieved in the incremental peak treadmill test on visit 1. This intensity and duration were chosen to replicate a typical prescription used for exercise training [23].

The PEP therapy intervention consisted of breathing through the PEP device for 15 breaths, followed by relaxed and deep breathing, huffing and coughing, according to the FET [24]. This cycle was repeated six times. The PEP hole diameter was chosen for each participant to achieve 10–20 cmH<sub>2</sub>O in mid expiration

3 Participants were taught to use the mouthpiece PEP device (PARI PEP System II; PARI, Starnberg, Germany) by a senior physiotherapist. If participants used PEP on a regular basis, corrections to their technique were made as necessary.

For the control intervention, participants received no intervention, i.e. they sat quietly for 20 min.

### Outcome measures

#### Mucus clearance

At each of visit 2, 3 and 4, subjects underwent a mucus clearance scan, which involved the inhalation of <sup>99m</sup>Tc-labelled sulfur colloid. The procedure was as follows: 1) radioaerosol inhalation; 2) dynamic imaging over 10 min to assess initial deposition and baseline clearance of the radioaerosol; 3) 20-min intervention; 4) dynamic imaging over 60 min to assess post-intervention mucus clearance.

The primary outcome was mucus clearance, measured using the radioaerosol technique and dynamic imaging with a double-headed gamma camera (E.Cam; Siemens, Hoffman Estates, IL, USA) as reported previously by our group [26–34]. The radioaerosol, <sup>99m</sup>Tc-sulfur colloid (CIS-US Inc., Bedford, MA, USA) was generated by a jet nebuliser (mass median aerodynamic diameter of the particles of 5.5 μm, span 1.9; Medic-Aid, Peckham, UK) at 7 L·min<sup>-1</sup>. Subjects inhaled the radioaerosol whilst following a target on a computer screen to produce a controlled breathing pattern aimed at maximising deposition in the conducting airways: 450 mL tidal volume, short inspiratory time (0.6–1.4 s, individually set according to the participant's airway obstruction, with shorter time for those with less airway obstruction), 0.2 s inspiratory hold time and 2 s expiratory time. The breathing pattern aimed at a peak inspiratory flow of approximately 45 L·min<sup>-1</sup>. Approximately 5 min after radioaerosol inhalation, simultaneous anterior and posterior dynamic imaging commenced, with a 1-min frame rate and the patient in a supine position. In addition, on visit 2 only, the participant's lung fields were delineated from a transmission scan with a cobalt-57 sheet source before any other procedures were undertaken.

All images were decay-corrected to the imaging start time. The anterior and posterior emission images were combined into geometric mean images. The right lung was divided into central, intermediate and peripheral regions. The central region was a rectangle comprising the middle half of the vertical and horizontal dimensions of the right lung, and the intermediate and peripheral regions were concentric bands surrounding the central region [35]. The defined regions were stored as a template for use on each mucus clearance scan. The initial lung radioaerosol distribution was defined in terms of the penetration index, which is the ratio of mean counts per pixel in the peripheral region to mean counts per pixel in the central region, multiplied by 100 (with lower numbers representing more central deposition of the radioaerosol). The first image was obtained 5 min after radioaerosol inhalation. The total counts of the whole right lung and defined regions in the dynamic emission geometric mean images were expressed as a percentage of the counts at the end of the 10-min baseline scan (i.e. 100% retained immediately before the intervention). Activity that had not been retained had been cleared. The mucus clearance scans were later analysed by an assessor blinded to the interventions.

#### Cough

All coughs (spontaneous and those directed according to the FET) were manually counted during each 20-min intervention and 60-min follow-up recovery period.

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#### Sense of chest congestion

Participants recorded their subjective sense of chest congestion on 10-cm visual analogue scales (0=very congested, 10=very clear) immediately before, during and at the end of 60 min following the intervention. The visual analogue scales were later measured by an assessor blinded to the interventions.

## Data analysis

For the mucus clearance scans, a random coefficients model was fitted using general linear mixed models to model the relationship between the percentage of retention and time after the 20-min intervention. The primary outcome was the mucus cleared immediately after finishing the 20-min intervention, measured by the intercept of the regression coefficient of retention. The secondary outcomes were the mean retention over the 60 min following the 20-min intervention, the subjective sense of chest congestion and the number of coughs. Repeated measures ANOVA were performed on the secondary outcome measures to compare differences between the interventions. Statistical significance was set at  $p < 0.05$ .

Data from a previous study involving eight subjects with chronic bronchitis resulted in a mean $\pm$ SD within-subject increase in mucus clearance with exercise of  $7.5 \pm 5.8$  [14]. Sample size calculations showed that 13 participants would be required to provide 90% power to detect the anticipated between-group differences in the primary outcome measure as significant ( $\alpha = 0.05$ ). We sought to recruit 15 participants to allow for a 15% dropout and increase precision around our estimates.

## Results

### Flow of participants through the study

A total of 15 adults with mild to severe CF lung disease were recruited and 14 completed the study (one participant withdrew after visit 2 owing to an allergic reaction that may have been a delayed response to the inhaled radioaerosol). Participant baseline characteristics are presented in table 1 and the supplementary material [36–38]. Routine mucolytic therapy was hypertonic saline only for two participants; recombinant human deoxyribonuclease (rhDNase) only for three participants; both hypertonic saline and rhDNase for four participants; and both denufosal and rhDNase for one participant. No participant used mannitol and five participants did not use any mucolytic or osmotic medication. No participant was prescribed a cystic fibrosis transmembrane conductance regulator (CFTR) corrector or potentiator medication. All but one participant were prescribed bronchodilators and/or inhaled corticosteroids. Five participants with a history of exercise-induced bronchoconstriction took 200  $\mu$ g of salbutamol 30 min before the intervention on visits 2, 3 and 4. All 15 participants performed exercise regularly when well and 14 performed some form of airway clearance routinely (four only exercised; five performed established airway clearance techniques only; five performed a combination of exercise and airway clearance techniques), including eight who performed PEP therapy on a regular basis.

There were no significant differences in the initial distribution of radioaerosol between the study days, with an mean $\pm$ SD penetration index of  $27.8 \pm 13.8$  for all scans, meaning that approximately 3.5 times the amount of radioaerosol was deposited in the central region compared to the peripheral region. There were no significant differences in pre-intervention mucus clearance during the 10-min baseline scan between any of the interventions (figure 2) and no carry-over or order effect between the interventions was detected.

TABLE 1 Participant characteristics

Characteristic (n=15)	Mean $\pm$ SD	Range
Age years	27 $\pm$ 9	18–48
Male sex n %	10 (67)	
BMI kg·m <sup>-2</sup>	22.2 $\pm$ 2.7	18.1–27.4
FEV <sub>1</sub> L	2.45 $\pm$ 0.94	1.16–4.78
FEV <sub>1</sub> % pred	65 $\pm$ 23	31–113
FVC % pred	88 $\pm$ 18	64–119
FEV <sub>1</sub> /FVC	0.61 $\pm$ 0.16	0.34–0.84
RV/TLC % <sup>#</sup>	32 $\pm$ 11	10–50
Treadmill V'O <sub>2peak</sub> mL·kg <sup>-1</sup> ·min <sup>-1</sup>	36.1 $\pm$ 10.4	18.9–53.7
Treadmill V'O <sub>2peak</sub> % pred	94 $\pm$ 25	49–136



