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EXERCISE TRAINING IN PULMONARY REHABILITATION: ARE FUNCTIONAL EXERCISES AND ELASTIC RESISTANCE TRAINING EFFECTIVE STRATEGIES?

PRESIDENTE PRUDENTE

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FABIANO FRANCISCO DE LIMA

Exercise Training in Pulmonary Rehabilitation: Are Functional Exercises and Elastic Resistance Training Effective Strategies?

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DEDICATION

I dedicate this thesis to everyone who was with me along this journey, for those who are happy with me with this achievement, especially my parents, Paulo Manoel de Lima and Clarice Francisco de Lima.

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EPIGRAPH

"Every day I live, I am more convinced that the waste of life is in the love that we do not give, in the forces that we do not use, in the selfish prudence that risks nothing and that, avoiding suffering, we also lose the happiness"

"A cada dia que vivo, mais me convenço de que o desperdício da vida está no amor que não damos, nas forças que não usamos, na prudência egoísta que nada arrisca e que, esquivando-nos do sofrimento, perdemos também a felicidade."

Carlos Drummond de Andrade

ABSTRACT

Introduction: A key priority in Pulmonary Rehabilitation (PR) programs is to increase their accessibility. Elastic resistance training stands out for its low cost, practicality, and portability, allowing people to perform resistance training in their home environment. Lemgruber® Elastic tubing (LET) has been proposed as a tool for such an end. Exercise training in PR programs commonly involves aerobic and resistance training, showing clinically relevant results when combined. PR programs provide significant functional gains for patients with Chronic Obstructive Pulmonary Disease (COPD). The evidence for increasing physical activity in daily life (PADL) with PR is contradictory and inconsistent. It is suggested an small effect on PADL with an inconsistent translation of functional gains into increased PADL. Functional exercise training can be a promising alternative. **Objectives:** This thesis presents the following objectives: To assess the length-resistance relation of elongation and resistance of five Lemgruber® elastic tubings (LET) of different diameters; Conduct a systematic review to investigate the effectiveness of elastic resistance training on improving muscle strength, functional exercise capacity, health-related quality of life (HRQoL) and dyspnea in patients with stable COPD; To evaluate the short term (8 weeks) and sustained effects (12 weeks post-training follow-up) of the combination of a functional exercise training, with a training program consisting of aerobic and resistance exercise in patients with COPD. **Methods:** Four studies were conducted to answer the objectives of this thesis and are presented as separated articles: 1) a descriptive laboratory study to evaluate the LET; 2) a systematic review and meta-analysis on the effectiveness of elastic resistance training in patients with COPD; 3) a study protocol and a randomized clinical trial on the effects of the combination of functional exercises with exercise training in patients with COPD. **Results:** The main findings of this thesis were that the large array of resistances delivered by LET, along with its safety and reasonable estimation of reference values, support its use in clinical practice. Elastic resistance training is an effective intervention to improve muscle strength in patients with COPD. Further, compared to resistance training using weight machines, elastic resistance training demonstrated similar effects on muscle strength, functional exercise capacity, HRQoL and dyspnea. The inclusion of a functional exercise training protocol in training conventionally performed by patients with COPD could not improve the PADL and activities in daily living limitations.

Keywords: Chronic Obstructive Pulmonary Disease, Physical exercise, Physical activity

RESUMO

Introdução: Uma prioridade chave dos programas de Reabilitação Pulmonar (RP) é aumentar sua acessibilidade. O treinamento resistido elástico se destaca pelo baixo custo, praticidade e portabilidade, permitindo que as pessoas realizem o treinamento resistido no ambiente domiciliar. Os tubos elásticos Lemgruber® (LET) tem sido proposto como uma ferramenta para este fim. O treinamento físico em programas de RP geralmente envolve treinamento aeróbico e resistido, mostrando resultados clinicamente relevantes quando combinados. Os programas de RP fornecem ganhos funcionais significativos para pacientes com Doença Pulmonar Obstrutiva Crônica (DPOC), entretanto, as evidências para o aumento da atividade física na vida diária (AFVD) com RP são contraditórias e inconsistentes, sugerindo um pequeno efeito na AFVD com uma tradução inconsistente de ganhos funcionais em aumento de AFVD. O treinamento físico funcional pode ser uma alternativa promissora. **Objetivos:** Esta tese apresenta os seguintes objetivos: Avaliar a relação comprimento-resistência de alongamento e resistência de cinco tubos elásticos Lemgruber® (LET) de diferentes diâmetros; Conduzir uma revisão sistemática para investigar a eficácia do treinamento resistido elástico na melhora da força muscular, capacidade funcional de exercício, qualidade de vida relacionada à saúde (QVRS) e dispneia em pacientes com DPOC estável; Avaliar os efeitos de curto prazo (8 semanas) e sustentados (12 semanas de acompanhamento pós-treinamento) da combinação de um treinamento físico funcional, com um programa de treinamento composto por exercício aeróbico e resistido em pacientes com DPOC. **Métodos:** Quatro estudos foram realizados para responder aos objetivos desta tese e são apresentados como artigos separados: 1) um estudo laboratorial descritivo para avaliação dos LET; 2) uma revisão sistemática e meta-análise sobre a eficácia do treinamento utilizando resistência elástica em pacientes com DPOC; 3) um protocolo de estudo e um ensaio clínico randomizado sobre os efeitos da combinação de exercícios funcionais com treinamento físico em pacientes com DPOC. **Resultados:** Os principais achados desta tese foram que a grande variedade de resistências fornecidas por LET, juntamente com sua segurança e estimativa razoável de valores de referência, suportam seu uso na prática clínica. O treinamento utilizando resistência elástica é uma intervenção eficaz para melhorar a força muscular em pacientes com DPOC. Além disso, em comparação ao treinamento resistido com aparelhos de musculação, o treinamento utilizando resistência elástica demonstrou efeitos semelhantes na força muscular, capacidade funcional de exercício, QVRS e dispneia. Por fim, a inclusão de um protocolo de treinamento físico funcional no treinamento convencionalmente realizado por pacientes com DPOC não não foi capaz de melhorar a AFVD e limitações nas atividades de vida diária.

Palavras-chave: Doença Pulmonar Obstrutiva Crônica, Exercício físico, Atividade física

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PRESENTATION

This thesis contemplates the material originated from the research entitled: “Exercise training in pulmonary rehabilitation: are functional exercises and elastic resistance training effective strategies?” held at the Faculty of Science and Technology - FCT / UNESP, campus of Presidente Prudente, in partnership with the Hasselt University, Diepenbeek, Belgium, and financed by the São Paulo Research Foundation (FAPESP).

In line with the roles of the UNESP post-graduation program in Physiotherapy (home institution), this material is divided into the following sessions:

Background: Introduction and objectives of the researched topic.

Scientific article I: Mechanical Properties, Safety and Resistance Values of Lemgruber® Elastic Tubing. Published in the journal: ***Brazilian Journal of Physical Therapy.*** (Impact Factor: 2.1)

Lima FF*, Camillo CA, Reis EAPD, Job AE, Silva BSA, Topalovic M, Ramos D, Ramos EMC. Mechanical properties, safety and resistance values of Lemgruber® elastic tubing. Braz J Phys Ther. 2019;23:41–47. DOI: 10.1016/j.bjpt.2018.07.001.*

Scientific article II: Elastic Resistance Training Produces Benefits Similar to Conventional Resistance Training in People with Chronic Obstructive Pulmonary Disease: Systematic Review and Meta-Analysis. Published in the journal: ***Physical Therapy.*** (Impact Factor: 3.1)

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Scientific article III: Effects of Combining Functional Exercises with Exercise Training on Daily Physical Activities and Functionality in Patients With COPD: A Protocol for a Randomized Clinical Trial. Published in the journal: ***Trials.*** (Impact Factor: 1.8)

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Scientific article IV: Combining Functional Exercises with Exercise Training in COPD: A Randomized Clinical Trial

Authors: Fabiano Francisco de Lima; Carlos Augusto Camillo; Isis Grigoletto; Juliana Souza Uzeloto; Franciele Marques Vanderlei; Dionei Ramos; Chris Burtin; Ercy Mara Cipulo Ramos

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Final Conclusions: Obtained from the research carried out.

Activities developed during the doctorate period.

1. BACKGROUND

Chronic obstructive pulmonary disease (COPD) is a preventable and treatable disease characterized by persistent respiratory symptoms and airflow limitation associated with airway and alveolar abnormalities caused by significant exposure to noxious particles or gases[1]. COPD is the 3rd leading cause of death and responsible for approximately 6% of total deaths worldwide[2]. According to the Global Burden of Disease, COPD is the most prevalent chronic respiratory disease worldwide responsible for roughly half of the prevalence of all chronic respiratory diseases among men (55.1% of total) and women (54.8% of total)[3].

Despite its primarily respiratory character, COPD also presents significant extrapulmonary (systemic) consequences, including skeletal muscle dysfunction, contributing to exercise intolerance[1]. These patients are less physically active than age-matched healthy individuals[4-9], and lower levels of physical activity in daily life (PADL) are associated with hospitalizations[10], worse prognosis[11], disease progression[12], and increased risk of premature death in COPD[13].

Pulmonary rehabilitation (PR) programs are well established as essential for the treatment of patients with COPD[14]. Exercise training is considered the cornerstone of PR[15, 16] and commonly comprises structured sessions of aerobic training (e.g., ground/treadmill walking and cycling) and resistance training for the muscle groups of the upper and lower limbs. Resistance training elicits lower cardiopulmonary stress and fewer symptoms than aerobic training[17] in COPD, promoting improves of functional exercise capacity, dyspnea, muscle strength, and health-related quality of life (HRQoL) in this population[18-24]. Of note, resistance training is commonly performed in PR programs using weight machines and dumbbells[25].

Over the past decade, studies have been conducted to investigate the effects of resistance training using elastic bands and tubing (i.e. elastic resistance training) in people with COPD[26-30], exploring whether these tools could be performed as an alternative to resistance training that uses weight machines[28-30]. Elastic resistance training stands out for its low cost[31], practicality and, mainly, for its portability, which allows people to perform resistance training in their home environment. Therefore, it can be used as an alternative type of resistance training in people with COPD, increasing accessibility. Unlike free weights, elastic resistance does not rely on gravity to provide resistance allowing people to perform exercises in the horizontal plane[32] (i.e. when lying or reclining). This can be considered an advantage in significantly functionally impaired people with COPD.

Despite the compelling evidence for the benefits of conventional center-based exercise training in people with COPD, exercise training reaches less than 10% of patients worldwide[33]. Access is particularly challenging in rural settings, where COPD is often prevalent, and programs may not be available. However, uptake and completion are also poor in metropolitan areas[34]. Up to 50% referred to PR do not attend it. Among those who attendat least once, up to a third dropout the program[34]. Frequent travel to a center-based program, in the setting of distressing dyspnea and mobility limitation, is regularly reported as a barrier to attendance[34]. A key priority identified by the American Thoracic Society/European Respiratory Society Policy Statement on Pulmonary Reabilitation was to increase the accessibility of PR programs[35]. Although elastic resistance may be an up-and-coming alternative to increasing the accessibility to resistance training, a systematic review of this intervention's effectiveness specifically in COPD has not been undertaken.

Furthermore, among studies conducted using elastic resistance in patients with COPD, different elastic materials have been used[26-28, 30]. Lemgruber® elastic tubing (LET) is an affordable type of elastic tubing used in exercise training programs with positive effects on peripheral muscle force and functional exercise capacity in healthy adults[31] and patients with COPD[28, 29, 36]. Despite the potential benefits, there is only limited information regarding the mechanical properties of LET, such as details about the reproducibility of repeated elongations or the maximal elongation considered safe. The manufacturer typically provides this information; however, it is common that only limited details are described[37]

In addition, in clinical practice, it is difficult to estimate the force generated by the elastic material during movements in different ranges of motion (ROM), hampering therapists from being confident about the magnitude of resistance offered through the ROM (i.e. elongation of the tubing) during training. Details about the mechanical properties also help to guarantee safety during exercise as improper use of various elastic materials has been reported to be harmful[38]. Increased knowledge of the problems mentioned above would certainly help therapists be more confident in elaborating and prescribing exercise training protocols using LET.

As mentioned before, exercise training in PR programs commonly involves aerobic and resistance training, showing promising results when combined[19], and is recommended by international guidelines[39, 40]. PR programs improve the functional exercise capacity in this population[14, 16]. However, the evidence for increasing PADL with PR is contradictory and inconsistent.[16, 41] It is suggested a negligible effect on PADL with an inconsistent translation of functional gains into increased PADL[42].

In older adults, functional exercise training improves the performance in activities in daily living (ADL), and mobility[43-45]. This training involves coordinated patterns of multi-joint movements and dynamic tasks[44]. Even combined with another exercise modality, this type of exercise has demonstrated positive effects for patients with COPD[46]. However, despite the benefits obtained on PADL and ADL performance in a short-term training program combining functional exercises with aerobic and home training in patients with COPD, the authors evaluated the responses only after the end of the training program[46]. Thus, it is not possible to know if the effects were maintained for a more extended period than the program. Furthermore, it did not include progressive resistance training, an essential component related to improvements in ADL performance in patients with COPD[24]. In this sense, the short term and sustained effects of the combination ofaerobic, resistance and functional exercise training (based on limitations for performing ADL) in a randomized trial are still to be investigated in patients with COPD.

1.1. Objectives

Given the context presented, the objectives of this thesis were:

- To assess the length-resistance relation of elongation and resistance of five Lemgruber® Elastic Tubing of different diameters; to describe the safe use of LET; to establish reference equations of resistance according to elongation of the five LET, and to describe elongation of LET during movements at different degrees of ROM.
- Conduct a systematic review including two-fold: (i) to investigate the effectiveness of elastic resistance training on improving muscle strength, functional exercise capacity, HRQoL and dyspnea in patients with stable COPD; and (ii) to compare the effects of elastic resistance training with those of conventional resistance training (using weight machines) on the same outcomes.
- Evaluate the short term (8 weeks) and sustained effects (12 weeks post-training follow-up) of the combination of functional exercise training, with a training program consisting of aerobic and resistance exercise, on PADL, ADL limitations, functional exercise capacity, and peripheral muscle strength of patients with COPD.

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2. ARTICLE I

ORIGINAL RESEARCH

Lima FF et al

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ORIGINAL RESEARCH

Mechanical properties, safety and resistance values of Lemgruber® elastic tubing

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Mechanical Properties, Safety and Resistance Values of Lemgruber® Elastic Tubing

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ABSTRACT

Background: Lemgruber® elastic tubing (LET) has been used as an adjunct to exercise training with positive effects in healthy adults and in patients with chronic lung disease. Despite its benefits, there is a lack of information on the specific resistance, elongation, reproducibility and safety of the different types of LET. **Objectives:** The primary outcome was to assess the length-resistance relation (E/R) of five LET of different diameters. Secondary outcomes included the development of reference equations of resistance according to elongation of LET types and; the descripton of LET safety and; the description of elongation of LET using a clinically useful outcome (i.e. range of motion [ROM], in degrees). **Methods:** The relation between elongation and resistance of LET was investigated in a laboratory environment. Secondly, reference equations for the resistance according to the elongation in each LET were calculated. Finally, the elongation of the tubing during movements in different degrees of ROM were estimated using mathematical models, so that the resistance provided by the tubing for any exercise could be predicted. **Results:** LET provided a large array of resistance varying from 3±0.1N to 537±13N (mean ± standard deviation). The maximal resistance deemed safe for each of the five LET were: 173±25N, 280±23N, 409±40N, 395±37N and 537±13N. Reference equations had nearly perfect predictive power (r^2=0.99) for all polynomial non-linear models ($p<0.001$ for all). **Conclusions:** Lemgruber elastic tubing progressively increased resistance with increased elongation. The large array of resistances delivered by LET, along with its safety and good estimation of reference values, support its use in clinical practice.

Keywords: Elastic resistance; exercise; resistance training.