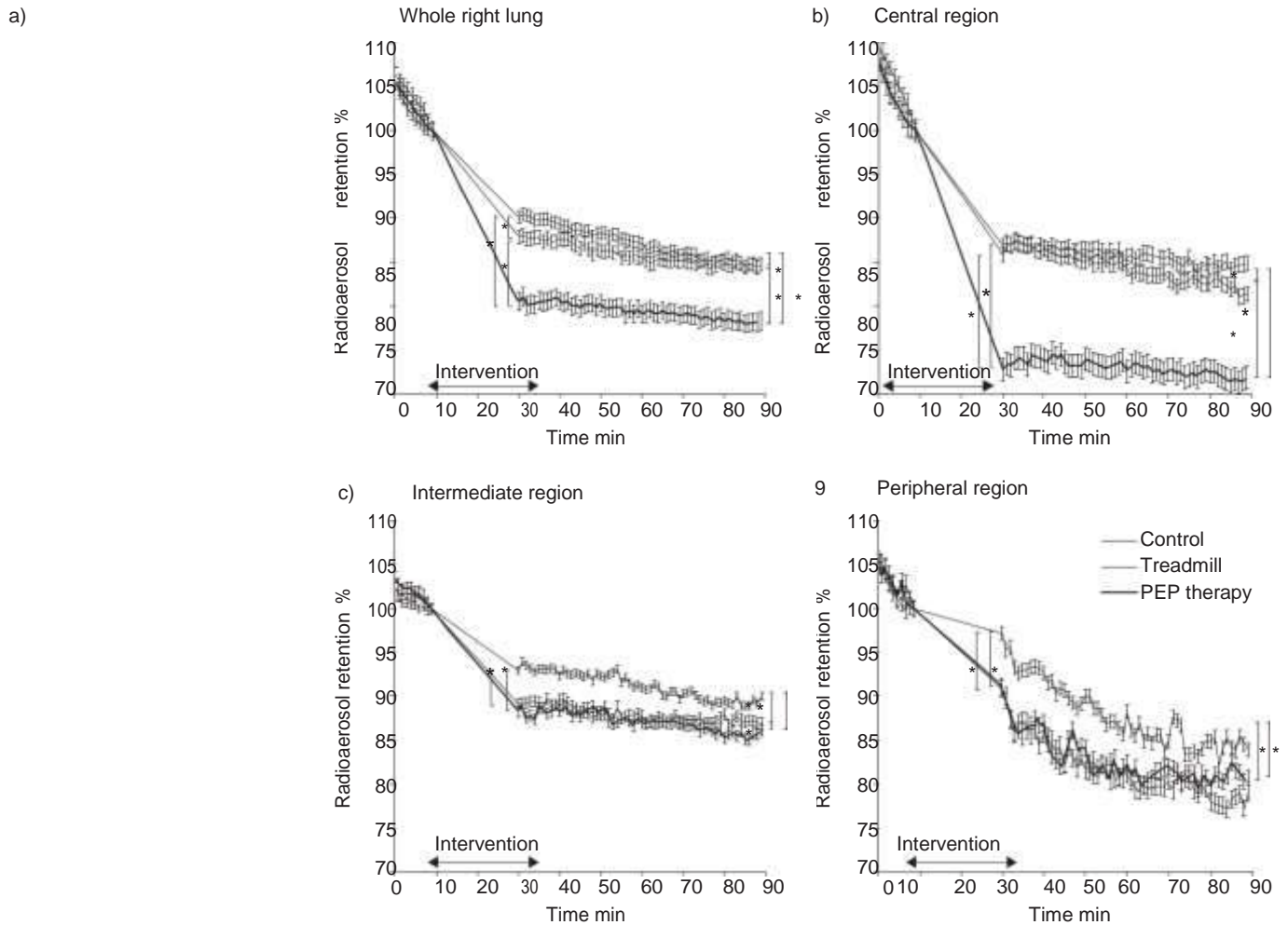


FIGURE 2 Mucus clearance scans for the control (solid line), treadmill exercise (dashed line) and positive expiratory pressure (PEP) therapy (dotted line) interventions (mean±SE), expressed as percentage of radioaerosol retention immediately before the intervention in a) whole right lung; b) central lung region; c) intermediate lung region; and d) peripheral lung region. \*: p<0.01.

Treatment descriptors

Pulse rate, oxygen saturation and treatment descriptors (work rate and perceived intensity during treadmill exercise [39, 40], PEP hole diameter and average expiratory pressure) for the 20-min interventions are presented in table 2. Treadmill exercise intensity was rated somewhat severe for breathlessness and strong/ heavy for perceived exertion. All treatments were well tolerated with no adverse events.

TABLE 2 Treatment descriptors

	PR bpm	SpO <sub>2</sub> %	Treatment descriptors
Control	83±14	98±2	Resting breathing
Treadmill	134±14	96±3	5.7±0.6 km·h <sup>-1</sup> at 5±3% incline <sup>#</sup> Dyspnoea <sup>  </sup> 4±2 RPE <sup>+</sup> 5±2 3.8±0.5 mm <sup>3</sup> 20±4 cmH <sub>2</sub> O <sup>f</sup>
PEP	89±12	97±3	

### Effect of exercise

Treadmill exercise cleared significantly more mucus during the intervention compared to control for the whole right lung and intermediate and peripheral regions (table 3 and figure 2) but there was no significant difference in the mucus cleared from the central region. When including the 60-min follow-up period, treadmill exercise cleared significantly more mucus compared to control for the whole right lung and intermediate and peripheral regions (table 3 and figure 2), but significantly less mucus compared to control for the central region. The improvement in mucus clearance with exercise was primarily achieved during the 20-min intervention, as there was no persistent benefit in the 60-min follow-up period.

There was a nonsignificant trend for participants to do more spontaneous coughs during treadmill exercise compared to control, but there were no differences in the number of coughs between the interventions in the 60-min follow-up period (table 4).

There were no significant differences in the change in sense of chest congestion following treadmill exercise compared to control either immediately after or 60 min after the intervention (table 5).

### Effect of PEP therapy

PEP therapy cleared significantly more mucus during the intervention compared to control for the whole right lung and all lung regions (table 3 and figure 2). When including the 60-min follow-up period, PEP therapy cleared significantly more mucus compared to control for the whole right lung and all lung regions (table 3 and figure 2). The improvement in mucus clearance with PEP therapy was primarily achieved during the 20-min intervention; there was no persistent benefit in the 60-min follow-up period.

There were significantly more coughs with PEP therapy compared to control during the intervention but no significant difference in the 60 min following the interventions (table 4).

There was significantly more improvement in the sense of chest congestion following PEP therapy compared to control both immediately after the interventions and 60 min after the interventions (table 5).

TABLE 3 Mucus clearance

	Mucus clearance <sup>#</sup> %					
	Interventions			Difference between interventions		
	Tread	PEP	Con	Tread minus Con	PEP minus Con	Tread minus PEP
Subjects n	15	14	14			
Whole lung						
Post-0	13.4 (7.1–19.7)	20.3 (14.0–26.7)	10.8 (5.5–16.1)	2.6** (1.6–3.6)	9.5** (8.5–10.5)	–6.9** (–5.9––7.9)
Post-60	15.4 (9.7–21.0)	21.8 (16.2–27.5)	14.0 (8.4–19.7)	1.3** (0.8–1.8)	7.8** (7.3–8.3)	–6.5** (–7.0––6.0)
Central region						
Post-0	14.2 (6.1–22.3)	27.1 (19.0–35.2)	14.0 (7.3–20.7)	0.2 (–1.2–1.6)	13.1** (11.7–14.5)	–12.9** (–11.5––14.3)
Post-60	15.7 (8.4–22.9)	28.4 (21.1–35.7)	17.1 (9.8–24.3)	–1.4** (–2.1––0.7)	11.3** (10.6–12.0)	–12.7** (–13.4––12.0)
Intermediate region						
Post-0	11.4 (6.3–16.5)	11.8 (6.7–16.9)	6.9 (2.7–11.1)	4.5** (3.6–5.4)	4.9** (4.0–5.8)	–0.4 (–1.3–0.5)
Post-60	12.9 (8.5–17.2)	13.6 (9.2–17.9)	9.5 (5.2–13.9)	3.3** (2.9–3.8)	4.0** (3.6–4.5)	–0.7* (–1.2––0.3)
Peripheral region						
Post-0	14.2 (6.7–21.7)	15.5 (8.0–23.0)	7.5 (1.6–13.4)	6.7** (5.2–8.3)	8.0** (6.4–9.6)	–1.3 (–2.9–0.3)
Post-60	19.4 (12.9–25.9)	19.0 (12.5–25.5)	13.4 (6.9–19.8)	6.1** (5.3–6.8)	5.6** (4.8–6.4)	0.4 (–0.4–1.2)