2.1 INTRODUCTION

Elastic resistive devices such as bands and tubing are tools that are frequently used in exercise programs. The low cost and portability compared to conventional weight machines allow it to be easily used at home as well as in environments with limited space[1-5]. The American College of Sports Medicine recommends exercise training using elastic resistance as a valid therapeutic option[6-8]. Unlike the constant resistance occurring during conventional resistance exercise (i.e. using dumbbells/barbells or weight machines), resistance when using elastic bands or tubing varies according to the elongation of the elastic material[9]. Consequently, highest resistance during concentric exercise is delivered at the point where muscles are at their shortest length (i.e. end of the elongation of the LET) [10,11]. Interestingly, positive effects of elastic resistance are observed and comparable to conventional resistance training [12-16]. Additionally, elastic bands can be used as an adjunct during exercise. For example, it has been shown that the bands improve joint balance during walking exercise (i.e. by reducing rearfoot eversion) [17].

Lemgruber® elastic tubing (LET) is an affordable type of elastic tubing that has been used in exercise training programs with positive effects on peripheral joint muscle force and functional exercise capacity in healthy adults[18] as well as in patients with chronic lung diseases[1,19,20]. Despite their potential benefits, there is only limited information regarding the mechanical properties of LET, such as details about the reproducibility of repeated elongations, or the maximal elongation considered safe. This information is typically provided by the manufacturer; however, it is common that only limited details are described[21]. In addition, in clinical practice, it is difficult to estimate the force generated by the elastic material during movements in different ranges of motion (ROM) hampering therapists from being confident about the magnitude of resistance offered through the ROM (i.e. elongation of the tubing)duringtraining. An increased knowledge of the above mentioned problems would certainly help therapists to be more confident in elaborating and prescribing exercise training protocols. Details about the mechanical properties also help to guarantee safety during exercise as improper use of different elastic materials has been reported to be harmful[9]. Therefore, the aims of this study were: 1) to assess the length-resistance relation of elongation and resistance of five LET of different diameters; 2) to describe the safe use of LET; 3) to establish reference equations of resistance according to elongation of the five LET and; 4) to describe elongation of LET during movements at different degrees of ROM.

2.2. METHODS

2.2.1. Study design

In this descriptive laboratory study[22], the main goal was to investigate the clinical applicability of LET. This was done by analysing the mechanical properties, safety and the resistance delivered during elongation of tubes adopting the following strategy: Firstly, LET of five different diameters had the relation between their elongation and resistance investigated using a laboratory experiment. Secondly, reference equations for the resistance according to the elongation in each LET were calculated. Finally, the elongation of the tubing during movements in different degrees of ROM were estimated using mathematical models, so that the resistance provided by the tubing for any exercise could be predicted.

2.2.2. Length-resistance relation of elongation and resistance.

Five LET sizes were used (**Figure 1A**). Internal (ID) and external diameter (ED) of each tube are described according to manufacturer specification: LET#200 (ID:3,0 millimetres (mm) , ED: 5,5mm); LET#201 (ID:4,0mm, ED: 5,5mm), LET#202

(ID: 4,0mm, ED:8,0mm), LET#203 (ID: 6,0mm, ED:9,0 mm) and LET#204 (ID: 6,0mm, ED: 11,5mm).

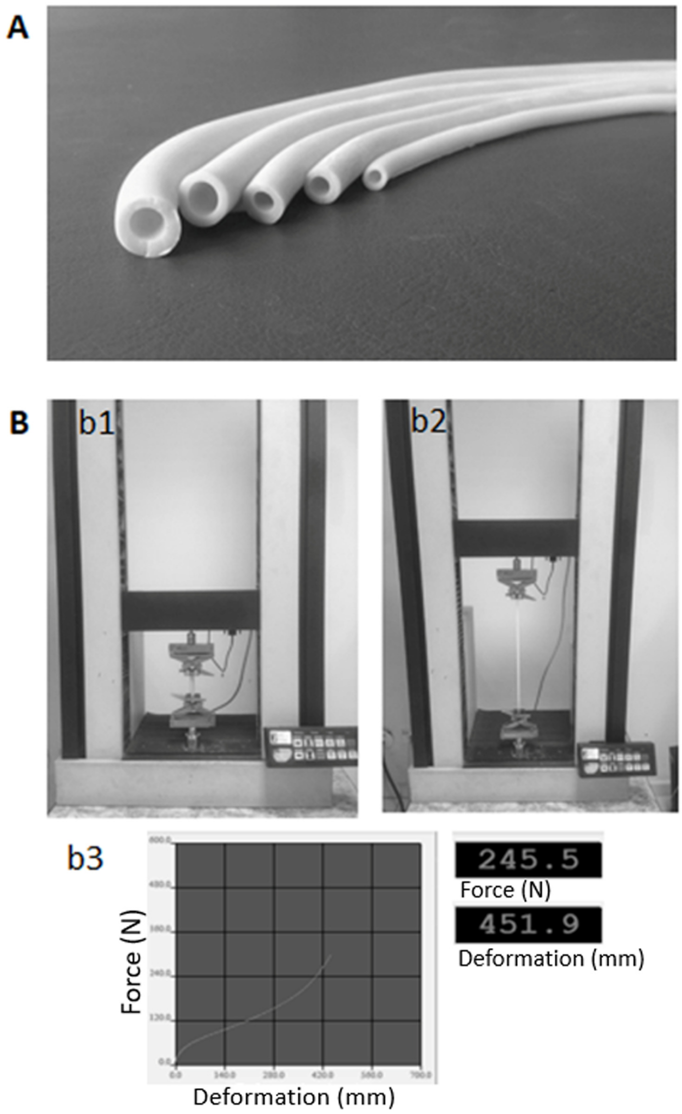

Figure 1: A: Lemgruber® elastic tubing; From the left to the right: LET#204; LET#203; LET#202; LET#201 and LET#200. B: Visual representation of the mechanical testing. Tubes are clamped on the machine by two pressure claws (b1) and subsequently stretched at the rate of 500 mm/min (b2) . The equipment was composed of a load cell, which in turn collected the force values applied by the equipment every deformed millimetre. This force was sent to a specific software (Maqtest), which reported, in real time, the length of the deformation (in millimetres - mm) and the force that the equipment performed for such deformation. The software also performed in real time a plotting of force versus deformation (b3), presenting the characteristic curve of the material under analysis.

The different sizes (mm) of tubing were submitted to experimentation using a mechanical testing machine following the standard testing method for vulcanized rubber and thermoplastic elastomers tension (ASTM D412-06a)[23]. In summary, the tubing were fastened to the testing machine (EMIC model DL 2000) and elongated at a constant speed of 500 mm/min until maximum capacity (i.e. the point where tubing were damaged or the point where the values of resistance stopped increasing despite further elongation) was reached [5]. The procedure was repeated five times with each LET size (with each repetition using a different tube sample of the same size) and the average of measurements was used as the resistance for each point of elongation. Reference equations were calculated using linear and non-linear curve-fit models for each of the five LET sizes. A visual description of the mechanical testing is provided in the figure 1B.

Maximum elongation deemed safe (MES) was defined as the length 10% lower than the maximum length of the samples achieved during the mechanical testing (e.g. if a tube would rupture or present damage in the mechanical testing at 50cm, the MES would be 45cm). In clinical practice, the knowledge of the MES would allow the therapist to easily calculate maximal length of the tube deemed safe in different initial lengths. Mathematically, maximal safe length to be used during exercising is calculated using the following equation (Equation 1):

Equation 1: Maximal length (cm) = Initial Length(cm) × MES (%).

2.2.3. Elongation during different ROM

The resistance delivered by LET during resistive dynamic exercises can be derived from the extent to which tubing elongates for the various ranges of motion (expressed in degrees). To this end, the elongation of tubing at different ranges of motion was calculated based on the general law of cosines using the following equation (Equation 2):

$$\text{Equation 2: } \gamma^2 = b^2 + c^2 - (2 \times b \times c \times \cos \alpha)$$

Where: 'γ' is the length of the elongated tube, 'b' is the length of the lever of the movement, 'c' is the length between the fulcrum and the fixation point of LET and 'α' is the angle between 'b' and 'c'. An illustrative example of this calculation during a shoulder abduction movement is described in **Figure 2**. On the left-hand side of the figure (i.e. before the movement), the lengths of both the tube and the lever of movement (i.e. subject's right arm) are equal. In the right-hand side of the figure (i.e. during the movement), the tube elongates as the shoulder abducts (the length of the lever, however, remains the same). During the movement, α increases and, consequently, the length of tube increases. The percentage of elongation is given using the following equation (Equation 3):

$$\text{Equation 3: elongation (\%)} = (\gamma / \chi) \times 100$$

Where 'γ' is the length of the elongated tube and 'χ' is the initial tube length. A reference equation to estimate elongation according to the range of motion was calculated using an ideal lever of one metre and LET without pre-elongation of the same length at angles varying from zero to 270 degrees. The resulting equation is provided in the results section.

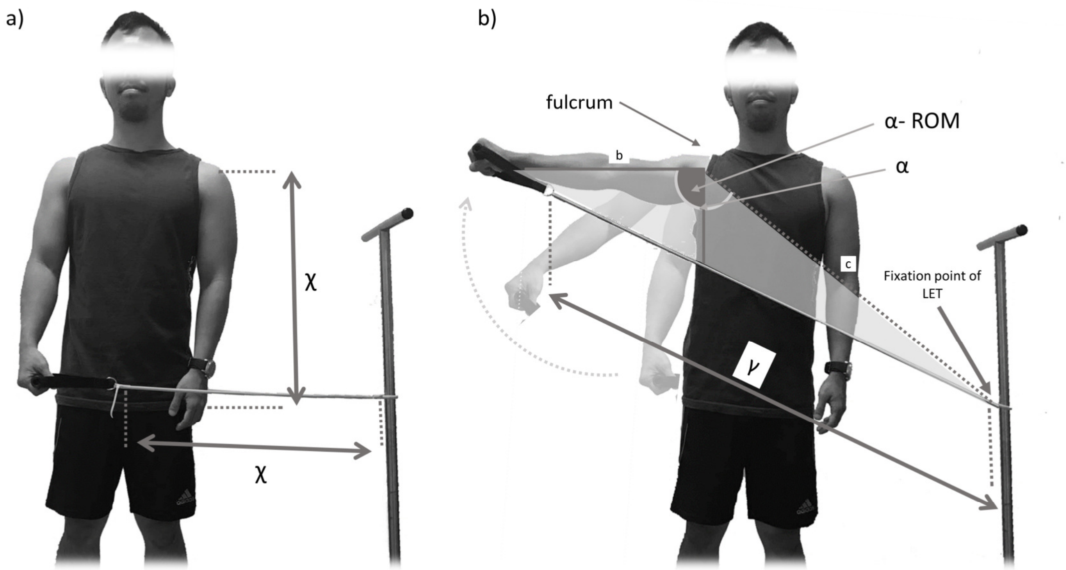

Figure 2. Example of the calculation of elongation during a shoulder abduction movement. a) Initial tube length (without pre-elongation) and lever of movement were equal in size (χ); b) After the complete desired movement (α=90° shoulder abduction) the total length of the tube was calculated as: Length= χ + tube elongation.

2.2.4. Data analysis

The trigonometry functions used to estimate elongations of LET according to the different ROM (i.e. general law of cosines) were calculated using Excel (Microsoft Corporation, USA) for every angle between 0 and 270°. Data analysis was conducted using the software Prism (Graphpad, USA). Shapiro-Wilk tests were used to test the normality of the data. Comparison of maximal resistance and elongation between tubes was performed using One-Way ANOVA with post hoc of Dunns. The equations to 1) estimate resistance according to elongation and to 2) estimate elongation according to ROM were performed using linear and non-linear regression models. The comparison of the slopes generated in '1' was calculated using the Zar's method (F test). Linearity of slopes was calculated using piecewise regression in

MatLab(MathWorks, USA) and values of the first and second inflection points of the curves were deemed the points where change in linearity occurred. A P value lower than 0.05 was considered to be statistically significant.

2.3. RESULTS

2.3.1. Mechanical testing measurements

Figure 3 shows the results of the elongation in the five different sizes of LET. Values reported were limited to 800% of initial length. All tubing presented similar and non-linear behaviour in the length-resistance slopes. The slopes demonstrated steeper increase in resistance at the beginning (68±3% of initial length) of the elongation (1^{st} inflection point of slopes) followed by a steady increase until 475±44% of initial length, when it becomes steeper again (2^{nd} inflection point of slopes). The length-resistance comparisons demonstrated differences between all five slopes ($p<0.0001$, $F=79461$).

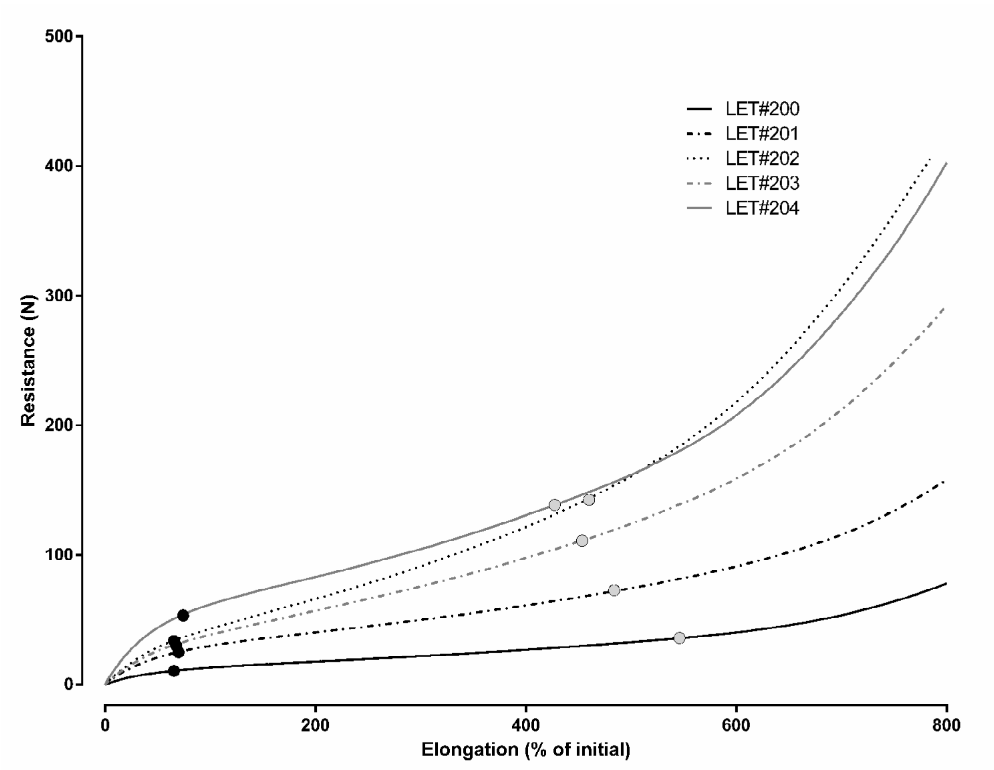

Figure 3: Length-resistance slopes of the five LET. #200 - #204 Lemgruber® elastic tubing. Black dots represent the 1st inflection point. Grey dots represent the 2nd inflection point. The areas between the black and grey dots are linear zones; areas outside the dots (left of black dots and right of grey dots) are the non-linear zones. $p<0.0001$ for comparison between all slopes (Zar's method).

Since the slopes were statistically different, reference equations were generated for each tubing size instead of one general equation for all. Two regression models were adopted (i.e. linear and polynomial non-linear) with equations and respective statistical significance and r^2 values reported in **Table 1.** All equations reached r^2 between 0.88 – 0.94 for the linear models and r^2 of 0.99 for the polynomial non-linear models ($p<0.001$ for all).

Table 1. Reference equations for the resistance according to elongation.

Tubing	*Linear model*	r^2	*p*	*Polynomial non-linear model*	r^2	*p*
#200	$y=(0.1159)X - 2.745$	*0.88*	<0.0001	$y= (3.795\times10^{-7})X^3 + (-0.0003623)X^2 + (0.14388)X + 1.896$	*0.99*	<0.0001
#201	$y=(0.2042)X + 1.144$	*0.91*	<0.0001	$y= (6.443\times10^{-7})X^3 + (-0.0006386)X^2 + (0.2913)X + 4.994$	*0.99*	<0.0001
#202	$y=(0.4097)X - 3.978$	*0.94*	<0.0001	$y= (1.287\times10^{-6})X^3 + (-0.0009377)X^2 + (0.4568)X + 4.811$	*0.99*	<0.0001
#203	$y= (0.3435)X - 3.927$	*0.94*	<0.0001	$y= (8.810\times10^{-7})X^3 + (-0.0007368)X^2 + (0.3824)X + 5.306$	*0.99*	<0.0001
#204	$y= (0.4501)X + 0.6974$	*0.91*	<0.0001	$y= (1.485\times10^{-6})X^3 + (-0.001311)X^2 + (0.5828)X + 11.30$	*0.99*	<0.0001

y= Resistance expressed in Newton; X= elongation expressed in percentage of initial.

Maximum elongation and resistance of all of the LET are described in **Figure 4A**. All tubes presented similar maximum distension except for tube LET#202 which had significantly smaller values than LET#200 and LET#201. There was an expected increase in maximum resistance from tubes LET#200 to LET#204. Maximal resistance was significantly different between LET#200 and LET#202 and between LET#200 and LET#204 ($p<0.001$ for both). Maximum values of resistance deemed safe of each tubing were 173±25N (LET#200), 280±23N (LET#201), 409±40N (LET#202), 395±37N (LET#203) and 537±13N (LET#204).

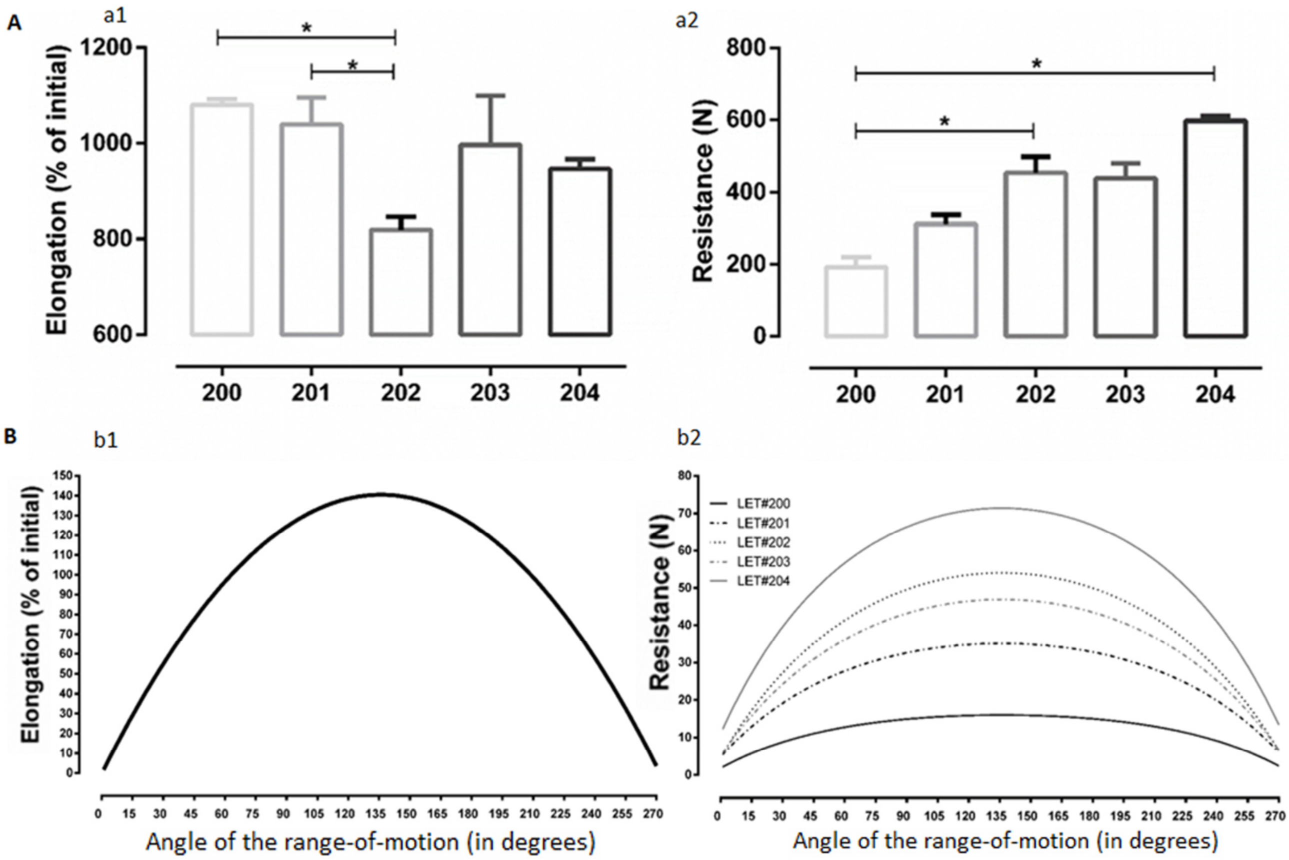

Figure 4. **A:** Maximum elongation and resistance of LET. a1) Maximum elongation expressed as a percentage of the initial length and; a2) Maximum resistance at the point of maximum elongation. B: Relation between elongation of tubes and the degrees of the range-of-motion; b1) plot describes changes in the elongation of the tubes as per the angle of the range-of-motion; b2) plot describes the resistance generated by each LET as per the angle of the range-of-motion. N= newton; #200 - #204= Lemgruber® Elastic tubing. *p<0,001.

2.3.2. Elongation according to ROM

The values of elongation according to ROM varied non-linearly. Assuming the length of the lever (i.e. the motion lever) and the tubing to be equal, the maximal elongation was obtained during 136 degrees of ROM with subsequent reduction of elongation despite increase in the ROM. Considering the anticipated non-linear behaviour of the slope, the polynomial non-linear regression model was used (r^2 = 0.99, p<0,0001) and the resulting reference equation for the calculation of elongation according to

ROM, of which “y” was the tubing elongation (in percent) and “x” was the ROM (in degrees) (Equation 4). **Figure 4B** depicts the slopes of elongation and the resistance created by each piece of tubing along the different degree points of the ROM.

Equation 4: $y = -0.4538 + (2.073)x + (-0.007623)x^2$

2.4. DISCUSSION

The present study has detailed the resistance values delivered by the Lemgruber® elastic tubing for elongations as large as 800% of initial length. Further, it created reference equations with nearly perfect precision to identify resistance according to elongation and identified maximal elongation considered safe for all the investigated tubing lengths. Last, it described the resistance of the tubing during movements in different degrees of ROM, so that the resistance of LET during any particular exercise could be predicted.

The mechanical analysis of LET confirmed a progressive increase in resistance during elongation. This is not particularly surprising and has been observed in other studies investigating different elastic materials[21,24]. The investigation of LET revealed an unexpected large array of resistance varying from 3±0.1N (10% of elongation in LET#200) up to 537±13N (880% of elongation in LET#204). This is of clinical relevance as therapists would require a large number of devices to deliver a similar resistance array using conventional resistance training such as dumbbells/barbells or multi-gym machines. Amongst the five investigated LET, LET#202 delivered the widest variation in resistance from 8.1±0.7N at 10% elongation to 405±38N at 785% elongation. Of note, LET #202 generated more resistance than #203. Although it seems intuitive that an increase in the size of the tubing should be followed with increased tubing resistance, the difference in the diameters of tubes explained the decay of the resistance. LET#202 have a larger internal diameter than #203 with similar external diameter (cfr. methods section). In practice, this meant that there was more elastic material being strained in #202 than in #203.

The investigation of elastic properties of elastic materials is not new. In fact, there have been studies with varied designs reporting similar behaviour of elastic materials as those observed in the present study[3,5,21,24,25]. Linearity of LET resistance was similar irrespective of diameter. There was a linear behaviour between 68% and 475% of elongation, which was in line with previous evidence investigating elastic material for muscle training[9]. It is important to state that the non-linear behaviour of the tubing outside the interval just described conferred the polynomial non-linear regression models nearly perfect predictive power (r^2=0.99) and better than linear models (r^2=088 – 0.94). Simoneau et al.[5] evaluated the resistance of tubes and elastic bands (i.e. yellow, green and black - The Hygenic Corporation). Values for 100% elongation of the three colors ranged from 14.4N (yellow) to 39.1N (black) in the elastic bands and 4.2N (yellow) to 34.2N (black) in the elastic tubes. In perspective, the LET used in the present study ranged from 13N (#200) to 58N (#204) for the same 100% elongation. Regarding the safety of tubes, LET could be safely elongated to a wider percentage(i.e. 800%) of initial length (compared to those recommended for Theraband® bands/tubes (i.e. not more than three times the initial length of the material)[21].

We observed a smaller elongation capacity of LET #202 compared to all other LETs. This was statistically smaller in comparison with #200 and #201. In practice, this does not seem to be specifically an issue as elongation values were as high as 8 times the initial length in LET#202. Further, this smaller elongation did not imply that less resistance was being generated as observed in figure 4A (a2). Lastly, in clinical practice, resistive dynamic exercises to upper and lower limbs are delivered within a pre-established ROM. In the present study, the elongation and their respective resistances for all of the five LET were thoroughly described. The information will help therapists deliver exercise with previous knowledge about the resistive load until a point considered unsafe. Importantly, the presented reference values were solely based on tubing without pre-elongation. This is not particularly an issue as resistance could be increased with additional parallel tubing or even using pre-elongation of tubing. When only tubes of the same diameter are available, the therapist could add pre-elongating tubes to increase resistance for a large array of exercises. In this specific case, we recommend using LET#200 as it delivered the widest variation in resistance and, therefore, could be seen as more versatile in such a scenario. For the convenience of the reader, the authors have provided an online supplement sheet with the calculation of estimated resistance of all tubing during eighteen different movements. The calculation provided account for differences between individual lever lengths (**online supplement 1**).

The results of the present study may affected by some potential limitations. The mechanical experimentation of the tubing was done using only pieces of the same length (50mm). A previous study, however, reported that different lengths deliver the same resistance when equal elongations (in percent) were compared [9]. The properties described in the present study were conducted under an ideal controlled situation. Real life situations will certainly have an impact on the durability of the LET and consequently, impact on the resistance available and the safety of the material. Although it is hard to estimate the durability of the LET, unpublished data from our research group has not demonstrated fragility of the material when used in a daily routine. Furthermore, safety is unlikely to be severely compromised, as LET were safely elongated to values as high as 800%, which are much larger than the ROM of common resistive dynamic exercises (Figure 4). In conclusion, Lemgruber elastic tubing (LET) progressively increased resistance with increased elongation. The large array of resistances delivered by LET associated with its safety and good reference values estimation, support its use in clinical practice.

Conflict of interest: The authors do not have any relation with the manufacturer of the LET, nor have received any funding or material for this specific investigation.

2.5. SUPPLEMENTARY DATA

Online supplement 1. Lemgruber® elastic tubing- Elongation by ROM. (Excel file).

Supplementary data associated with this article can be found, in the online version, at doi: 10.1016/j.bjpt.2018.07.001.

2.6. REFERENCES

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3. ARTICLE II

SYSTEMATIC REVIEW

de Lima FF et al

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Review

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Elastic Resistance Training Produces Benefits Similar to Conventional Resistance Training in People With Chronic Obstructive Pulmonary Disease: Systematic Review and Meta-Analysis

Fabiano F. de Lima, Vinicius Cavalheri, Bruna S.A. Silva, Isis Grigoletto, Juliana S. Uzeloto, Dionei Ramos, Carlos A. Camillo, Ercy M.C. Ramos

Elastic Resistance Training Produces Benefits Similar to Conventional Resistance Training in People with Chronic Obstructive Pulmonary Disease: Systematic Review and Meta-Analysis

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ABSTRACT

Objective: The purpose of this study was to investigate the effectiveness of elastic resistance training on improving muscle strength, functional exercise capacity, health-related quality of life (HRQoL), and dyspnea in people with stable chronic obstructive pulmonary disease (COPD). **Methods:** For this systematic review, PubMed, The Cochrane Library, Embase (OVID), PEDro, SciELO, and CINAHL were searched from inception to November 2019. Included studies were randomized clinical trials in which people with stable COPD were allocated to (1) an experimental group that received lower-limb resistance training, upper-limb resistance training, or both using elastic resistance; or (2) a control group that received no or sham resistance training or conventional resistance training using weight machines. Data extraction was performed by 3 review authors. The methodological quality of the studies was assessed using the PEDro scale. Eight studies on 332 participants were included. **Results:** Knee extensor strength was higher in the experimental group (standardized mean difference = 0.52, 95% CI = 0.09–0.95) compared with the non-exercise control group. Compared with the conventional exercise control, the experimental group presented similar effects for muscle strength, functional exercise capacity, HRQoL, and dyspnea (95% CI overlapped the line of no effect for all). **Conclusions:** Elastic resistance training improves muscle strength in people with COPD. The current review suggests elastic resistance as a potential alternative to conventional resistance training using weight machines, as they show similar effects on muscle strength, functional exercise capacity, HRQoL, and dyspnea. **Impact:** Due to its beneficial effects, including reduced risk of exacerbation-related hospitalizations, exercise training is viewed as the cornerstone of pulmonary rehabilitation in people with COPD. This study shows that elastic resistance training

can be an effective, portable, practical, and low-cost alternative to conventional weight resistance training.

Keyword: Chronic Obstructive Pulmonary Disease, Exercise, Rehabilitation, Muscle Strength

3.1. INTRODUCTION

The beneficial effects of exercise training in people with chronic obstructive pulmonary disease (COPD) are well established. It improves exercise capacity, health-related quality of life (HRQoL), muscle strength, and reduces the risk of hospitalizations due to an exacerbation of COPD[1-3]. Due to these beneficial effects, exercise training is seen as the cornerstone of pulmonary rehabilitation in this population[4,5].

Exercise training comprises structured sessions of aerobic training (such as ground-based or treadmill-walking and/or cycling) and resistance training for the muscle groups of the upper and lower limbs. Specifically, resistance training has been shown to elicit lower cardiopulmonary stress and fewer symptoms than aerobic training[6] in people with COPD, as well as to improve functional exercise capacity, dyspnea, muscle strength, and HRQoL in this population[7-13]. Of note, resistance training is commonly performed in pulmonary rehabilitation programs using weight machines and/or hand-held weights[14]. However, over the past decade studies have been conducted to investigate the effects of resistance training using elastic bands and/or tubing (i.e. elastic resistance training) in people with COPD[15-19], exploring whether these tools could be performed as an alternative to resistance training that uses weight machines[17-19].

Elastic resistance training stands out for its low cost[20], practicality and, mainly, for its portability, which allows people to perform resistance training in their home environment. Therefore, it has the potential to be used as an alternative type of resistance training in people with COPD, which could increase the access and tolerance to resistance training. That is, unlike free weights, elastic resistance does not rely on gravity to provide resistance, and allows people to perform exercises in the horizontal plane[21] (i.e. when lying or reclining). This can be considered an advantage in very functionally impaired people with COPD.

A key priority identified by the American Thoracic Society/European Respiratory Society Policy Statement on Pulmonary Rehabilitation was to increase the accessibility of pulmonary rehabilitation [22]. Although elastic resistance may be a very promising alternative to specifically increasing the accessibility to resistance training, a systematic review of the current evidence on the effectiveness of this intervention specifically in people with COPD has not been undertaken. Systematic reviews have been conducted to evaluate muscle strength in healthy elderly people and in different disease populations[23,24]. However, some of the limitations of these previous reviews (for clinicians working with people with COPD) were that: (i) only one or two studies in people with COPD were included; (ii) the reviews did not report on important variables for people with COPD (such as functional exercise capacity, HRQoL and dyspnea) and (iii) one of the reviews did not compare elastic resistance training to conventional resistance training[23]. Therefore, the aim of the current systematic review was two-fold: (i) to investigate the effectiveness of elastic resistance training on improving muscle strength, functional exercise capacity, HRQoL and dyspnea in people with stable COPD; and (ii) to compare the effects of elastic resistance training with those of conventional resistance training (using weight machines) on the same outcomes.

3.2. METHODS

This systematic review was registered on PROSPERO (CRD42018091731) and conducted in accordance with the PRISMA Statement for Reporting Systematic Reviews and Meta-Analyses[25]. We included randomized clinical trials in which people with stable COPD were allocated to an experimental group that received lower- and/or upper-limb resistance training via elastic resistance (i.e. elastic bands

[TheraBand] and/or elastic tubing) or to a control group that received either no/sham resistance training (non-exercise control) or conventional lower- and/or upper-limb resistance training using weight machines (conventional exercise control). Abstracts from conference presentations and study protocols were excluded. The outcomes included were muscle strength, functional exercise capacity, HRQoL and dyspnea.