Data are presented as the mean (95% CI), unless otherwise stated. Tread: treadmill; PEP: positive expiratory pressure therapy (including the forced expiratory technique); Con: control; Post-0: immediately following intervention; Post-60: 60 min post intervention. <sup>#</sup>: assessed immediately after the 20-min intervention, measured as the intercept of the regression coefficient of retention, and the mean retention during the 60-min resting breathing/recovery follow-up period; \*: p<0.01; \*\*: p<0.001.

TABLE 4 Cough

Outcome	Coughs n					
	Interventions			Difference between interventions		
	Tread	PEP <sup>#</sup>	Con	Tread minus Con	PEP minus Con	Tread minus PEP
Subjects n	15	14	14			
During 20-min intervention	16±23	73±59	4±6	13 (-2-27)	69* (33-105)	-56* (-87--26)
During 60-min follow-up	21±43	13±20	13±15	8 (-17-32)	0 (-11-11)	8 (-10-25)

Data are presented as mean±SD or mean (95% CI), unless otherwise stated. Tread: treadmill; PEP: positive expiratory pressure therapy (including the forced expiratory technique); Con: control. <sup>#</sup>: participants were instructed to cough 18 times and huff 12 times during the PEP therapy intervention; \*: p<0.01.

Effect of exercise compared to PEP therapy

Treadmill exercise cleared significantly less mucus during the intervention compared to PEP therapy for the whole right lung and central region but there was no significant difference in the mucus cleared from the intermediate or peripheral regions (table 3 and figure 2). When including the 60-min follow-up period, treadmill exercise cleared significantly less mucus compared to PEP therapy for the whole right lung and central and intermediate regions but there was no significant difference in the mucus cleared from the peripheral region.

There were significantly fewer coughs with treadmill exercise compared to PEP therapy during the intervention (table 4). There was no significant difference in the number of spontaneous coughs in the 60 min following the interventions (table 4).

There was significantly less improvement in the sense of chest congestion following treadmill exercise compared to PEP therapy both immediately after and 60 min after the interventions (table 5).

Discussion

This is the first study to measure mucus clearance, using the gold standard inhaled radioaerosol technique, with exercise alone in adults with CF. The main findings were that although treadmill exercise significantly increased mucus clearance from the whole lung compared to no intervention, treadmill exercise was significantly less effective compared to PEP therapy. There were no significant differences, however, in the amount of mucus cleared from the intermediate and peripheral lung regions when comparing treadmill exercise and PEP therapy.

These results demonstrate that exercise alone does act as an effective independent airway clearance technique for adults with mild to severe CF lung disease in clearing mucus from the intermediate and peripheral lung regions. Importantly, however, less mucus was cleared from the central lung region following treadmill exercise alone compared to PEP therapy, most likely due to the FET component in PEP therapy that involved directed huffing and coughing. Participants did ~60 more coughs during the

TABLE 5 Sense of chest congestion

	Interventions									Difference between interventions					
	Pre			Post-0			Post-60			Post-0 minus Pre			Post-60 minus Post-0		
	Tread	PEP	Con	Tread	PEP	Con	Tread	PEP	Con	Tread minus Con	PEP minus Con	Tread minus PEP	Tread minus Con	PEP minus Con	Tread minus PEP
Subjects n	15	14	14	15	14	14	15	14	14						
Chest congestion VAS <sup>#</sup> cm	5.2±1.9	4.2±1.9	5.9±1.8	6.1±1.9	5.9±2.2	6.4±1.9	5.4±2.1	6.1±1.7	6.0±2.0	0.5 (-0.3-1.3)	1.2* (0.1-2.3)	0.7* (0.1-1.4)	0.1 (-0.7-1.0)	1.8*** (0.9-2.7)	1.7** (0.7-2.7)

Data are presented as mean±SD or mean (95% CI), unless otherwise stated. Pre: pre intervention; Post-0: immediately post intervention; Post-60: 60 min post intervention; Tread: treadmill; PEP: positive expiratory pressure therapy (including the forced expiratory technique); Con: control. <sup>#</sup>: measured on a 10 cm VAS scale, where higher numbers represent less chest congestion and positive numbers represent a decrease in chest congestion from pre to post intervention; \*: p<0.05; \*\*: p<0.01; \*\*\*: p<0.001.

PEP intervention than during treadmill exercise, which in turn resulted in ~10 more coughs than during the control intervention. The absence of a matched “cough control” day in our study prevents the determination of how much the improvement in mucus clearance was due to treadmill exercise and PEP breathing, compared to the benefits achieved with cough alone. Previous studies have demonstrated that FET alone is an effective treatment [17, 41] and interventions that include FET and/or directed coughing clear mucus predominantly from the central regions [16, 18, 42]. Perhaps if FET or directed coughing had been included with the treadmill intervention there would have been more mucus cleared from the central region.

The baseline mucus clearance (i.e. that achieved during the resting breathing (control) intervention) in this study was very similar to that reported in the most comprehensive study of adults with CF (in our study ~15% was cleared from the whole lung 60 min post inhalation of the radioaerosol compared to 14% clearance in ROBINSON et al. [29]). This amount of mucus clearance in people with CF is about half that of the group of healthy aged-matched control participants, which was reported as 28% clearance from the whole lung [29]. Despite the vast majority of the participants in our study carrying out well-established airway clearance routines (14 out of 15 were prescribed mucolytic and/or osmotic medication and 14 out of 15 performed some form of airway clearance regularly), it would appear that mucus clearance remains markedly reduced in adults with CF, further highlighting the ongoing need to optimise airway clearance therapies.

The improvements in mucus clearance with exercise and PEP therapy were primarily achieved during the 20-min intervention. There was no persistent benefit or acceleration of mucus clearance created by the treatments in the 60-min follow-up period, which is consistent with every previous study that has included a follow-up period after an airway clearance treatment in adults with CF [15–18]. By contrast, the mucolytic and osmotic medications hypertonic saline [28, 30] and mannitol [31] improve mucus clearance immediately following inhalation and continue to accelerate mucus clearance in the follow-up period. One clinical implication is that, given that there is no continued benefit to mucus clearance after the initial effects of airway clearance interventions, people with CF will need to regularly perform these treatments to maintain adequate mucus clearance.

The improvement in whole lung mucus clearance with exercise (~3% more than during the control intervention) seen in our study was less than the 8–9% improvement found in earlier studies in people without lung disease [13] and adults with chronic bronchitis [14]. The improvement in peripheral lung region mucus clearance, however, was similar (~7% in our study compared to 6%) [14]. It is not clear why there was a discrepancy in the effect for the whole lung, given that participants in our study exercised at a similar intensity to those in the other two studies [13, 14]. The baseline mucus clearance in our study was greater than that seen in those with chronic bronchitis (in our study ~15% was cleared from the whole lung 60 min post inhalation of the radioaerosol compared to 10% clearance in those with chronic bronchitis) [14]. Perhaps because most of the participants in our study already had well-established airway clearance routines, there was less potential for an improvement in mucus clearance with exercise. Another possibility is that in our study radioaerosol deposition was predominantly in the central lung region, which had the least improvement in mucus clearance, and thus may have lowered the overall whole lung mucus clearance owing to the greater relative contribution of this region. It should also be noted that because mucus clearance from the peripheral and intermediate lung regions was greater with exercise compared to the control, more mucus would have been entering the central region during the exercise intervention, which would likely lower the net mucus clearance from this region.

The improvement in whole lung mucus clearance with PEP therapy in our study (~10% more than during the control intervention) is similar to the 5–20% improvement that has been reported previously [17, 18, 43]. Also similar to previous research, the main increase in mucus clearance was in the central lung region [18]. Interestingly, trials that have compared PEP therapy to FET or directed coughing alone have shown no between-group differences in mucus clearance [17, 44] or dry weight of expectorated sputum [45] immediately following the PEP interventions. Another study that investigated PEP therapy compared to PEP alone (i.e. no FET or directed coughing) found that although there were no between-group differences in lung function, expectorated sputum weight or exacerbation frequency, participants reported PEP alone to be ineffective in clearing mucus [46]. In combination, these studies would suggest that the FET component of PEP therapy makes an important contribution to the efficacy of PEP therapy.

Exercise cleared significantly less mucus than PEP therapy for the whole lung and central lung region (~7% and 13%, respectively) in our study, with no significant differences in the intermediate or peripheral lung regions. The only other study which compared exercise alone to PEP therapy found that exercise alone produced significantly less sputum than PEP therapy [47]. This study, however, has only been published in abstract form and lacks details on CF participant characteristics, exercise intensity, the PEP

protocol and results data. Two studies have compared exercise plus FET or directed coughing to PEP therapy and found no between-group differences in mucus clearance [19] or expectorated sputum weight

46. However, all of these studies, including our study, involved participants who were not taking CFTR modulators. Considering the likely improvement in mucus clearance with these highly effective therapies, it is possible that the effects of airway clearance techniques may change once patients with CF are routinely prescribed these new medications.

This study has demonstrated that a single bout of treadmill exercise improved whole lung mucus clearance compared to no intervention; however, exercise alone was less effective than the well-established airway clearance technique of PEP therapy, which includes huffing and coughing. In terms of the effects of the two interventions on the different lung regions, there were no differences in the amount of mucus cleared from the peripheral and intermediate regions, yet significantly less mucus was cleared from the central region with exercise alone. This difference was most likely due to the huffing and coughing in the FET component of PEP therapy. In clinical practice, therefore, it is recommended that FET is included with exercise if the aim is to improve central and whole lung mucus clearance. Longer-term studies investigating exercise (with huffing and coughing) as a standalone airway clearance technique are required to determine if it is as effective as established airway clearance techniques on clinically important outcomes, such as exacerbation frequency, quality of life and exercise capacity, which are related to morbidity and mortality in CF.

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### 3. JURNAL PNEUMONIA:

## Inpatient rehabilitation improves functional capacity, peripheral muscle strength and quality of life in patients with community-acquired pneumonia: a randomised trial

Anderson Jose´, Simone Dal Corso

Post-graduate Program in Rehabilitation Sciences, Universidade Nove de Julho, Saˆo Paulo, Brazil

#### KEY WORDS

Randomised controlled trial  
Physical therapy (specialty)  
Pneumonia  
Exercise  
Quality of life



#### ABSTRACT

**Question:** Among people who are hospitalised for community-acquired pneumonia, does an inpatient exercise-based rehabilitation program improve functional outcomes, symptoms, quality of life and length of hospital stay more than a respiratory physiotherapy regimen? **Design:** Randomised trial with concealed allocation, intention-to-treat analysis and blinding of some outcomes. **Participants:** Forty-nine adults hospitalised for community-acquired pneumonia. **Intervention:** The experimental group (n = 32) underwent a physical training program that included warm-up, stretching, peripheral muscle strength training and walking at a controlled speed for 15 minutes. The control group (n = 17) underwent a respiratory physiotherapy regimen that included percussion, vibrocompression, respiratory exercises and free walking. The intervention regimens lasted 8 days. **Outcome measures:** The primary outcome was the Glittre Activities of Daily Living test, which assesses the time taken to complete a series of functional tasks (eg, rising from a chair, walking, stairs, lifting and bending). Secondary outcomes were distance walked in the incremental shuttle walk test, peripheral muscle strength, quality of life, dyspnoea, lung function, C-reactive protein and length of hospital stay. Measures were taken 1 day before and 1 day after the intervention period. **Results:** There was greater improvement in the experimental group than in the control group on the Glittre Activities of Daily Living test (mean between-group difference 39 seconds, 95% CI 20 to 59) and the incremental shuttle walk test (mean between-group difference 130 m, 95% CI 77 to 182). There were also significantly greater improvements in quality of life, dyspnoea and peripheral muscle strength in the experimental group than in the control group. There were no between-group differences in lung function, C-reactive protein or length of hospital stay. **Conclusion:** The improvement in functional outcomes after an inpatient rehabilitation program was greater than the improvement after standard respiratory physiotherapy. The exercise training program led to greater benefits in functional capacity, peripheral muscle strength, dyspnoea and quality of life. **Registration:** ClinicalTrials.gov, NCT02103400 [Jose´ A, Dal Corso S (2016) Inpatient rehabilitation improves functional capacity, peripheral muscle strength and quality of life in patients with community-acquired pneumonia: a randomised trial. *Journal of Physiotherapy* 62: 96–102]

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#### Introduction

Community-acquired pneumonia is a highly prevalent adverse health condition with a high mortality rate. It involves substantial treatment costs and has significant social impact worldwide.<sup>1</sup> Patients who are hospitalised for community-acquired pneumonia experience a decline in functional capacity,<sup>2–4</sup> which is associated with higher rates of re-hospitalisation and death,<sup>3,4</sup> as well as reductions in both peripheral muscle strength and quality of life.<sup>2</sup> Moreover, such patients can endure a long period before the complete remission of symptoms and the return to previous activities of daily living.<sup>5</sup>

Although widely employed in clinical practice,<sup>6</sup> the current physiotherapeutic approach for patients with community-acquired pneumonia, which focuses on airway clearance, is not

supported by evidence<sup>7–10</sup> and the main guidelines for the management of this condition do not recommend it.<sup>1</sup> In patients who are hospitalised for acute exacerbations of chronic obstructive pulmonary disease (COPD), an inpatient rehabilitation program leads to some immediate improvements in functional capacity, quality of life, peripheral muscle strength, exercise tolerance,<sup>11,12</sup> anxiety and depression.<sup>13</sup> However, the recent publication of a major study by Greening and colleagues has indicated that very early exercise-based rehabilitation commenced during hospitalisation may reduce uptake of pulmonary rehabilitation and increase mortality after discharge.<sup>14</sup> Interpreting this study in the light of the existing evidence suggests that for patients who are hospitalised for acute exacerbations of COPD, pulmonary rehabilitation immediately after discharge may be more beneficial overall than commencing the exercise-based rehabilitation during hospitalisation.<sup>15</sup>

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In patients who are hospitalised for community-acquired pneumonia, early mobilisation has been applied only in one large study, but it was poorly described.<sup>16</sup> Therefore, in these patients, the effects of aerobic and resistance training on functional capacity, peripheral muscle strength and quality of life require thorough investigation during hospitalisation. Considering the high prevalence and treatment costs of community-acquired pneumonia, its social impact and the scarcity of evidence to support standard respiratory physiotherapy for such patients, it is crucial to investigate whether a physical training program can lead to better recovery of functional capacity at discharge from the hospital.