3.2.1. Data Sources and Searches

Studies were identified from PubMed, The Cochrane Library, Embase (OVID), PEDro, SciELO and CINAHL in November 5, 2019. The following search strategy was used and adapted according to each database: (COPD OR Chronic Obstructive Pulmonary Disease) OR pulmonary disease, chronic obstructive) AND (Resistance training OR rehabilitation OR elastic resistance OR elastic band OR elasticized band OR elastic tub*) AND (randomised OR randomized).

3.2.2. Study selection

After removing duplicates, two independent authors reviewed the titles and abstracts of all studies identified through the database search. The decisions of the two review authors were recorded and any disagreement was resolved by further discussion. If no consensus was reached, a third review author resolved the disagreement. Subsequently, the same two review authors independently examined the full texts of studies to be included. No language restrictions were adopted.

3.2.3. Data Extraction and Quality Assessment

A standardized form was used to extract data. This was performed by three review authors who divided the task and checked each other's work. Any disagreement was resolved by a fourth review author. Data were extracted of baseline characteristics, key methodologic descriptors and details of interventions and outcomes. Where studies had outcome data collected in different time points, data collected immediately after completion of the intervention were included in the meta-analyses.

The included studies were assessed for their methodological quality using the 11-item PEDro scale[26]. The process was independently carried out by two authors and overseen by a third author. The first item (eligibility criteria) is not scored, which is why the score of the PEDro scale ranges between 0 and 10.

3.2.4. Data Synthesis and Analysis

The statistical analyses were performed using RevMan 5.3 (The Nordic Cochrane Centre, The Cochrane Collaboration) following the recommendation of the Cochrane Handbook[27]. A random-effect model was utilized to calculate summary estimates. If the studies were homogeneous, a fixed-effect model was used. The mean difference (MD) or standardized mean difference (SMD) with their 95% confidence intervals (CI) were used in the meta-analyses; MD for outcomes assessed using the same outcome measures and SMD for outcomes assessed using different outcome measures across the included studies.

Where means and standard deviation (SD) for differences in outcome measures collected at baseline and post-intervention were not available, post-intervention data were used in the meta-analysis for studies in which no significant differences between the control group and experimental group were reported at baseline. For those studies that reported median and interquartile range, mean and SD were calculated[28].

Analyses were conducted to compare: (i) experimental group (i.e. elastic resistance) *versus* non-exercise control; and (ii) experimental group (i.e. elastic resistance) *versus* conventional exercise control (i.e. conventional resistance training using weight machines).

The heterogeneity across the included studies were assessed using I^2 statistic and considered substantial if $I^2 \geq 50\%$[27]. In the case of substantial heterogeneity, sensitivity analysis was undertaken, where possible, to investigate the potential causes[29]. For studies that included more than one experimental group that exercised with elastic resistance (e.g. one group that used elastic bands and one group that used elastic tubing), the results were not combined. Data from the group with the larger sample were used.

As suggested in the Cochrane Handbook[27], in meta-analyses that reported results as SMD, studies that reported post-intervention values and those that reported mean changes were placed in separate subgroups.The Grading of Recommendations Assessment, Development and Evaluation (GRADE)[30] recommendations was used to assess the certainty of evidence pertaining to each outcome.

3.3. RESULTS

The database search was conducted on November 5th 2019. The flow diagram is presented in Figure 1. A total of 5,434 records were identified and, after removing the duplicates, 3,738 records were screened by title and abstract. Full text articles assessed for eligibility totaled 432, and eight studies (in 332 people with COPD) met the eligibility criteria and were included in the review[15-19,31-33].

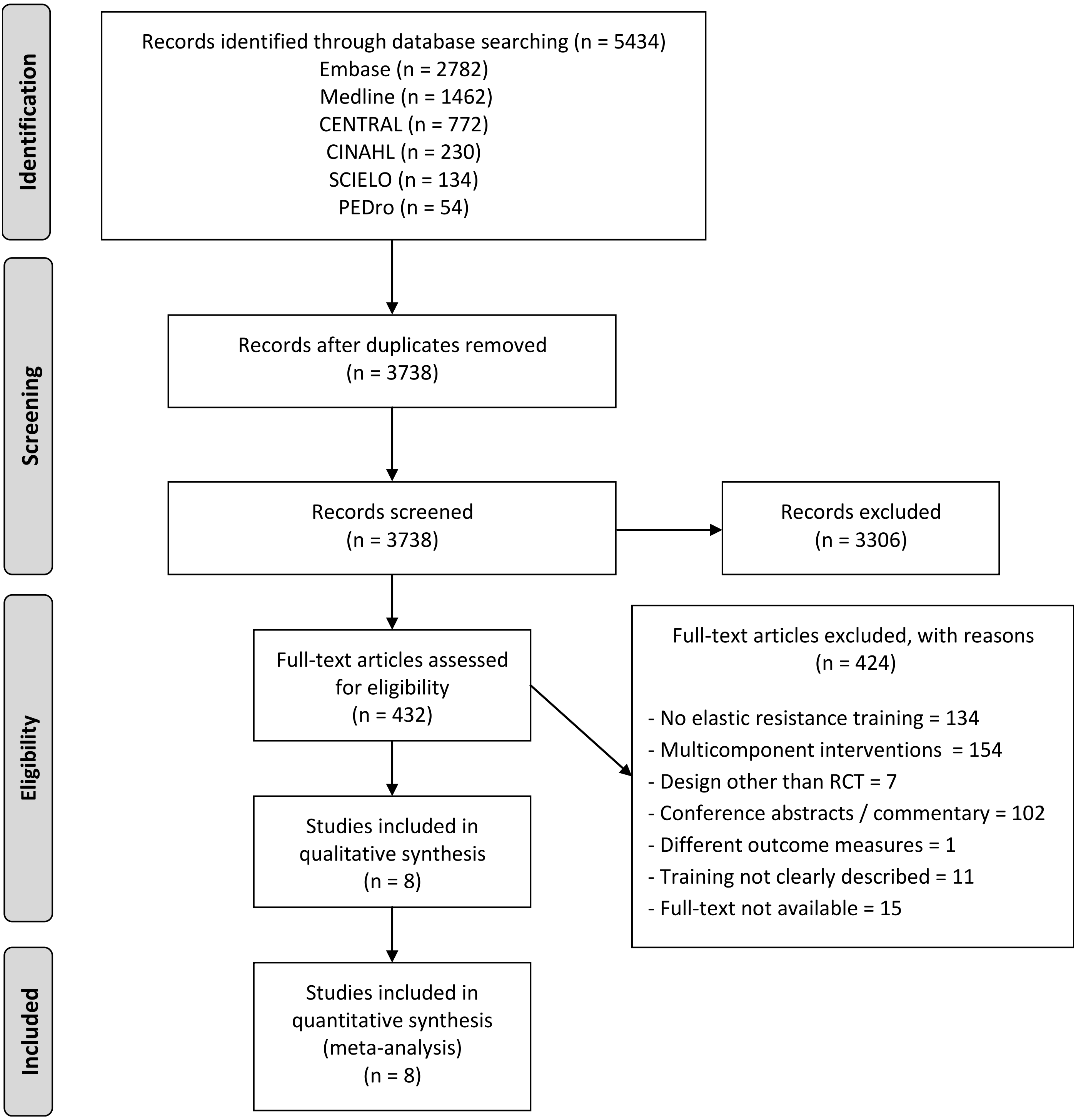

Figure 1: PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flow diagram.

Characteristics of the included studies and specific characteristics of the resistance training protocols are presented in Table 1. The sample size of the included studies ranged between 28 and 55 participants, with the mean age of the participants ranging between 62 and 69 years. The studies were based in Australia[16], Brazil[17-19,32,33], China[31] and Sweden[15]. Three studies[15,16,31] compared elastic resistance training to a non-exercise control (educational orientation[15,31] and any intervention)[16], whereas five studies[17-19,32,33] compared elastic resistance training to conventional resistance training using weight machines. Only one study did not include muscle strength as an outcome measure[32]. The frequency of exercise training programs was three times per week in all studies and the duration ranged between eight and 12 weeks. The exercise prescription varied from 2 to 7 sets. The studies included used Lemgruber elastic tubes[34] or /and TheraBand[35] for elastic resistance training. One study reported that training was performed with elastic resistance bands (no further information provided)[16].

Table 1. Characteristics of included studies.

Author	Participants	Experimental and control groups	Elastic training protocol (duration, frequency, sets, repetitions and progression)	Number and types of exercises	Elastic resistance used	Prescription of the initial elastic resistance load	Analysis type (n) and Attrition	Outcome Measures
Chen et al. (2018)[31]	n=55 Age (yr): EG: 69 (8) CG: 64 (11) Gender: EG: 22 (M)/3 (F) CG: 15 (M)/7 (F)	EG: n=29 Resistance training with elastic tools CG: n=26 No exercise intervention (one individual session of health education)	Duration and frequency 12 weeks, three times/week Sets and repetition: 8 to 12 repetitions (the patients should offer their best effort during training (20–30 min) Progression: No information on progression	6 sets of exercises: Straight-leg lifting exercises, prone hip extension exercises, thigh abduction exercises, posterior muscle group exercises, anterior muscle group exercises and standing calf raise	Elastic bands (TheraBand)	No information	Per protocol (EG: 25; CG: 22) Attrition EG: 4/29 (14%) CG: 4/26 (15%)	Muscle strength (Biomechanical Test and Training Systems) Functional exercise capacity (6MWT)
Nyberg et al. (2015)[15]	n=44 Age (yr): EG: 69 (5) CG: 68 (6) Gender: EG: 12 (M)/10 (F) CG: 11 (M)/11 (F)	EG: n=22 Supervised group-based progressive elastic resistance training CG: n=22 No exercise intervention (four sessions of face-to-face health education)	Duration and frequency 8 weeks, three times/week Sets and repetitions: 2x25 repetition maximum in each exercise Progression: was increased using Borg scale: if patient rates on Borg scale <4 and performs ≥20 repetitions on the training in at least three of six elastic band exercises in two out of three following sessions, it resulted in an increase of the resistance by increasing the tension of the elastic band (changing the color of the elastic band for a higher tension)	8 exercises: Heel-raise, step-up, latissimus row, chest press, leg extension, straight arm shoulder flex, leg curl and elbow flexion	Elastic bands (TheraBand)	RM test Performed using initial test 25 repetition maximum load	ITT analysis (EG: 22, CG: 22) Attrition EG: 2/22 (9%) CG: 2/22 (9%)	Muscle strength (Interchangeable stationary dynamometry) Functional exercise capacity (6MWT)

O'Shea et al. (2007)[16]	n=54 Age (yr): EG: 67 (7) CG: 68 (10) Gender: 22 (M)/35 (F)	EG: n=27 Progressive elastic resistance training CG: n=27 No exercise intervention	Duration and frequency 12 weeks, three times/week Sets and repetitions: 3x8-12 repetition maximum in each exercise Progression: was increased if patient could perform 3x12 repetition maximum with correct technique through the full range of movement was increased (changing the color of the elastic band for a higher tension)	6 exercises: Hip abduction in standing, simulated lifting, sit-to-stand, seated row, lunges and chest press	Elasticised resistance bands	Performed using a blue elastic band with 25%-250% elongation (all the exercises start or stop positions were within this interval)	<u>ITT analysis</u> (EG: 27, CG: 27) <u>Attrition</u> EG: 7/27 (26%) CG: 3/27 (11%)	Muscle strength (hand-held dynamometry) Functional exercise capacity (6MWT)
Ramos et al. (2014)[17]	n=45 Age (yr): EG: 67 [60–69] CG: 66 [61–68] Gender: EG: 11 (M)/6 (F) CG: 13 (M)/4 (F)	EG: n=22 Progressive elastic resistance training CG: n=23 Progressive resistance training using weight machines	Duration and frequency 8 weeks, three times/week Set and repetitions: 2 to 7 sets of the number of repetitions achieved during 20 seconds of the fatigue resistance test. Progression: was increased by adding a set every two sessions	5 exercises: Knee extension, knee flexion, shoulder abduction, shoulder flexion and elbow flexion	Elastic tubing (Lemgruber)	Fatigue Resistance test Performed to provoke task failure owing to fatigue (40–60 seconds) after the beginning of movement (full range of motion for the maximum number of repetitions and at maximum speed while free from signs or symptoms) The test was interrupted in the case of fatigue, significant reduction in the range of motion and speed, or muscle compensation	<u>Per-protocol analysis</u> (EG: 17, CG: 17) <u>Attrition</u> EG: 5/22 (23%) CG: 6/23 (26%)	Muscle strength (digital dynamometry) Functional exercise capacity (6MWT) HRQoL (CRDQ) Dyspnea (CRDQ)

Silva et al. (2016)[18]	n=28 Age (yr): EG: 62 (10) CG: 68 (7) No information on gender	EG: n=14 Supervised group-based progressive elastic resistance training CG: n=14 Supervised group-based progressive resistance training performed with weight machines	Duration and frequency 12 weeks, three times/week Set and repetitions: 2x15 to 4x6 maximum repetitions Progression: was increased adding tubes in parallel in fixed-hooks' chair	5 exercises: Knee flexors and extensors, shoulder flexors and abductors and elbow flexors	Elastic tubing (Lemgruber)	RM test Performed using initial test 15 RM Performed using a tube reference whose load only enabled performance of 15 RM (up to two additional RM were accepted)	<u>Per-protocol analysis</u> (EG: 9, CG:10) <u>Attrition</u> EG: 5/14 (36%) CG: 4/14 (29%)	Muscle strength (digital dynamometry) HRQoL (CRDQ) Dyspnea (CRDQ)
Silva et al. (2018a)*[32]	n=30 Age (yr): EG: 66 (2†) CG: 66 (3†) No information on gender	EG: n=14 Supervised group-based progressive elastic resistance training CG: n=16 Supervised group-based progressive resistance training performed with weight machines	Duration and frequency 12 weeks, three times/week Sets and repetitions: 2x15 to 3x15 repetition maximum Progression: was increased adding tubes in parallel in fixed-hooks' chair	5 exercises: Shoulder flexion, elbow flexion, shoulder abduction, knee extension and knee flexion	Elastic bands (TheraBand)	Performed using a tube reference whose load were enable the maximum number of repetitions determined for each training week Sufficient to promote only the established adaptations for each training week	<u>ITT analysis</u> (EG: 14, CG: 16) <u>Attrition</u> EG: 2/14 (14%) CG: 6/16 (38%)	Functional exercise capacity (6MWT)
Silva et al. (2018b)[19]	n=48 Age (yr): EG: 69 (8) CG: 64 (11) No information on	EG: n=32 Progressive elastic resistance training CG: n=16	Duration and frequency 12 weeks, three times/week Sets and repetitions: 2x15 to 3x15 repetition maximum Progression: was increased	5 exercises: Shoulder flexion, elbow flexion, shoulder abduction, knee extension and	Elastic bands (TheraBand) Elastic tubing (Lemgruber)	Performed using a tube reference or Elastic band whose load were enable the maximum number of repetitions determined for each training week During the first 2 weeks	<u>Per Protocol</u> <u>analysis</u> (EG: 24 CG: 11) <u>Attrition</u> EG: 8/32 (25%)	Muscle strength (digital dynamometry)

	gender	Progressive resistance training using weight machines	adding tubes in parallel in fixed-hooks' chair	knee flexion		of training, the patient's imposed load was enough to complete two sets of 15 repetitions.	CG: 5/16 (31%)	
Silva et al. (2019)[33]	n=28 Age (yr): EG: 63 (9) CG: 65 (8) Gender: EG: 9 (M)/5(F) CG: 10 (M)/4(F)	EG: n=14 Resistance training with the elastic tubing group CG: n=14 Resistance training with the weight-machine training group	Duration and frequency 12 weeks, three times/week Set and repetitions: 2x15 to 3x15 repetition maximum Progression: was increased adding tubes in parallel in fixed-hooks' chair	5 exercises: Shoulder flexion, elbow flexion, shoulder abduction, knee extension and knee flexion	Elastic tubing (Lemgruber)	RM test Performed using initial test 15 RM Performed using a tube reference whose load only enabled performance of 15 RM (up to two additional RM were accepted)	Per Protocol analysis (EG: 9 CG: 10) Attrition: EG: 5/14 (36%) CG:4/14 (29%)	Functional exercise capacity (6MWT)

Abbreviations: 6MWT: six-minute walk test; CG: control group; COPD: chronic obstructive pulmonary disease; CRDQ: Chronic Respiratory Disease Questionnaire; EG: experimental group; F: female; HRQoL: health-related quality of life; IQR: interquartile range; ITT: intention-to-treat; M: male; MRC: Medical Research Council Scale; RM: repetition maximum; SD: standard deviation; SF-36: Medical Outcomes Study short-form 36.Data are presented as mean (standard deviation) or median [interquartile range] unless otherwise stated. *: data provided by authors; †: standard error.