Therefore, the research question for this randomised trial was: Among people who are hospitalised for community-acquired pneumonia, does an inpatient exercise-based rehabilitation program improve functional outcomes, symptoms, quality of life and length of hospital stay more than a respiratory physiotherapy regimen?

Method

Design

This study was a randomised trial, with concealed allocation, blinding of assessors of some outcomes and intention-to-treat analysis. Patients who were hospitalised for community-acquired pneumonia were randomly assigned to receive either physical exercise training (experimental group) or respiratory physiotherapy (control group). After eligible patients were advised regarding the study and consented to participate, they were randomly allocated to one of the two groups. Upcoming random allocations

were concealed in opaque, sealed envelopes that had been prepared by a researcher who was not involved in the recruitment or assessment of the participants. Data were obtained before randomisation and 1 day after the 8-day intervention period. The length of the hospital stay was also recorded for all participants (Figure 1).

Participants, therapists and centre

The inclusion criteria for participation in the study were: being aged > 18 years, having a diagnosis of community-acquired pneumonia,<sup>1</sup> being hospitalised for < 48 hours, and having adequate awareness and independent ambulation. The exclusion criteria were: being unwilling to participate, having cognitive impairment, having osteoarticular disorders, and having other acute or chronic respiratory diseases. The researchers in the study applied the interventions. This study was conducted at Mandaqui Hospital, which is a tertiary hospital in São Paulo, Brazil.

Interventions

Control group

Participants allocated to the control group received standard respiratory physiotherapy in daily 50-minute sessions for 8 days; this involved secretion removal, breathing exercises and walking. The secretion removal techniques were percussion and vibrocompression in side lying for 10 minutes on each side, during and after which the participant was instructed to perform voluntary coughing and huffing to expectorate secretions until achieving a dry cough.<sup>17</sup>

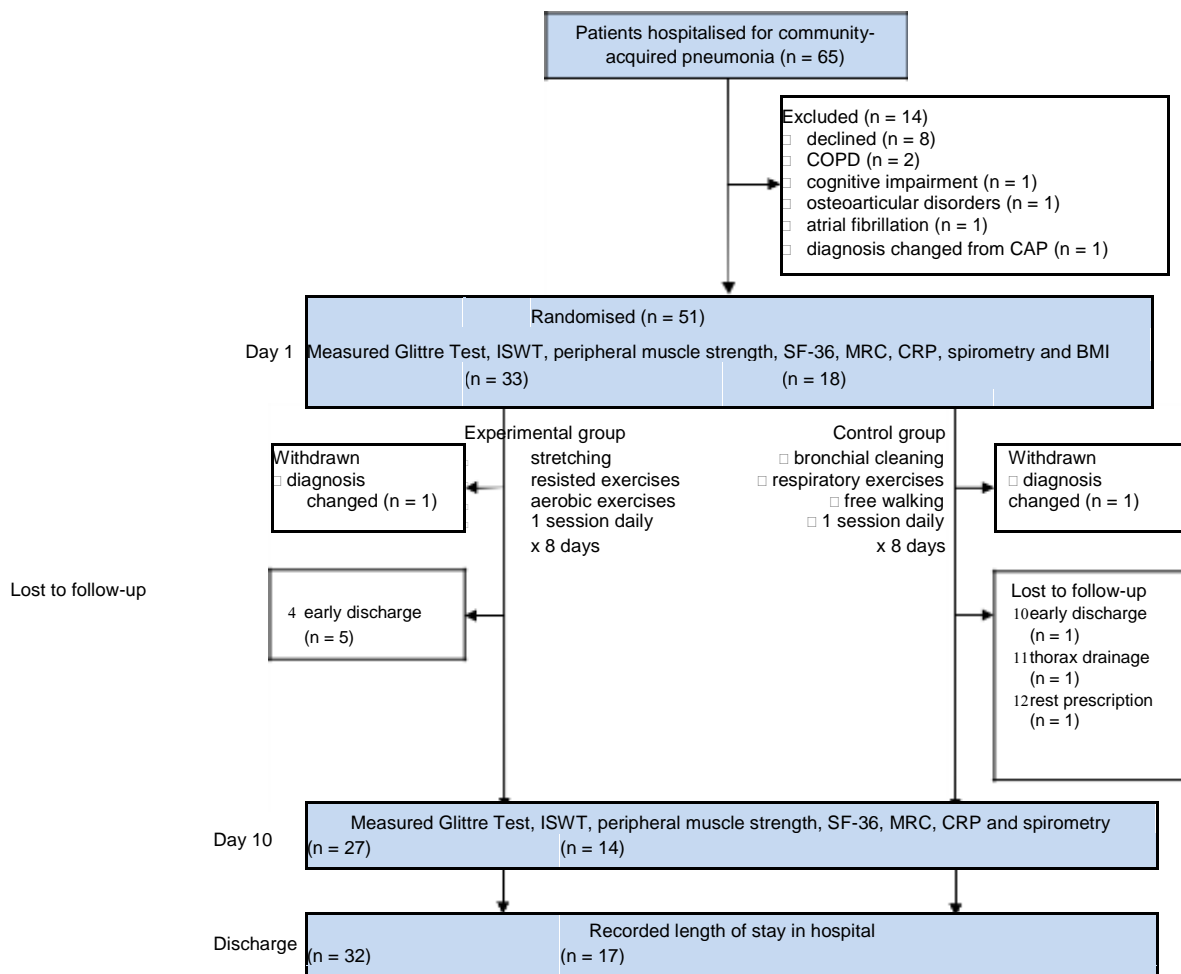


Figure 1. Design and flow of participants through the trial.

BMI = body mass index, COPD = chronic obstructive pulmonary disease, CRP = C-reactive protein, ISWT = incremental shuttle walk test, MRC = Medical Research Council Dyspnoea Scale, SF-36 = Short Form 36 questionnaire.



The breathing exercises were targeted at improving ventilation. They included diaphragmatic breathing exercises (three sets of 10 repetitions with a 1-minute rest period between sets) and inspiratory exercise with maximum inspiration and maximum inspiratory pause (three sets of 10 repetitions with a 1-minute rest period between sets).<sup>17</sup> Walking was self-paced with a prescribed duration of 10 minutes.

#### Experimental group

The participants allocated to the experimental group received physical training in daily 50-minute sessions for 8 days; this involved warm-up, stretching, resistance exercises for peripheral muscles and aerobic walking training.

The warm-up involved active movements of the upper and lower limbs for approximately 5 minutes. Stretching targeted the pectoralis major, latissimus dorsi, trapezius, quadriceps femoris and hamstring muscles. Participants held each stretch for 30 seconds and stretched for approximately 5 minutes in total.

Peripheral muscle strengthening exercises were performed for approximately 25 minutes. The exercises were performed with three sets of eight repetitions with a 1-minute rest period between sets for both limbs simultaneously using an elastic band<sup>a</sup>. The targeted muscles were biceps brachii, deltoids, quadriceps femoris and hamstrings. The initial workload was 70% of maximum peripheral muscle strength.<sup>18</sup> At the end of each set, dyspnoea and fatigue were measured using the Borg scale,<sup>19</sup> with participants aiming to score between 4 and 6 at the end of the three sets. If the fatigue score was below this level, the workload was increased by exchanging the elastic band for one more resistant, and if above this level, the workload was decreased.

Aerobic training was performed in a flat corridor that was 10 m long. Participants walked for 15 uninterrupted minutes, with their speed guided by the auditory recording of the endurance shuttle walk test<sup>20</sup> set at a speed corresponding to 70% of the speed reached on the incremental shuttle walk test (ISWT).<sup>21</sup> If the participant was unable to tolerate this time or exhibited a drop in pulse oxygen saturation (SpO<sub>2</sub>) < 84%, he or she was allowed to rest on a chair, at which point the timer was paused. Upon feeling capable of proceeding, the participant continued to walk until completing the entire 15 minutes. Adjustments in the training intensity were made according to symptoms (dyspnoea and fatigue between 4 and 6 on the Borg scale)<sup>19</sup> and/or 70% of the predicted maximum heart rate, which was established using Karvonen's equation.<sup>22</sup> If a participant reported a dyspnoea score < 4 and/or the heart rate remained below the rate established by Karvonen's equation, the speed of the walk was increased the following day, and if dyspnoea was > 6 and/or the heart rate was above the rate established in the equation, the speed of the walk was diminished the following day.

#### Outcome measures

All evaluations were conducted on the first and tenth days of the study (Figure 1). The data that were collected to characterise the participants at baseline included age, gender, body mass index and the CURB-65 score, which is a tool for predicting risk of death from community-acquired pneumonia.<sup>23</sup> [6T\$DIF]

#### Primary outcome

Functional exercise capacity was measured using the Glittre Activities of Daily Living test,<sup>24</sup> which consists of a set of functional activities (eg, rising from a chair, walking, stairs, lifting and bending). The participant performs the sequence of activities five times as quickly as possible. Each participant performed the entire test twice, and the main outcome was the better time taken to complete five laps.

#### Secondary outcomes

Exercise capacity was measured using the ISWT,]FID\$T3[performed as previously described.<sup>21</sup>]FID\$T7[Two tests were performed on the same

day, and the longer distance that was walked was used for the analysis.

Peripheral muscle strength was measured using a dynamometer<sup>b</sup>. The peak of isometric contraction was recorded for the biceps brachii, deltoid, quadriceps femoris and hamstring muscles. Three maximum isometric contractions were performed, and the highest value was considered in the analysis.<sup>25</sup>

Quality of life was measured using the Short Form 36 question-naire (SF-36),<sup>26</sup> which has eight subscales: physical functioning, physical role functioning, pain, general health state, vitality, social role functioning, emotional role functioning, and mental health. The score for each subscale ranges from 0 to 100 points, with higher scores denoting better quality of life.

Dyspnoea was measured using the Medical Research Council scale,<sup>27</sup>]FID\$T8[which is composed of five activities on which breathlessness is scored from 1 to 5. Higher scores denote greater limitations to activities of daily living.

Pulmonary function was measured using a portable spirometer<sup>c</sup>. The technical procedures were based on Brazilian guidelines.<sup>28</sup> The data were expressed as absolute and percent-tages of predicted values for the forced expiratory volume in one second (FEV<sub>1</sub>) and the forced vital capacity (FVC).<sup>29</sup> Blinded assessors determined the following outcomes: inflammation was measured based on C-reactive protein (CRP) using a venous blood sample. The respiratory physician, who was blinded to the participants' group allocation, decided on the length of hospital stay. Hospital records were used to confirm whether there were any deaths before discharge.

The safety of the interventions was evaluated based on the observation and occurrence of adverse events such as nausea, lightheadedness, significant dyspnoea, extreme fatigue, chest pain, arrhythmia, syncope, altered consciousness or severe desaturation (SpO<sub>2</sub> 80%).

#### Data analysis

The sample size was calculated in relation to the Glittre Activities of Daily Living test<sup>24</sup> as the main outcome and was based on results obtained from a pilot study with five participants in each group. An effect size of 1.3 was estimated from a mean time of 213 seconds to perform the Glittre Activities of Daily Living test in the control group and 153 seconds for the experimental group, with a SD within each group of 45 seconds. Unequal treatment allocation (2:1) was assumed due to ethical reasons for maximising participants' exposure to the experimental group. Assuming an  $\alpha$  error of 0.05, a  $\beta$  error of 0.20 and an allocation ratio of 2:1, the sample size was determined to be 24 participants in the intervention group and 12 in the control group.

The Shapiro-Wilk test was used to determine the distribution (normal or non-normal) of the data. Baseline characteristics were summarised using mean (SD) for parametric data and median (IQR) for non-parametric data. The continuous outcome data were analysed as mean (SD) of two groups, mean (SD) within-group difference and mean (95% CI) between-group difference. The standardised effect size was calculated using Cohen's *d*. Pearson's correlation coefficients were calculated to determine the strength of correlations between variables. The data were analysed based on intention-to-treat analysis. A *p*-value < 0.05 was considered significant.

## Results

### Compliance with the study protocol

The target sample size in the registered protocol was 30 participants. This was based on a calculation using the difference to be detected from a study by Skumlien and colleagues<sup>24</sup> and the SD from a study by Jose´ and colleagues.<sup>2</sup> When the results of our pilot study became available early in the

Table 1  
Baseline characteristics of participants.

Characteristic	Randomised (n = 49)	
	Exp (n = 32)	Con (n = 17)
Age (yr), mean (SD)	51 (21)	59 (18)
Gender, n males (%)	17 (53)	10 (59)
Body mass index, (kg/m <sup>2</sup> ), mean (SD)	23 (4)	25 (6)
CURB-65, median (IQR)	1 (1 to 1)	1 (1 to 2)

Exp = experimental group, Con = control group.

conduct of the present study, the sample size calculation outlined in the Data analysis section, above, was considered to be the better choice for the present study. This exceeded the registered target sample size.

One registered outcome measure, Tumour Necrosis Factor-alpha (TNF $\alpha$ ), was not reported. In principle, the analysis of TNF $\alpha$  should have been carried out in the hospital. However, the hospital carried out the analysis on seven participants and did not allow further collection due to the high cost of the test. The limited data are available from the authors on request.

#### Flow of participants through the study

Of the 65 patients admitted with an initial diagnosis of community-acquired pneumonia during the study recruitment period, 14 were excluded based on the eligibility criteria (Figure 1).

A further two participants were withdrawn after randomisation because their diagnosis of community-acquired pneumonia changed during reassessment by a physician; they were not included in the intention-to-treat analysis. Therefore, the study reports data on 49 participants: 32 in the experimental group and 17 in the control group. Five participants in the experimental group and one in the control group were discharged before the scheduled post-intervention reassessment on Day 10, but these participants could be included in the analysis of length of hospital stay. A further two participants in the control group withdrew from the

Table 2

Mean (SD) of groups, mean (SD) difference within groups and mean (95% CI) difference between groups for functional capacity tests, peripheral muscle strength, dyspnoea and inflammation.

Outcomes	Groups				Difference within groups		Difference between groups
	Day 1		Day 10		Day 10 minus Day 1		Day 10 minus Day 1
	Exp (n = 32)	Con (n = 17)	Exp (n = 32)	Con (n = 17)	Exp	Con	Exp minus Con
Glittre ADL Test (s)	229(86)	223(52)	177 (93)	211(46)	-52 (40)	-12(26)	-39 (-59 to -20)
Incremental Shuttle Walk Test (m)	355 (126)	313(91)	517 (184)	346(94)	162(110)	33 (71)	130 (77 to 182)
Biceps brachii strength (kgf)	12.9 (4.7)	12.9(5.6)	15.7 (4.8)	12.2(4.6)	2.7(2.5)	-0.7(4.8)	3.5 (0.9 to 6.0)
Deltoids strength (kgf)	5.4 (2.0)	5.3(2.5)	7.6(2.5)	5.3(2.4)	2.2(1.8)	0.0 (1.5)	2.2 (1.2 to 3.2)
Quadriceps strength (kgf)	25.6 (5.7)	24.2(8.3)	32.5 (8.5)	22.6(6.7)	6.9(6.1)	-1.6(5.5)	8.5 (4.6 to 11.6)
Hamstrings strength (kgf)	15.5 (5.7)	14.4(5.8)	21.4 (7.6)	13.9(4.2)	5.9(4.7)	-0.5(3.5)	6.5 (4.0 to 8.8)
MRC Dyspnoea scale (1 to 5)	3.1 (1.1)	2.5(0.9)	1.6(0.9)	1.9(0.7)	-1.5 (1.1)	-0.6(0.7)	-0.9 (-1.4 to -0.4)
C-reactive protein (mg/l)	14 (14)	11(13)	5(7)	5(5)	-9(14)	-7 (13)	-2 (-10 to 6)

ADL = activities of daily living, Con = control group, Exp = experimental group, MRC = Medical Research Council.