The PEDro score of the included studies ranged between 3 and 8 (Table 2) and the mean (SD) score was 5.3 (1.6). This moderate methodological quality was mainly due to lack of blinding of participants and therapists across all included studies as well as lack of blinding of outcome assessors, adequate follow-up and intention-to-treat analysis in 5 studies.

Table 2. Quality assessment of randomized clinical trials - PEDro Scale.

Authors	Eligibility criteria *	Random allocation	Concealed allocation	Baseline comparability	Blind participants	Blind therapists	Blind assessors	Adequate follow-up	Intention-to-treat analysis	Between-group comparisons	Point estimates and variability	TOTAL
Chen et al. (2018)[31]	Yes	Yes	No	Yes	No	No	No	Yes	No	Yes	Yes	5
Nyberg et al. (2015)[15]	No	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes	8
O'Shea et al. (2007) [16]	Yes	Yes	Yes	Yes	No	No	Yes	No	Yes	Yes	Yes	7
Ramos et al. (2014)[17]	No	Yes	Yes	Yes	No	No	No	No	No	Yes	Yes	5
Silva et al. (2016)[18]	Yes	Yes	No	Yes	No	No	No	No	No	Yes	Yes	4
Silva et al. (2018a) [32]	No	Yes	No	No	No	No	No	No	No	Yes	Yes	3
Silva et al. (2018b)[19]	Yes	Yes	Yes	Yes	No	No	No	No	No	Yes	Yes	5
Silva et al. (2019)[33]	Yes	Yes	Yes	Yes	No	No	No	No	No	Yes	Yes	5

* This item does not contribute to the total PEDro score.

3.3.1. Muscle strength

The three studies (on 145 participants) that compared elastic resistance training to a non-exercise control[15,16,31] reported data on knee extensors strength. On completion of the intervention period, knee extensors strength was higher in the experimental group compared to the non-exercise control group (SMD 0.52; 95% CI 0.09 to 0.95, I^2=40%; low certainty) (Figure 2a and Supplementary material 1). Two studies [15,16] (on 98 participants) that compared elastic resistance training to a non-exercise control reported data on shoulder flexors strength. On completion of the intervention period, there was an uncertain effect on shoulder flexors strength (SMD 0.35, 95% CI -0.05 to 0.75, I^2=0%; low certainty) (Figure 2b and Supplementary material 1).

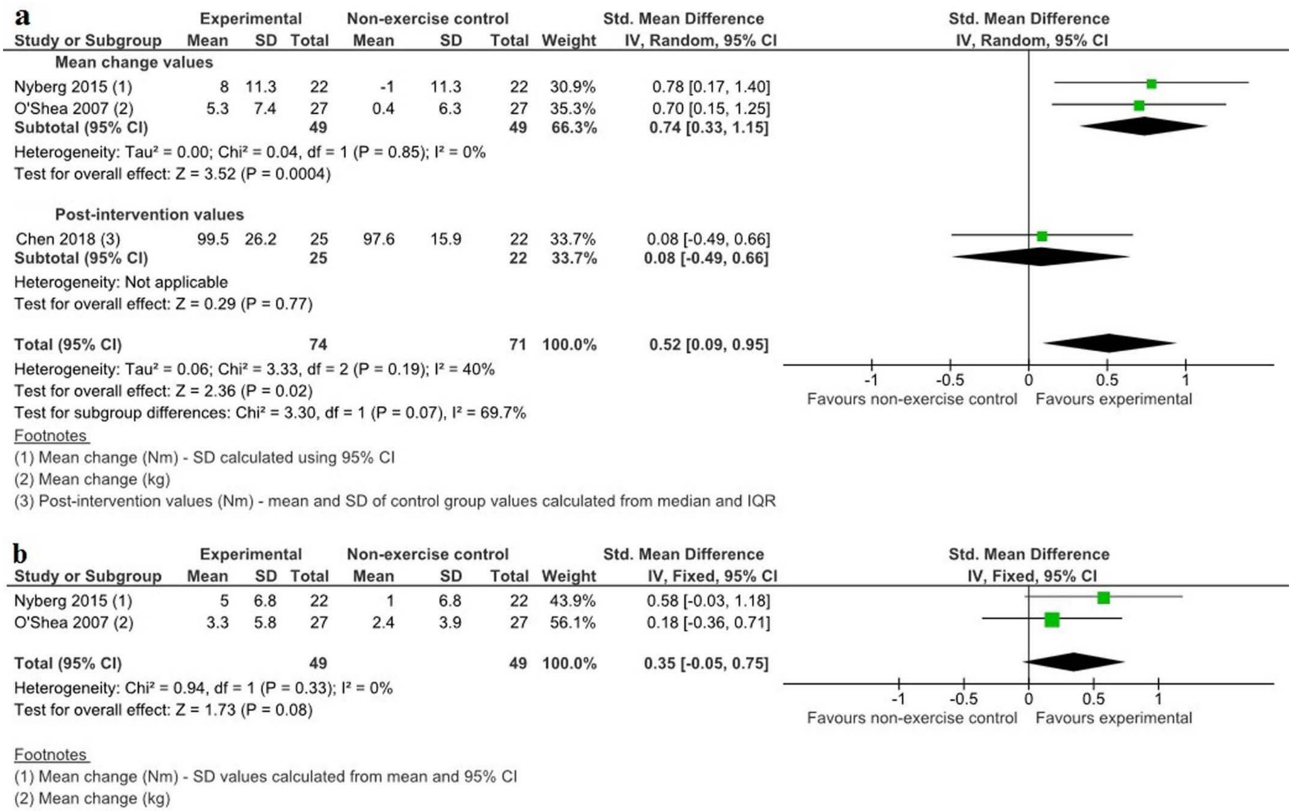

Figure 2: Forest plot of muscle strength comparison between the experimental group (elastic resistance) *versus* non-exercise control; a: knee extensors; b: shoulder flexors.

Three studies[17-19] (on 88 participants) that compared elastic resistance training to conventional resistance training using weight machines reported data on knee extensors strength; two studies[17,18] (on 53 participants) reported data on shoulder flexors strength and 3[17-19] (on 88 participants) reported data on elbow flexors strength. On completion of the intervention period, similar knee extensors strength (SMD = −0.14, 95% CI = −0.58 to 0.29, I^2 = 0%; low certainty) (Figure 3a and Supplementary material 1)[17-19], shoulder flexors strength (MD = 4.02 N, 95% CI = −7.81 to 15.84 N, I^2 = 42%; very low certainty) (Figure 3b and Supplementary material 1)[17,18], and elbow flexors strength (SMD = 0.07, 95% CI = −0.36 to 0.50, I^2 = 0%; moderate certainty) (Figure 3c and Supplementary material 1)[17-19] was demonstrated between the two groups. Muscle strength data from one[33] of the studies had already been reported[18], so did not enter the muscle strength meta-analysis.

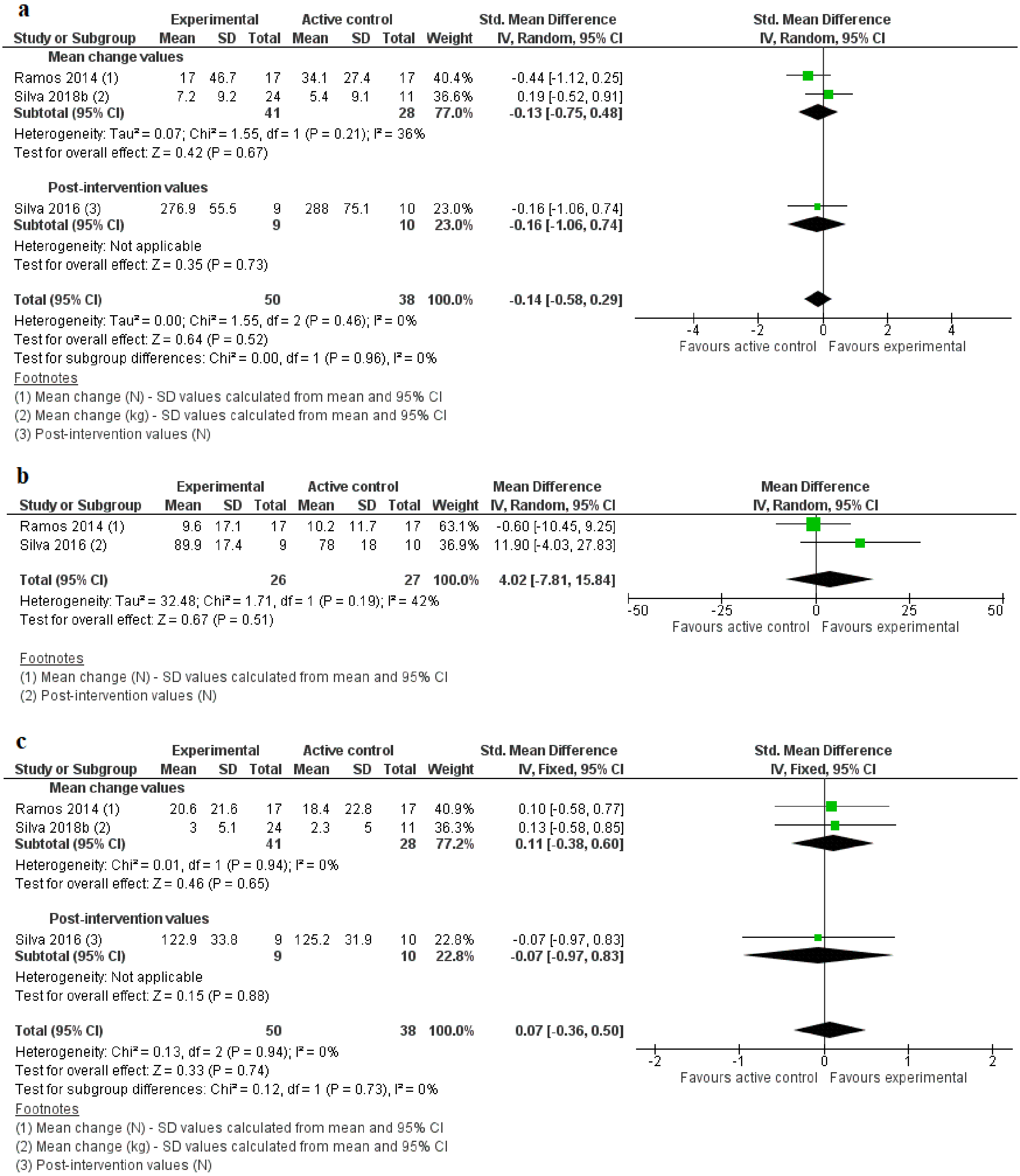

Figure 3: Forest plot of muscle strength comparison between the experimental group (elastic resistance) *versus* conventional exercise control group; a: knee extensors; b: shoulder flexors; c: elbow flexors.

3.3.2. Functional exercise capacity

Three studies[15,16,31] (on 145 participants) that compared elastic resistance training to non-exercise control reported data on functional exercise capacity as measured via the six-minute walk test (6MWT). On completion of the intervention period, there was an uncertain effect on functional exercise capacity (MD 17.24, 95% CI -6.33 to 40.58, I^2=57%; very low certainty) (Figure 4a and Supplementary material 1)[15,16,31].

Three studies[17,32,33] (on 83 participants) that compared elastic resistance training to conventional resistance training using weight machines reported data on functional exercise capacityas measured via the 6MWT. On completion of the intervention period, similar effect on functional exercise capacity (MD 10.94, 95% CI -8.65 to 30.53, I^2=0%; low certainty) was demonstrated between the two groups (Figure 4b and Supplementary material 1).

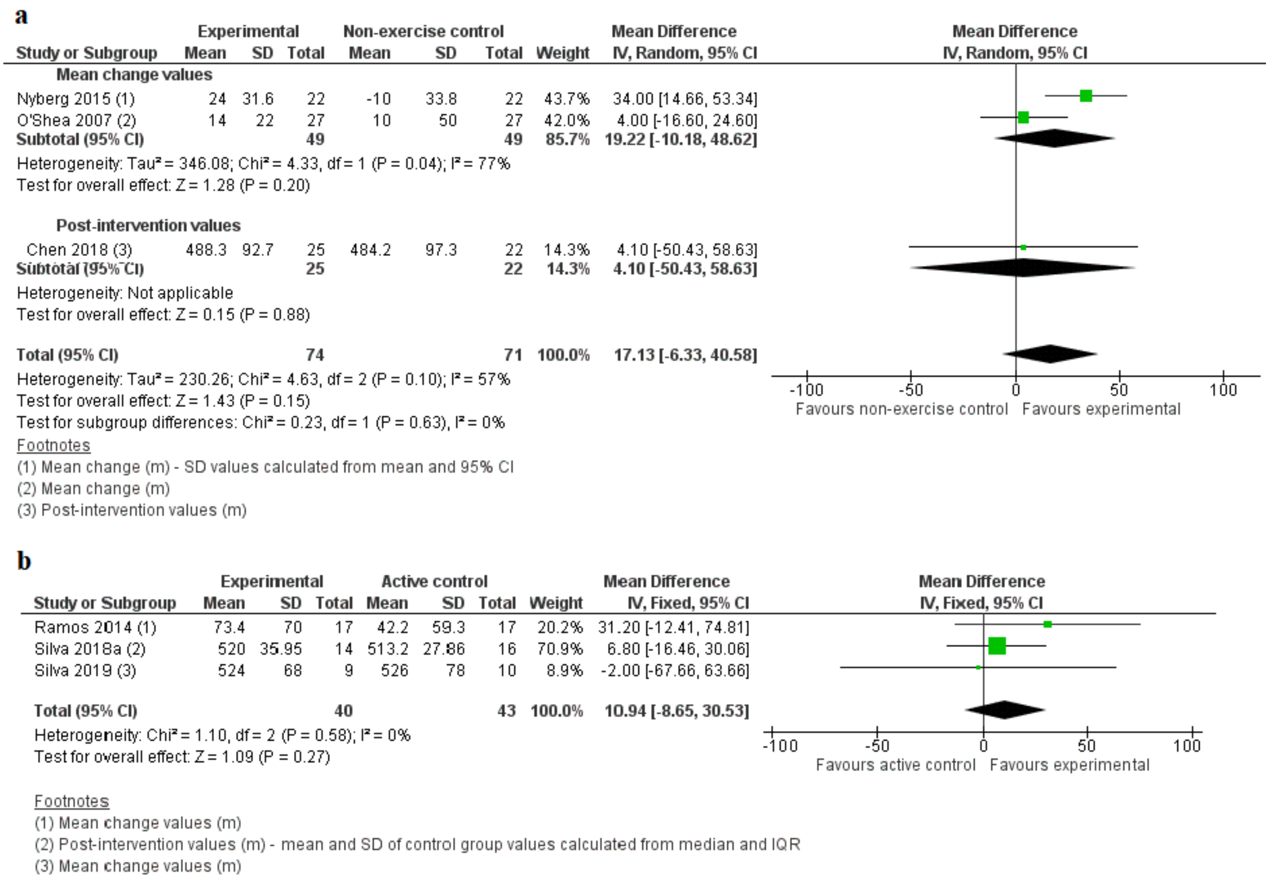

Figure 4: Forest plot of functional exercise capacity comparison; a: experimental (elastic resistance) *versus* non-exercise control; b: experimental (elastic resistance) versus conventional exercise control group.