Table 3

Mean (SD) of groups, mean (SD) difference within groups, and mean (95% CI) difference between groups for health-related quality of life assessed using the Short Form 36 (SF-36) questionnaire.

Domains	Groups				Difference within groups		Difference between groups
	Day 1		Day 10		Day 10 minus Day 1		Day 10 minus Day 1
	Exp (n = 32)	Con (n = 17)	Exp (n = 32)	Con (n = 17)	Exp	Con	Exp minus Con
Physical functioning	52 (20)	52 (26)	80 (21)	66 (20)	28(22)	14 (24)	13 (1 to 28)
Physical role functioning	37 (31)	40 (37)	58 (30)	45 (36)	21(28)	5 (26)	16 (-1 to 32)
Pain	41 (22)	37 (26)	55 (23)	43 (20)	14(16)	6 (28)	8 (-8 to 23)
General health state	58 (16)	56 (23)	70 (12)	63 (22)	12(13)	7 (18)	5 (-5 to 15)
Vitality	48 (13)	48 (20)	69 (16)	68 (15)	21(21)	20 (23)	0 (-13 to 14)
Social role functioning	62 (24)	43 (21)	68 (22)	54 (24)	7 (17)	11 (14)	-5 (-14 to 5)
Emotional role functioning	43 (35)	22 (29)	57 (32)	38 (39)	15(21)	16 (29)	-2 (-18 to 15)
Mental health	53 (20)	49 (18)	60 (19)	53 (19)	7(9)	4 (17)	3 (-6 to 12)

Exp = experimental group, Con = control group.

study due to the constraints of their medical management (Figure 1). All participants permitted their length of stay to be recorded.

The baseline characteristics of the groups were similar. These data are presented in Table 1 and the first two data columns of Table 2, Table 3 and Table 4. Individual participant data are presented in Table 5 on the eAddenda.

#### Effect of interventions

##### Primary outcome

Functional exercise capacity, as measured by the Glittre Activities of Daily Living test, improved by a mean of 52 seconds (SD 40) in the experimental group, whereas the control group improved by a mean of 12 seconds (SD 26). This was a statistically significant difference (MD 39 seconds, 95% CI 20 to 59), as shown in Table 2. When calculated as a standardised effect size, the between-group difference of 39 seconds equated to a Cohen's d of 1.19.

##### Secondary outcomes

The improvement in functional capacity, as evaluated by the distance walked on the ISWT, was significantly greater in the experimental group than in the control group (MD 130 m, 95% CI 77 to 182). When calculated as a standardised effect size, the between-group difference equated to a Cohen's d of 1.39. No significant between-group differences occurred in the variables monitored during the ISWT: heart rate, percentage of predicted maximal heart rate, SpO<sub>2</sub> and Borg dyspnoea and fatigue scales (data not shown). The SpO<sub>2</sub> during the aerobic training did not show any desaturation < 84%, as outlined in the Methods section.

All muscles that were analysed demonstrated mean improvement in strength in the experimental group and mean deterioration in the control group, as presented in Table 2. The between-group difference in change in strength was statistically significant for all four muscle groups. The between-group differences in change in strength were: 3.5 kgf for biceps brachii (Cohen's d = 0.76); 2.2 kgf

Table 4  
Mean (SD) of groups, mean (SD) difference within groups, and mean (95% CI) difference between groups for lung function.

Outcome	Groups				Difference within groups		Difference between groups
	Day 1		Day 10		Day 10 minus Day 1		Day 10 minus Day 1
	Exp (n = 32)	Con (n = 17)	Exp (n = 32)	Con (n = 17)	Exp	Con	Exp minus Con
FEV <sub>1</sub> (l)	2.05 (0.66)	2.20(0.86)	2.21 (0.63)	2.15(0.59)	0.16(0.26)	-0.06 (0.62)	0.21 (-0.11 to 0.54)
FEV <sub>1</sub> (% pred)	69 (11)	75(12)	74 (10)	75(12)	6(8)	1 (15)	5 (-3 to 13)
FVC (l)	2.55 (0.74)	2.66(0.97)	2.71 (0.65)	2.67(0.76)	0.16(0.29)	0.01 (0.49)	0.15 (-0.12 to 0.42)
FVC (% pred)	69 (11)	71(10)	74 (8)	73 (9)	5(8)	2 (11)	3 (-3 to 9)

Con = control group, Exp = experimental group, FEV<sub>1</sub> = forced expiratory volume in one second, FVC = forced vital capacity, % pred = percentage of the predicted value.<sup>29</sup> JFIDST5[

for deltoids (Cohen's *d* = 1.45); 8.1 kgf for quadriceps (Cohen's *d* = 1.46); and 6.4 kgf for hamstrings (Cohen's *d* = 1.54).

The domain 'physical functioning' of the SF-36 quality of life questionnaire improved significantly more in the experimental group than in the control group (MD 14 points, 95% CI 1 to 28, Cohen's *d* = 0.48). None of the other domains of the SF-36 showed statistically significant effects (Table 3).

Both groups showed an improvement on average in the severity of dyspnoea, as measured on the Medical Research Council scale during the 10 days of the study. However, the experimental group showed significantly greater improvement (MD 0.9 points, 95% CI 0.4 to 1.4, Cohen's *d* = 0.98).

Pulmonary function was reduced to a similar degree compared to predicted values in both groups (Table 4). After the interventions, no substantial change in pulmonary function was detected. Both groups showed a reduction on average in CRP during the 10 days of the study. The amount of reduction was similar in the two groups. No correlations were found between CRP and the other variables studied. Moreover, the change in CRP was not correlated with peripheral muscle strength or improvement in the performance of the functional capacity tests.

All participants survived long enough to be discharged from the hospital. The type of treatment did not significantly influence length of stay in hospital: median 12 days (IQR 10 to 18) in the experimental group and median 13 days (IQR 11 to 25) in the control group. None of the adverse events listed in the Methods section were identified during the application of the allocated interventions.

## Discussion

It is believed that this is the first study to investigate the effects of an inpatient rehabilitation program on patients with community-acquired pneumonia by comparing them with those of standard respiratory physiotherapy. The results were superior to those of standard respiratory physiotherapy.

Although it is common practice,<sup>6</sup> JFIDST5[ there is no evidence to support the routine use of standard respiratory physiotherapy in patients who are hospitalised for community-acquired pneumonia. A randomised clinical trial examined intervention for pneumonia that included postural drainage, percussion, thoracic vibration and positive pressure, but failed to demonstrate changes in fever, the extent of radiographic impairment, length of hospital stay, or mortality.<sup>7</sup> These results are in line with the results of another study of techniques such as postural drainage, external support for breathing, percussion and vibration in pneumonia.<sup>8</sup> There was no overall effect and in younger patients, smokers and patients with interstitial pneumonia specifically, the intervention led to an increase in the duration of fever and length of hospital stay.<sup>8</sup> A systematic review of adjunctive therapies for patients hospitalised for community-acquired pneumonia has shown that clinical trials with such respiratory physiotherapy techniques are scarce and do not provide evidence of benefits from their routine use in these patients.<sup>9</sup>

In a recent meta-analysis, Yang et al<sup>10</sup> compared standard respiratory physiotherapy to usual care and found no significant differences regarding mortality, the resolution of the disease, improvement in chest radiography or healing time. The same was

observed when comparing the active cycle of breathing techniques with usual care, including no difference regarding hospitalisation length, duration of antibiotic therapy, mean duration of sputum production or inpatient sputum weight.