3.3.3. HRQoL and dyspnea

The studies that compared elastic resistance training to non-exercise control did not report sufficient data on HRQoL or dyspnea and, therefore, meta-analysis was not conducted. However, two studies[17,18] (on 53 participants) that compared elastic resistance training to conventional resistance training using weight machines reported data on HRQoL (Chronic Respiratory Disease Questionnaire (CRDQ) and dyspnea. Of note, dyspnea was assessed by the dyspnea domain of the CRDQ. On completion of the intervention period, similar effect in all HRQoL domains was demonstrated between the two groups (Supplementary material 1 and 2a to 2d): fatigue: MD = –0.14, 95% CI = –1.24 to 0.97, I^2= 53%; very low certainty; (b) emotional function: MD = 0.15, 95% CI = –0.53 to 0.83, I^2= 13%; very low certainty;

(c) mastery: MD = –0.35, 95% CI = –1.08 to 0.38, I^2= 0%; very low certainty; and (d) dyspnea: MD = –0.27, 95% CI = –0.95 to 0.27, I^2= 0%; moderate certainty.

3.4. DISCUSSION

This systematic review suggested that elastic resistance training potentially improves muscle strength in people with COPD. When compared to conventional resistance training using weight machines, elastic resistance training has similar effect on muscle strength, functional exercise capacity, HRQoL and dyspnea. The results should be interpreted with caution as the certainty of the evidence ranged between very low and moderate using the GRADE.

People with COPD commonly present muscle dysfunction[36], which can contribute to impairments in physical activity level, exercise capacity, HRQoL and premature mortality[36]. Conventional resistance training using weight machines and/or hand-held weights is well established in this population, with current guidelines suggesting that it should be performed two to three days a week [5]. The optimal prescription of resistance training in this population is not yet determined, mainly due to the wide variation on the type of exercises prescribed as well as on their intensity, number of sets and number of repetitions. The findings of this review adds to the existing literature on resistance training by suggesting that, compared to a non-exercise control group, people with COPD who exercised using elastic bands and/or tubing improve muscle strength. This finding demonstrates that this type of resistance training prescription can also be considered in this population.

Although conventional resistance training is known to improve muscle strength, the effects of conventional lower limb resistance training on exercise capacity is less consistent. It seems that training load may play a partial role on the capacity of increased lower limb muscle strength to translate into increased exercise capacity. That is, previous studies that used training load ≥ 80% of one repetition maximum have demonstrated improvements in exercise capacity[11,12,37]. Resistance training programs that used more modest loads have been shown ineffective at improving exercise capacity[16]. The uncertain effect of elastic resistance training on functional exercise capacity demonstrated in this review may be due to modest loads used to prescribe resistance training in the included studies. Of note, in one of the studies included in this review[15], participants performed a low-load, but high-repetition, elastic resistance training. The study demonstrated that specific resistance training program to improve in functional exercise capacity. This finding can be explained by the endurance nature (i.e. low-load and high-repetition) of the elastic training program prescribed in that specific study.

In fact, resistance training is recommended and commonly performed in clinical practice and in pulmonary rehabilitation programs using weight machines and/or hand-held weights[14]. This review demonstrated that, in addition to improving muscle strength in people with COPD, when compared to conventional resistance training using weight machines, elastic resistance training had similar effect on muscle strength, functional exercise capacity, HRQoL and dyspnea. Therefore, the results of this systematic review provide evidence for a potential alternative way of delivering resistance exercise training (as part of pulmonary rehabilitation) to this population.

Despite the compelling evidence for the benefits of conventional center-based exercise training in people with COPD, exercise training is delivered to fewer than 10% of those would benefit[38]. Access is particularly challenging in rural settings, where COPD is often prevalent and programs may not be available. However, uptake and completion are also poor in metropolitan areas[39]. Up to 50% of those who are referred to pulmonary rehabilitation will never attend and of those who present at least once, up to a third will not complete the program[39]. Frequent travel to a center-based program, in the setting of distressing dyspnea and mobility limitation, is regularly reported as a barrier to attendance[39]. Elastic resistance training is simple, easy to administer, has low cost, and is practical and portable, allowing people with COPD to perform the training in small spaces, including their home environment. It can be easily administered in rural and remote areas where lack of funds limits the amount of exercise equipment available and for those who have difficulties to commute to rehabilitation centers[17,40,41]. Furthermore, unlike weights, elastic resistance does not depend on the action of gravity to provide resistance[21], which can be an alternative for patients with major functional impairments due to the possibility of performing resistance exercise training in a horizontal position (i.e. when lying or reclining).

Although we have run a comprehensive search across several databases, the findings of the current systematic review should be interpreted with caution due to the limited number of studies included in the meta-analyses and the small sample size across the studies. Additionally, the methodological quality of the included studies was moderate. Besides the high risk of performance bias (i.e. bias due to lack of blinding of subjects and therapists) which is common in studies of exercise training, the majority of included studies did not blind the assessor (i.e. high risk of detection bias), reported substantial loss to follow-up (i.e. high risk of attrition bias), and did not perform intention-to-treat analysis.

In summary, the current systematic review and meta-analyses suggest that elastic resistance training is an effective intervention to improve muscle strength in people with COPD. Further, compared to resistance training using weight machines, elastic resistance training demonstrated similar effects on muscle strength, functional exercise capacity, HRQoL and dyspnea. Our findings suggest elastic resistance as a potential alternative to conventional resistance training using weight machines in people with COPD.

ACKNOWLEDGMENTS

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Conflict of Interest: none declared.

3.5. REFERENCES

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3.6. SUPPLEMENTARY MATERIALS

Supplementary material 1. Grading of recommendations Assessment, Development and Evaluation Summary of Findings.

Experimental group versus no-exercise control										
	Certainty Assessment							No. of Participants		Certainty
	No. of Studies	Study Design	Risk of Bias	Inconsistency	Indirectess	Imprecision	Other Considerations	Experimental group	No-exercise control	
Peripheral muscle force (knee extension)	3	RCT	Serious[a,b]	Not serious	Not serious	Serious[c]	None	74	71	⊕⊕OO Low
Peripheral muscle force (shoulder flexion)	2	RCT	Not serious	Not serious	Not serious	Very serious[c,d]	None	49	49	⊕⊕OO Low
Functional exercise capacity	3	RCT	Serious[a,b]	Serious[e]	Not serious	Very serious[c,d]	None	74	71	⊕OOO Very low

Experimental group versus conventional resistance training										
	Certainty Assessment							No. of Participants		Certainty
	No. of Studies	Study Design	Risk of Bias	Inconsistency	Indirectess	Imprecision	Other Considerations	Experimental group	Conventional resistance training	
Peripheral muscle force (knee extension)	3	RCT	Serious[a,b]	Not serious	Not serious	Serious[d]	None	50	38	⊕⊕OO Low
Peripheral muscle force (shoulder flexion)	2	RCT	Serious[a,b]	Serious[e]	Not serious	Serious[d]	None	26	27	⊕OOO Very low
Peripheral muscle force (elbow flexion)	3	RCT	Serious[a,b]	Not serious	Not serious	Not serious	None	50	38	⊕⊕⊕O Moderate

Functional exercise capacity	3	RCT	Very serious[a,b,f]	Not serious	Not serious	Not serious	None	40	43	⊕⊕◯◯ Low
Health-related quality of life (fatigue)	2	RCT	Very serious[a,b]	Very serious[e]	Not serious	Serious[d]	None	26	27	⊕◯◯◯ Very low
Health-related quality of life (emotional functional)	2	RCT	Very serious[a,b]	Serious[e]	Not serious	Not serious	None	26	27	⊕◯◯◯ Very low
Health-related quality of life (mastery)	2	RCT	Very serious[a,b]	Very serious[e]	Not serious	Serious[d]	None	26	27	⊕◯◯◯ Very low
Health-related quality of life (dyspnea)	2	RCT	Serious[a,b]	Not serious	Not serious	Not serious	None	26	27	⊕⊕⊕◯ Moderate

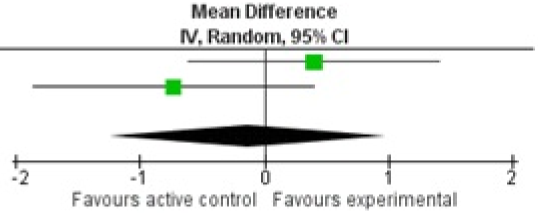
a: Some lack of blinding of outcome assessor. b: Some lack of allocation concealment. c: Small sample size across the studies. d: Large varibility (95% confidence interval) around the central tendency. e: Substantial heterogeneity (I^2> 50%). f: Some high risk of attrition bias.

Supplementary material 2: Forest plot of HRQoL comparison: experimental (elastic resistance) *versus* conventional exercise control group; a: Fatigue; b: Emotional function; c: Mastery; d: Dyspnea.

a

Study or Subgroup	Experimental Mean	Experimental SD	Experimental Total	Active control Mean	Active control SD	Active control Total	Weight	Mean Difference IV, Random, 95% CI
Ramos 2014 (1)	0.7	1.6	17	0.3	1.4	17	52.7%	0.40 [-0.61, 1.41]
Silva 2016 (2)	4.17	1.45	9	4.9	1	10	47.3%	-0.73 [-1.86, 0.40]
Total (95% CI)			**26**			**27**	**100.0%**	**-0.14 [-1.24, 0.97]**

Heterogeneity: Tau² = 0.34; Chi² = 2.13, df = 1 (P = 0.14); I² = 53%
Test for overall effect: Z = 0.24 (P = 0.81)

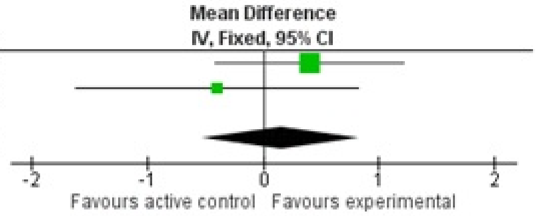


Footnotes
(1) Mean change - CRDQ - SD values calculated from mean and 95% CI
(2) Post-intervention values - CRDQ

b

Study or Subgroup	Experimental Mean	Experimental SD	Experimental Total	Active control Mean	Active control SD	Active control Total	Weight	Mean Difference IV, Fixed, 95% CI
Ramos 2014 (1)	0.8	1.4	17	0.4	1	17	68.9%	0.40 [-0.42, 1.22]
Silva 2016 (2)	5.1	1.7	9	5.5	0.8	10	31.1%	-0.40 [-1.62, 0.82]
Total (95% CI)			**26**			**27**	**100.0%**	**0.15 [-0.53, 0.83]**

Heterogeneity: Chi² = 1.14, df = 1 (P = 0.28); I² = 13%
Test for overall effect: Z = 0.44 (P = 0.66)

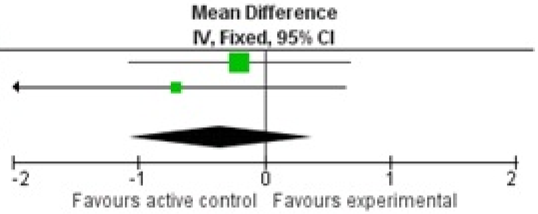


Footnotes
(1) Mean change - CRDQ - SD values calculated from mean and 95% CI
(2) Post-intervention values - CRDQ

c

Study or Subgroup	Experimental Mean	Experimental SD	Experimental Total	Active control Mean	Active control SD	Active control Total	Weight	Mean Difference IV, Fixed, 95% CI
Ramos 2014 (1)	0.5	1.4	17	0.7	1.2	17	69.9%	-0.20 [-1.08, 0.68]
Silva 2016 (2)	5.3	1.9	9	6	0.8	10	30.1%	-0.70 [-2.04, 0.64]
Total (95% CI)			**26**			**27**	**100.0%**	**-0.35 [-1.08, 0.38]**

Heterogeneity: Chi² = 0.38, df = 1 (P = 0.54); I² = 0%
Test for overall effect: Z = 0.94 (P = 0.35)

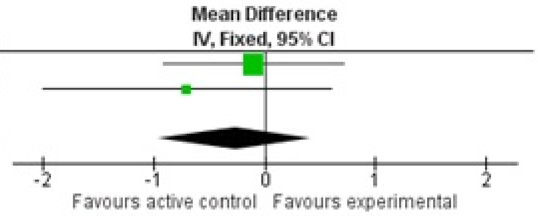


Footnotes
(1) Mean change - CRDQ - SD values calculated from mean and 95% CI
(2) Post-intervention values - CRDQ

d

Study or Subgroup	Experimental Mean	Experimental SD	Experimental Total	Active control Mean	Active control SD	Active control Total	Weight	Mean Difference IV, Fixed, 95% CI
Ramos 2014 (1)	0.9	1.2	17	1	1.2	17	72.3%	-0.10 [-0.91, 0.71]
Silva 2016 (2)	4	1.4	9	4.7	1.5	10	27.7%	-0.70 [-2.00, 0.60]
Total (95% CI)			**26**			**27**	**100.0%**	**-0.27 [-0.95, 0.42]**

Heterogeneity: Chi² = 0.59, df = 1 (P = 0.44); I² = 0%
Test for overall effect: Z = 0.76 (P = 0.45)



Footnotes
(1) Mean change - CRDQ - SD values calculated from mean and 95% CI
(2) Post-intervention values - CRDQ

4. ARTICLE III

STUDY PROTOCOL

de Lima FF et AL

Published in the journal: ***Trials*** (Impact Factor: 1.8)

Trials

STUDY PROTOCOL Open Access

Effects of combining functional exercises with exercise training on daily physical activities and functionality in patients with COPD: a protocol for a randomized clinical trial

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Effects of Combining Functional Exercises with Exercise Training On Daily Physical Activities and Functionality in Patients with COPD: A Protocol for a Randomized Clinical Trial

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ABSTRACT

Introduction: Functional training has been shown to be a viable alternative for elderly and patients with chronic obstructive pulmonary disease (COPD). However, whether or not the combination of this type of training with aerobic and resistance training, commonly performed in pulmonary rehabilitation (PR) programs induces more pronounced effects on daily physical activities and functionality remains unclear. The aims of the study will be to evaluate the short term and sustained effects of the combination of a functional circuit program with a training program consisting of aerobic and resistance exercise. **Methods**: In this randomized controlled trial, patients with COPD will be randomized (1:1:1) to an eight-week training program to follow one of the three a priori defined groups: I) resistance and aerobic and functional exercises or; II) a conventional program including only resistance and aerobic exercises or; III) a usual care program. Patients will be evaluated before and upon completion of eight weeks of training regarding physical activity in daily life (PADL) using an activity monitor (accelerometer), activities of daily living (London Chest Activity of Daily Living), functional exercise capacity (six-minute walk test), and muscle strength (dynamometry). Additionally, the sustained effects of the interventions will be evaluated 22 weeks after commencing the study. **Discussion:** The inclusion of a protocol of functional physical training in the training conventionally performed by patients with COPD as an alternative to increase PADL and functionality may provide subsidies for the treatment of these patients, representing an advance and impacting on the physical training of patients with COPD.

Keywords: Chronic Obstructive Pulmonary Disease, Exercise Training,Physical Activity levels, Follow-up.

4.1. INTRODUCTION

Despite its primarily respiratory character, Chronic Obstructive Pulmonary Disease (COPD) also presents extrapulmonary consequences, including the reduction in functional exercise capacity and musculoskeletal function (i.e. strength and peripheral muscular resistance)[1, 2]. It is known that, to avoid the symptoms of the disease, these patients are less active when compared to healthy individuals of the same age group, presenting less time in physical activity, at a lower intensity and number of movements per day[3-8]. Lower levels of physical activity in daily life (PADL) are associated with a higher risk of hospitalizations and worse prognosis in COPD[9, 10], besides contributing to the progression of the disease[11].

As an attempt to counteract these consequences, pulmonary rehabilitation (PR) programs including physical training have been proposed as a key element in the treatment of individuals with COPD[12, 13]. Physical training is associated with an improvement in the functional exercise capacity and a reduction in dyspnea in these individuals[14, 15]. Resistance and aerobic training are among the exercises commonly proposed for these patients[12, 13, 16]. The combination of these modalities has been shown to be the best form of training for these individuals[17], as well as being recommended by international guidelines for the clinical treatment of these patients in PR programs[13, 18]. Despite the functional gains obtained in PR programs, the evidence for increased PADL in COPD patients is still contradictory and inconsistent[19], especially in short-term PR programs[20-24].

Functional physical training has been shown to be an effective alternative for improving mobility, functionality, and performance in the activities of daily living (ADL) of older adults[25-27]. This type of training includes muscle work involving coordinated patterns of multi-joint movements and dynamic tasks in order to improve functionality.

Studies demonstrate positive functional effects of this type of exercise for patients with COPD[22, 28].

Sewell et al.[28], demonstrated improvement in PADL and ADL performance after a short-term training program combining functional exercises with aerobic and home training in patients with COPD. Despite the benefits obtained, the authors did not evaluate whether or not the responses were maintained for a longer period of time than the program period, and did not include the progressive resistance training, an essential component for these patients. It is still unknown whether the addition of a functional circuit training (structured based on the limitations during ADL) to a conventional combined aerobic and resistance training program, commonly performed and well established in PR programs, can improve PADL, ADL performance, and functionality of patients with COPD in the short term. In addition, it is unknown if possible functional and PADL gains obtained in this type of training are maintained during a three months follow-up.

This randomized clinical superiority trial aims to evaluate the effects of the addition of a circuit of functional physical training to a eight-week combined training (aerobic and resistance) on PADL, ADL performance, functional exercise capacity, and peripheral muscle strength of patients with COPD. In addition, the effects of the interventions will be re-evaluated three months after the training completion. It is hypothesized that the proposed functional training will lead to behavioral changes, influencing the improvement in the performance of ADLs and, consequently, PADL, accompanied by functional improvement in patients with COPD.

4.2. METHODS

4.2.1 Study design

A randomized clinical trial with follow-up will be conducted at the Center for Studies and Care in Physical Therapy and Rehabilitation of the UniversidadeEstadualPaulista (FCT/UNESP), Presidente Prudente, Brazil. The study protocol was developed following the SPIRIT 2013 Checklist guidelines[29]. The trial was registered at www.ensaiosclinicos.gov.br (ID:RBR-3zmh3r).The study design is shown in **figure 1**.

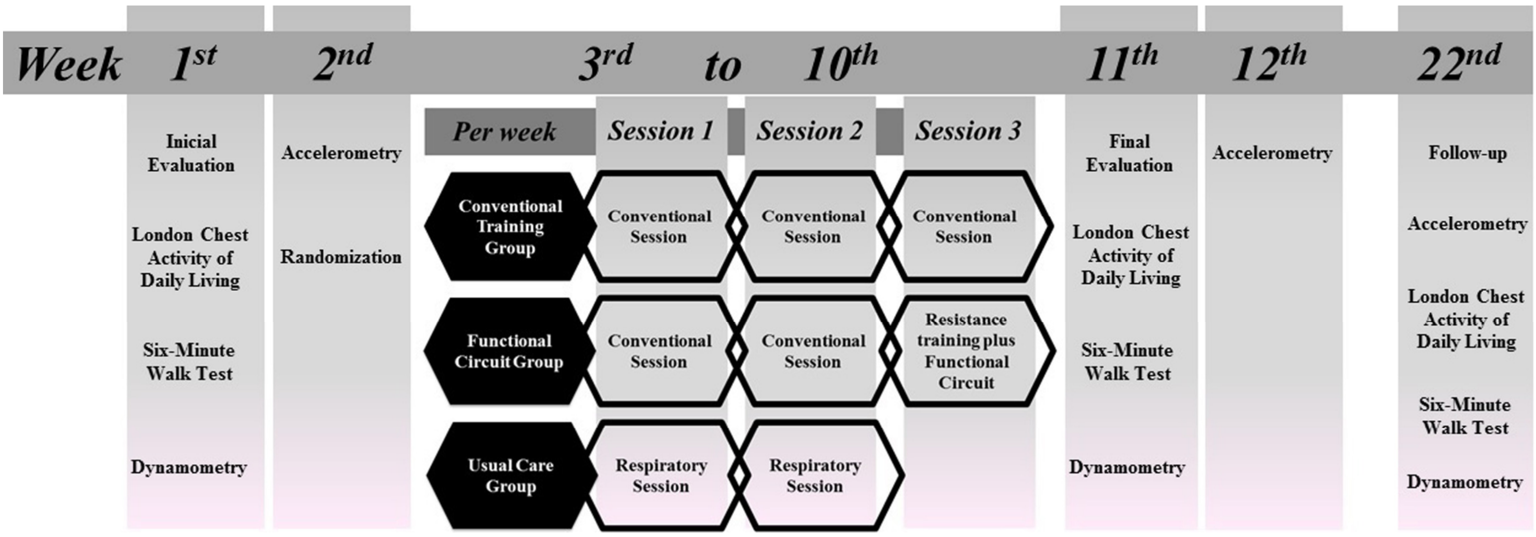

Figure 1. Experimental design of the study

Initially, participants will participate in an assessment process over two weeks on non-consecutive days. The first day of evaluation will consist of anamnesis, obtaining personal identification data and investigation of preexisting comorbidities, and performing spirometry to confirm the diagnosis of COPD by means of a portable spirometer MIR-Spirobank version 3.6. The interpretation will be in accordance with the *American Thoracic Society* (ATS) and *European Respiratory Society* (ERS)[30], with values of normality relative to the Brazilian population[31]. Limitations of ADLs will be evaluated by the *London Chest Activity of Daily Living* scale (LCADL)[32, 33].It should be emphasized that the questionnaire will be applied through an interview, always by the same evaluator, who will carry out prior training to avoid possible biases in the interpretation of questions and answers. On the second day, a functional capacity evaluation will be performed using the six-minute walk test (6MWT). On the third day of evaluations, the measurement of peripheral muscle strength will be performed by means of a digital dynamometer. Patients will receive a physical activity monitor (accelerometer) which will be used during seven days before the beginning of the training period, together with the basic guidelines for using the equipment. After the initial evaluation period, the training phase will begin. Conventional sessions will include resistance training and aerobic training. Resistance training plus functional circuit will include resistance training and performing a functional training circuit. Respiratory sessions will include only respiratory physiotherapy techniques.

After the end of the training period (eight weeks), all the evaluations described above will be repeated, except for the spirometry. Finally, a follow-up will be performed three months after the end of the training period, evaluating the PADL, limitations in the performance of ADL, functional exercise capacity, and muscle strength.

4.2.2. Participants

For the present study, 75 patients with COPD from the municipality of Presidente Prudente and region will be recruited through telephone contact and the distribution of leaflets and medical referrals. The following inclusion criteria will be considered: (1) patients diagnosed with COPD according to the *Global Initiative for Chronic Obstructive Lung Disease* (GOLD)[34]; (2) clinically stable patients, without exacerbations or changes in medications for at least 30 days; (3) patients who do not use long-term oxygen therapy at home; (4) patients without pathological conditions that prevent the performance of physical activity; (5) absence of severe or unstable heart disease and; (6) do not participate in another structured exercise program. The study was approved by the Research Ethics Committee of the FCT/UNESP, Presidente Prudente/Brazil (#77909317.2.0000.5402).

4.2.3. Analysis of the population

Will be considered exclusion criteria: complications that prevent the continuity of the training protocol, as well as low adhesion rate to the training protocol (below 75% of all sessions)[35]. In the event of two consecutive absences from training sessions, patients will be contacted by telephone to confirm the reason. An intention-to-treat analysis will be performed using the patient's most recent assessment in case of withdrawals or absence of data. In case of possible injuries occurring during the intervention period, the individuals will be referred for appropriate treatment.

4.2.4. Randomization

The sample will be randomly allocated into three groups: functional circuit training group (FTG), conventional training group (CTG), and usual care group (UCG). The randomized allocation sequence will be performed by a researcher who will not be involved in the recruitment, evaluation, or training of patients, using an online platform (www.sealedenvelope.com) and concealed brown envelopes. The randomization process will be carried out in blocksdefined a priori. Evaluators will be blind as to the allocation of participants to interventions. The training will be supervised by trained physiotherapists not involved in the randomization process or evaluations.

4.3. PROCEDURES

4.3.1. Interventions

The physical exercise program will take place over 8 weeks with a frequency of three weekly sessions of approximately 60 minutes each, totaling 24 training sessions. The sessions will begin with dynamic general stretching, after which the aerobic training will be carried out on a treadmill with a duration of 30 minutes, followed by the resistance training of upper limbs and lower limbs. These dynamics will occur for both the FTG and CTG groups, except for the third weekly session in which the FTG will perform functional training in circuit format. At the beginning, during, and at the end of the sessions, vital signs will be checked. The UCG will perform only usual care involving respiratory physiotherapy sessions that include inhalation therapy, pulmonary deflation techniques, diaphragmatic awareness, and inspiratory muscle exercise.

4.3.2. Resistance training

For the training prescription, a 1-repetition maximum test (1RM) will be performed according to a previously described protocol[36, 37], of the following muscle groups: elbow flexors, and knee extensors and flexors. The resistance training will be performed using weight machines: extensor chair and flexor chair (Ipiranga® - Brazil) for lower limbs; and simple pulley equipment (Ipiranga® - Brazil) for upper limbs. The intensity of training will follow the protocol recommended for patients with COPD[38, 39], 60 to 80% of the 1RM test, with 3 sets of 10 repetitions, and 2 minute intervals between sets. The load increase will be performed every four stimuli (sessions), with a 5% increase in the intensity of the 1RM test until reaching 80%. The trained muscle groups will be the same as previously described in the 1RM test.

4.3.3. Aerobic training

The aerobic training will be performed on an ergometric treadmill and will begin with an intensity of 80% of the average speed reached in the 6MWT[40]. In addition, the increase in aerobic training intensity will be performed based on the subjective sensation of dyspnea of the individuals, measured by the Borg scale[38]. Thus, when the individual reports a dyspnea sensation with values between 4 and 6 on the Borg scale, the intensity will be maintained, this being considered an adequate training intensity[38, 41]; however, when the intensity is less than 4, there will be a 5% increase in training intensity.

4.3.4. Functional circuit training

In order to maintain the same increment dynamics of resistance training in both training groups (FTG and CTG), the session that will include circuit format functional training in the FTG will be divided into two stages: Functional circuit and resistance training (elbow flexion, knee extension and flexion). The circuit training will be composed of 12 exercises (stations) that will simulate ADL, elaborated based on previous identification (telephone interview) of the main limitations for performing ADL, reported by patients with COPD from the database of the care center where the study will be conducted.

Each exercise will last 2 minutes and 30 seconds, so the total duration of the functional circuit will be 30 minutes, as performed in aerobic training. Following the same method of aerobic training, the increment in the training intensity will be performed based on the subjective sensation of dyspnea of the individuals, measured usuing the Borg scale[38, 41]. Thus, when the individual reports a dyspnea sensation with values between 4 and 6 on the Borg scale, the intensity will be maintained, this being considered an adequate training intensity[38, 41], however, when the intensity is less than 4, the training intensity will be increased, that is, an increase in the speed/number of repetitions of the exercises until the 8 weeks of training is completed. A pilot session was conducted with patients with COPD to evaluate the viability and execution time of functional training in circuit format. There were no problems in the execution and time of the exercises, and these were shown to be feasible by the patients.

The functional circuit will include the exercises/stations described below and illustrated in figure 2: **Exercise 1**: Simulate drying the back: pass the stick behind the back (as if drying the back with a towel, change hands every 5 movements); **Exercise 2**: Simulate sweeping the floor: With shoulder flexion at approximately 75º, hold the stick with the forearm pronated, perform a movement similar to "rowing"; **Exercise 3**: Simulate Tying Shoes: Sitting in a chair with 90° elbow flexion, hold a ball with their hands, then perform knee flexion, touching the lateral malleolus on the contralateral knee, with the ball touching the medial malleolus; **Exercise 4**: Simulate passing a squeegee on the floor: Holding a stick (the stick should touch the ground) with the hands, move the stick anteriorly to the left and then later to the right, and after repeat on the contralateral side; **Exercise 5**: Simulate bath movements to wash the hair: Holding a small ball in the hands, perform simultaneous movements: 90° shoulder flexion, 90° elbow flexion, and touch the ball on the head; **Exercise 6**: Simulate picking up objects in high and low places: In front of a bookcase in the orthostatic position, pick up a ball from a high shelf (head level) and then put it on two lower shelves (chest level and waist level); **Exercise 7**: Simulate squatting: Squat holding a fixed bar; **Exercise 8**: Simulate walking on uneven ground using ramps and stairs: Rise and descend steps/ramp; **Exercise 9**: Simulate standing up and sitting in a chair: get up from the chair, walk a short distance (3 meters), and sit in the chair again; **Exercise 10**: Simulate changing clothes: With a hula hoop on the ground, step with both feet inside the circle, crouch to pick up the hula hoop with both hands, rise up holding the hula hoop and perform shoulder flexion by lifting the hula hoop so that it runs all over the body of the individual; reverse the movement with the same steps, ending by placing it on the floor again; **Exercise 11**: Simulate the avoidance of obstacles during gait: With five hula hoops on the ground, walk among the hula hoops; **Exercise 12**: Simulate picking up objects: In front of three small cones on the floor, perform trunk flexion and touch the tip of one of the cones and return to the starting position and repeat the movement until having touched all the cones; When finishing the three movements, perform them with the other hand (**figure 2**).

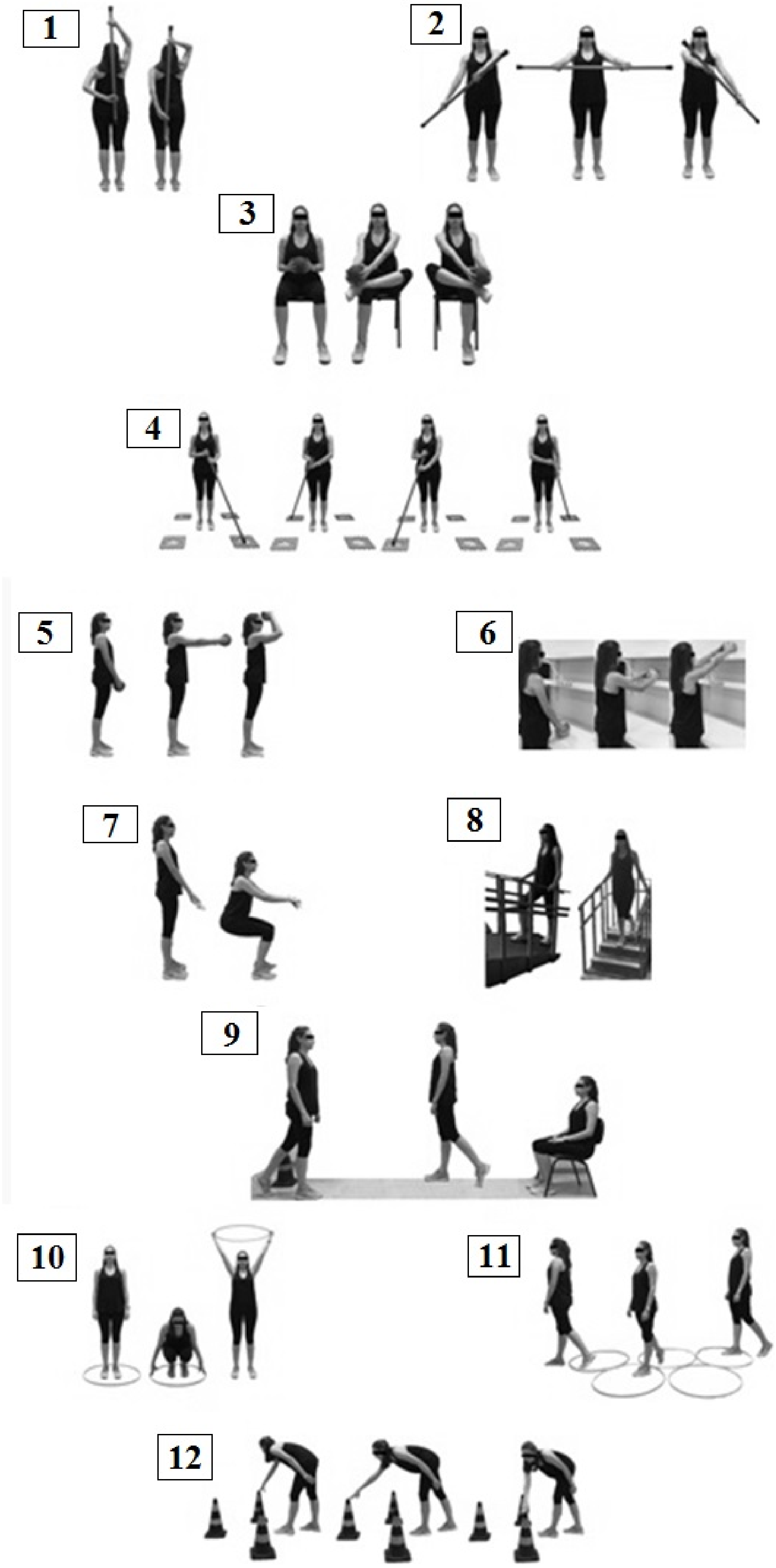

Figure 2. Functional circuit exercises

4.3.5. Participant timeline

The time schedule of enrollment, interventions, and assessments is outlined in **figure 3**. Recruitment of study participants began in July 2018.