As previous studies have demonstrated that standard respiratory physiotherapy has no impact on clinical measures of the resolution of pneumonia, it is interesting to observe (albeit without a no-intervention control group for comparison) the change in functional outcomes in the group that received respiratory therapy in the present study. This group did not show substantial improvement in the distance walked on the ISWT. There is no minimum clinically important difference established for the ISWT specifically for patients hospitalised for community-acquired pneumonia, but the magnitude of the average improvement observed in this group was inferior to that found after an outpatient rehabilitation program for both patients with non-cystic fibrosis bronchiectasis (37 m)<sup>30</sup> and with COPD (48 m).<sup>31</sup> The same lack of substantial improvement was observed in the group that received respiratory therapy for the Glittre Activities of Daily Living test, where again the best estimate of the minimum clinically important difference is indirect because it comes from patients with COPD (53 seconds).<sup>24</sup>

No association was found between hospital length of stay and type of treatment. However, in a study conducted by Mundy et al, a reduction in hospital length of stay was found when early mobilisation was performed.<sup>16</sup> This divergence may have occurred because the hospital length of stay in the present study depended on factors other than clinical criteria, such as the economic status of the patient, the ability to afford antibiotic therapy, cognition, capacity to self-medicate correctly and administrative aspects of the hospital such as availability of hospital beds.

All participants were discharged, so there was no association between mortality and the type of treatment. This was due to the low severity of cases, as represented by the low CURB-65, corresponding to prognosis of a low degree of lethality.<sup>23</sup> A previous study had demonstrated that early mobilisation did not interfere in the mortality of these patients, with no change in the re-hospitalisation rate within a 90-day period.<sup>16</sup>

No important complications occurred due to the intervention protocols, indicating that the protocols are safe and could be performed on patients with community-acquired pneumonia whose characteristics are similar to those of the present sample. Physical exercise with early mobilisation of hospitalised patients

has previously been performed and appears to be safe for patients with COPD,<sup>11-13</sup> asthma,<sup>32</sup> interstitial lung disease<sup>33</sup> and community-acquired pneumonia.<sup>16</sup> However, as discussed above, exercise-based rehabilitation commenced during hospitalisation for COPD exacerbation may reduce uptake of pulmonary rehabilitation and increase mortality after discharge,<sup>14</sup> so pulmonary rehabilitation immediately after discharge may be more beneficial for patients with COPD.<sup>15</sup>

Previous studies have demonstrated that short-term hospitalisation reduces functional capacity, even in patients who are not bedridden, regardless of age or initial functional status.<sup>34</sup> In a recent study, a decline in functional capacity as well as reductions in both peripheral muscle strength and quality of life<sup>2</sup> were demonstrated in patients hospitalised for community-acquired

pneumonia. Therefore, interventions to minimise such declines are crucial for these patients.

Mundy et al evaluated the effects of early mobilisation performed by nurses on 456 patients who were hospitalised for community-acquired pneumonia and found that hospitalisation length and costs were reduced, with no adverse events.<sup>16</sup> However, this intervention was poorly described and the control group did not receive any kind of standard respiratory physiotherapy. The present study is the first to demonstrate the relative effects of a physical training program on functional capacity for hospitalised patients with community-acquired pneumonia. The aerobic and resistance training provided a more effective recovery of functional capacity than standard respiratory physiotherapy.

The loss of peripheral muscle strength is a common adverse change in hospitalised patients, even during short periods of hospitalisation.<sup>34</sup> The interventions performed in the present study led to a significant increase in peripheral muscle strength of the exercised muscles, whereas no such increase occurred in the control group. The training to improve peripheral muscle strength was performed with elastic bands due to the difficulty in transporting and storing weights in a hospital setting with limited space. Elastic bands are a low-cost, highly practical alternative with no need for more expensive equipment, which hospitals often cannot provide, and are as effective as other resources.<sup>35</sup>

The evaluation of dyspnoea using the Medical Research Council scale revealed a greater reduction in the experimental group than in the control group, although both groups improved substantially. However, if a reduction of 0.58 is considered clinically significant for the Medical Research Council scale,<sup>36</sup> this reduction occurred in both groups. Besides the improvement in the clinical status and the resolution of the lung disease, it is possible that the 10-minute walk in the control group as well as the aerobic and resistance training in the experimental group both led to a lower sensation of dyspnoea upon discharge from the hospital.

The magnitude of change in CRP was similar in both groups, suggesting that the common management or natural recovery (rather than the randomised interventions) determined the reduction in CRP. The association between CRP and functional capacity was also investigated in the present study, but was not significant. This was likely due to the low severity of community-acquired pneumonia, since previous studies with severe patients with high levels of CRP found such an association, along with a worse prognosis. Moreover, a high level of CRP upon admission to the hospital, the maintenance of this level after treatment and a small reduction in comparison to the initial level have also been associated with a worse prognosis as well as greater morbidity and mortality rates.<sup>37,38</sup>

A limitation of the present study was that the researchers who evaluated the Glitter Activities of Daily Living test, ISWT, quality of life, dyspnoea, peripheral muscle strength and spirometry were the same as those who performed the therapeutic interventions. However, the evaluations were standardised with written guide-lines to minimise the potential for bias from unblinded assessors. Furthermore, the assessors were blinded for some key study outcomes such as CRP, length of stay and outcome (death or hospital discharge).

In summary, this study identified significant improvements in functional capacity, peripheral muscle strength, dyspnoea and quality of life with inpatient exercise rehabilitation as opposed to respiratory interventions. It is believed that these benefits, in conjunction with other evidence about the benefits of inpatient exercise in this population,<sup>16</sup> are sufficient to recommend the use of an inpatient rehabilitation program – especially where the current routine treatment for these patients is respiratory physiotherapy techniques, since the latter lacks robust evidence to support its routine use in this population. Given the unexpected effects of inpatient exercise rehabilitation in COPD exacerbations,<sup>14</sup> however, further research should investigate the effects of the intervention of people with community-acquired pneumonia after discharge from hospital.

What is already known on this topic: People who are hospitalised for community-acquired pneumonia experience a decline in functional capacity that is associated with higher rates of re-hospitalisation and death. Existing evidence does not support the use of respiratory techniques, although these remain standard practice in some hospitals.

What this study adds: Among people who are hospitalised for community-acquired pneumonia, an exercise training pro-gram led to greater benefits in functional capacity, peripheral muscle strength, dyspnoea and quality of life than a regimen that included respiratory techniques and self-paced walking.

Footnotes: <sup>a</sup>Thera Band™, The Hygenic Corporation, Akron, Ohio, USA.

<sup>b</sup>FIDST443Kratos, Saõ Paulo, Brazil. FIDST51<sup>c</sup> FIDST61[Pony, Cosmed, Rome, Italy. eAddenda: Table 5 can be found online at doi:10.1016/j.jphys.

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Correspondence: Simone Dal Corso, Post-graduate Program in Rehabilitation Sciences, Universidade Nove de Julho, Saõ Paulo, Brazil. Email: dr\_andersonjose@yahoo.com.br, simonedc@uninove.br

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