	STUDY PERIOD					
	Enrollment	**Allocation**	**Post-allocation**			**Close-out**
TIMEPOINT**	***-t₁***	**0**	***Baseline***	***Post-intervention***	***Follow-up***	***tₓ***
ENROLLMENT:						
Eligibility screen	X					
Informed consent	X					
Allocation		X				
INTERVENTIONS:						
[FTG]			X	X	X	
[CTG]			X	X	X	
[UCG]			X	X	X	
ASSESSMENTS:						
[Pulmonary Function]	X					
[LCADL]			X	X	X	X
[Functional exercise capacity]			X	X	X	X
[Muscle strength]			X	X	X	X
[PADL]			X	X	X	X

Figure 3. Content for the schedule of enrollment, interventions, and assessments; FTG: Functional Circuit Training Group; CTG: Conventional Training Group; UCG: Usual Care Group; LCADL: London Chest Activity of Daily Living – scale; PADL: Physical Activity in Daily Life.

4.4. RESULTS

The primary outcome will be the PADL assessment using accelerometry. Secondary outcomes include limitations on performance in ADL, functional exercise capacity, and peripheral muscle strength. The evaluations will be carried out by the same evaluators at all described moments.

4.4.1. Primary outcome

The PADL will be used as the primary outcome of the study, measured by step counts days and time spent on activities, using an accelerometer type movement sensor, Actigraph, GT3X (Actigraph LLC, Pensacola, FL), which measures and records acceleration variations with magnitudes ranging from approximately 0.05 to 2.5 G (g=9.8 m/s^2) within a frequency range of 0.25 to 2.5 Hertz. Each sample of counts will be summarized over a specific time interval of 60 seconds, called an epoch. Accelerometers will be placed on the waist immediately below the umbilical scar and individuals will wear the equipment for seven days. The accelerometer will be removed during the nighttime sleep period and when the participant has contact with water (personal hygiene or water activities). Participants will wear the device before and after the intervention periods and soon after the three-month post-intervention follow-up. For analysis of the data, specific *software* will be used (ActiLife5 – Data Analysis Software by Actigraph).

4.4.2. Secondary outcomes

The study will include three evaluations of secondary outcomes: limitations during ADL performance, functional exercise capacity, and peripheral muscle strength. These outcomes will be evaluated before and after the intervention period, as well as after the post-intervention follow-up period of three months.

4.4.2.1. Limitations during Activities of Daily Living

Limitations during the performance of ADL will be evaluated by the LCADL scale, developed by Garrod et al., 2000[42], translated to Portuguese and validated for use in COPD in Brazilian patients[32, 33]. This scale contains 15 items divided into four domains: Personal care (four items), domestic (six items), physical activity (two items), and leisure (three items)[33]. The total score can vary from 0 to 75 points, and the higher the score, the greater the limitation in ADL[32].

4.4.2.2. Functional exercise capacity

Functional exercise capacity will be evaluated through the 6MWT, performed according to the guidelines established by the ATS[43].

4.4.2.3. Peripheral Muscle Strength

Measurement of muscle strength will be performed in the dominant member using a Force Gauge® digital dynamometer, model FG-100kg, and the results will be expressed in Newtons (N). The patient will be instructed to perform the movements of elbow flexion, and knee flexion and extension, resisted by a steel cable coupled to the dynamometer. The measurement will be repeated five times with an interval of 1 minute between attempts and the highest value among the three closest measurements will be recorded[44].

4.5. Sample size calculation

This is a superiority trial in which sample size determination was performed through prior study[45] information based on the primary PADL variable. With the expectation of an increase in the number of steps of 45% (approximately 2260 steps) in the FTG group compared to the CTG and UTG (both with no expected increase), using a standard deviation of 2,603 steps, and loss at follow-up of 20% of individuals (values commonly found in the study population)[44] , 25 individuals will be required in each of the three groups to obtain a power of 80%, adopting an α of 5%.

4.6. Statistical analysis

The statistical program SPSS 22.0 will be used. The data will be submitted to the normality test of Kolmogorov-Smirnov and if they present normal distribution the descriptive variables will be expressed as mean and standard deviation, if they do not fit the Gaussian distribution model, data will be presented as median and interquartile range. The Mauchly's sphericity test will be performed. Once the sphericity is assumed, two-way ANOVA will be performed to evaluate the possible intra and inter-group differences (FTG, CTG, and UCG) at pre-intervention, post-intervention, and post *follow-up*. The Tukey post-hoc will be used to identify the specific differences in the variables in which the F values found are higher than the established statistical significance criterion. To evaluate the effect size between interventions, the Cohen's d test will be used. The level of significance adopted will be 5%. Data integrity will be monitored by regularly scrutinizing data files for omissions and errors. Participants will be given an anonymous study ID to protect confidentiality, and only study investigators will have access to the final trial data set.

4.7. DISCUSSION

4.7.1. Potential impact and significance of the study

The present proposal was developed through extensive literature research on this topic. Through the interpretation of the results found in several studies it was possible develop this concise and structured training protocol. The use of this protocol in the treatment of patients with COPD will confirm whether the addition of functional physical training to a conventional training will promote positive effects on PADL and functionality, as well as whether there will be maintenance of possible gains at the three month post-training follow-up.

4.7.2. Strengths and limitations of the study

This study presents as a strong point the follow-up three months after training as this allows evaluation of whether the possible changes resulting from the protocol will be maintained. The assessment of PADL via accelerometers as primary outcome, is a strong point as it is an objective measurement and do not suffer influence of personnel involved in the study. Another strong point that can be considered, is the fact of this being a randomized clinical trial, which makes the study more reliable.The fact that the study is performed in only one center is considered a limitation, as well as the inability to blind the therapists and patients to the training protocol.

4.7.3. Contribution and clinical applicability

The results obtained in the proposed protocol may provide subsidies via publication for the implementation and insertion of a physical training circuit in the rehabilitation of patients with COPD. In addition, the proposed functional exercises are easily applicable, and simulate ADLs not requiring specific equipments, and can therefore be implemented in several PR centers.

DECLARATIONS

Ethics approval and consent to participate

Ethical approval has been granted by the Human Ethics Committee of the FCT/UNESP (#77909317.2.0000.5402).Informed consent will be obtained by researchers from all study participants.

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5. ARTICLE IV

ORIGINAL RESEARCH

de Lima FF et al

Will be submitted to the journal**: Respiratory Medicine.** (Impact factor 3.09)

Combining Functional Exercises with Exercise Training in COPD: A Randomized Clinical Trial

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Trial registration: Brazilian Clinical Trials Registry (ReBEC), ID:RBR-3zmh3r.

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ABSTRACT

Background: It is unclear whether the combination of functional exercises with aerobic and resistance trainingcan improve physical activity in daily life (PADL) and limitations in chronic obstructive pulmonary disease (COPD). This study evaluated the short term and sustained effects of the combination of functional exercises with aerobic and resistance training. **Methods**: 76 patients with COPD were randomized to: I) a Functional Training Group (FTG) performing resistance and aerobic and functional exercises or; II) a Conventional Training Group (CTG) including only resistance and aerobic exercises or; III) a Usual Care Group (UCG). Patients were evaluated before and upon completion of eight weeks of training regarding PADL, activities of daily living (ADL) limitations, functional exercise capacity, and muscle strength. Sustained effects were evaluated 12 weeks after the end of the training. **Results:** There was no change in steps/day and time in moderate to vigorous physical activity post-intervention and 12 weeks post-training in any of the groups, as well as, there were no differences between groups (p>0.05). Only CTG showed reduction in LCADL total score after the intervention and increase at follow-up (20±8; 17±6; 19±8, pre and post-intervention, and 12 weeks post-training, respectively) (p=0.001), without difference between groups (p=0.375). **Conclusion:** Combined aerobic and resistance training with functional exercises failed to improve PADL and ADL limitations in patients with COPD. Eight weeks of conventional training improved ADL limitations.This, however, was not superior to the results from the other groups and was not sustained at 12 weeks post-training follow-up.

Trial registration: Brazilian Clinical Trials Registry (ReBEC) ID: RBR-3zmh3r.

Keywords: Chronic Obstructive Pulmonary Disease, Exercise Training, Physical Activity

5.1. INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD)Chronic obstructive pulmonary disease (COPD) is a preventable and treatable disease characterized by persistent respiratory symptoms and airflow limitation.COPD is a preventable and treatable public health challenge, and one of the leading causes of chronic morbidity and mortality worldwide[1],being responsible for approximately 6% of total deaths worldwide[2]. COPD is a disease with primarily respiratory characteristics. However, the patients also present significant extrapulmonary consequences, including skeletal muscle dysfunction, contributing to exercise intolerance[1]. These patients are less physically active than age-matched healthy individuals[3-8], and lower levels of physical activity in daily life (PADL) are associated with hospitalizations[9], worse prognosis[10], disease progression[11], and increased risk of premature death in COPD[12].

Pulmonary rehabilitation (PR) is well established as essential andaintegral part of the care of patients with COPD[13]. Exercise training is considered the cornerstone of PR[14, 15], and aerobic, and resistance training have been commonly proposed for these patients showing promising results when combined[16], besides, it is recommended by international guidelines[17, 18]. PR programs improve the functional exercise capacity in this population[13, 15], however, the evidence for increased PADL in patients with COPD is contradictory and inconsistent[15, 19], suggesting a small effect on PADL and inconsistent translation of functional gain into increased PADL[20].

In older adults, functional exercise training improves the performance in daily living activities (ADL), and mobility[21-23]. This training involves coordinated patterns of multi-joint movements and dynamic tasks[22]. Even combined with another exercise modality, this type of exercise has been demonstrated positive effects for patients with COPD[24]. However, despite the benefits obtained on PADL and ADL performance in a short-term training program combining functional exercises with aerobic and home training in patients with COPD, the authors evaluated the responses only after the end of the training program[24]. Thus, it is not possible to know if the effects were maintained for a more extended period than the program. Furthermore, it did not include progressive resistance training, an essential component related to improvements in ADL performance in patients with COPD[25].

The present study evaluated the short term (8 weeks) and sustained effects (12 weeks post-training follow-up) of functional exercise training combined with aerobic and resistance exercise training on PADL, subjective ADL limitations, functional exercise capacity, and peripheral muscle strength of patients with COPD. It is expected that the inclusion of functional training promotes behavioral change by improving ADL limitations, PADL and exercise tolerance in patients with COPD.

5.2. METHODS

Patients with COPD from the municipality of Presidente Prudente and region, Brazil, were recruited between July 2018 and January 2020 through telephone contact and the distribution of leaflets and medical referrals. The following inclusion criteria were considered: patients diagnosed with COPD according to the *Global Initiative for Chronic Obstructive Lung Disease* (GOLD)[1]; clinically stable patients, without exacerbations or changes in medications for at least 30 days; patients who do not use long-term oxygen therapy at home; patients without pathological conditions that prevent the performance of exercise training; absence of severe or unstable heart disease and; do not participate in another structured exercise program. Exclusion criteriato consider dropoutswere: complications that prevent the continuity of the training protocol and low adhesion rate to the training protocol (below 75% of all sessions). The trial was registered (RBR-3zmh3r) and approved by the Research Ethics Committee of the São Paulo State University – Faculty of Science and

Technology (UNESP/FCT), Presidente Prudente, Brazil (#77909317.2.0000.5402). All participants provided written informed consent. Specific details of the methods have been previously reported[26].

5.2.1. Study design

A randomized controlled trial was conducted at the Center for Studies and Care in Physical Therapy and Rehabilitation of the UNESP/FCT, Presidente Prudente, Brazil. Participants underwent an initial assessment including: anamnesis, lung function (spirometry)[27,28], ADL limitations, functional exercise capacity, peripheral muscle strength, and PADL. After the initial assessments, participants were randomly allocated into three groups: functional training group (FTG), conventional training group (CTG), and usual care group (UCG). The randomized allocation sequence was performed by a researcher not involved in the recruitment, evaluation, or training of patients, using an online platform (www.sealedenvelope.com) and concealed brown envelopes. Evaluators were blinded as to the allocation of participants to interventions, as well as, trained to carry out the evaluations. FTG performed resistance, aerobic and functional exercise training; CTG performed aerobic and resistance exercise, and UCG performed respiratory physiotherapy techniques. After eight weeks of training, the initial assessments were repeated. 12-weeks after the end of the training, the PADL, ADL limitations, functional exercise capacity, and muscle strength were assessed again (12-weeks post-training follow-up).

5.2.2. Intervention protocol

The exercise training program lasted 8 weeks, with a frequency of three weekly sessions of approximately 60 minutes each, totalling 24 sessions. The sessions started with general dynamic stretching; the aerobic training was performed on a treadmill for 30 minutes starting with an intensity of 80% of the average speed reached in the 6MWT and the progression was based on the subjective sensation of dyspnea of the individuals (4 – 6 in the Borg scale)[29]; the resistance training was performed using weight machines: extensor chair and flexor chair for lower limbs (knee extensors and flexors) and simple pulley equipment for upper limbs (elbow flexors) with intensity from 60 to 80% of the 1RM testwith 3 sets of 10 repetitions). These dynamics were performed by both the FTG and CTG groups, except for the third weekly session in which the FTG performed the functional training in circuit format instead of aerobic training. The functional circuit training was composed of 12 exercises (stations) that simulate ADL. These exercises were identified based on telephone interviews with patients with COPD discussing the perceived main limitations during ADL. Each exercise lasted 2 minutes and 30 seconds, so the functional circuit's total duration was 30 minutes, as performed in aerobic training. Following the same aerobic training method, the increment in the training intensity was performed based on the subjective sensation of dyspnea of the individuals, measured using the Borg scale[30]. The UCG performed only respiratory physiotherapy twice a week. Details of the training protocol, as well as the functional training, were described previously[26].

5.2.3. PADL and ADL Limitations Measurements

The PADL was the primary outcome, and was assessed using an activity monitor (Actigraph-GT3X, Actigraph LLC, Pensacola, FL). Participants were instructed to use the device for seven days. For analysis of the data, specific *software*was used (ActiLife5 – Data Analysis Software by Actigraph). Days with at least 8 hours of wearing time were considered valid[31]. A measurement was considered valid when patients had at least 3 valid days, including at least 2 weekdays[4, 32]. Perceived ADL Limitations were evaluated by the *London Chest Activity of Daily Living* scale

(LCADL)[33], validated for use in Brazilian patients with COPD[34, 35]. The total score can vary from 0 to 75 points, and the higher the score, the greater the limitation in ADL[34].

5.2.4. Functional Exercise Capacity and Muscle Strength Measurements

Functional exercise capacity was evaluated by the 6MWT, performed according to international guideline[36]. Muscle strength was evaluated using a digital dynamometer (Force Gauge®, model FG-100kg) and the results were expressed in Newton (N). The movements evaluated were: elbow flexion, knee flexion and knee extension.

5.2.5. Statistical analysis

The sample size determination was performed based on the PADL[37]. Anticipating an increase in the number of steps of 45% (approximately 2260 steps) in the FTG, using a standard deviation of 2603 steps, and attrition of 20%, 25 individuals were required in each group ($\alpha = 0.05$, $1-\beta = 0.8$). The statistical program SPSS 22.0 was used for data analyses. The data were submitted to the Shapiro-Wilk normality test. Categorical data were described as frequency, and the Chi-square test was performed. One-way ANOVA or Kruskal-Wallis test was performed to compare the baseline characteristics according to the data distribution. Two-way ANOVA was performed to compare intra and inter-group differences (FTG, CTG, and UCG) at baseline, final, and follow-up moments. Bonferroni post-test was used to identify specific differences. The level of significance adopted was 5%. As established in the study protocol, previously published[26], an ITT analysis was carried out including all participants. In case of absence of data (i.e. attrition or attendance less than 75% of total) the results of the last available assessment were carried forward.

5.3. RESULTS

The study flow is described in figure 1.

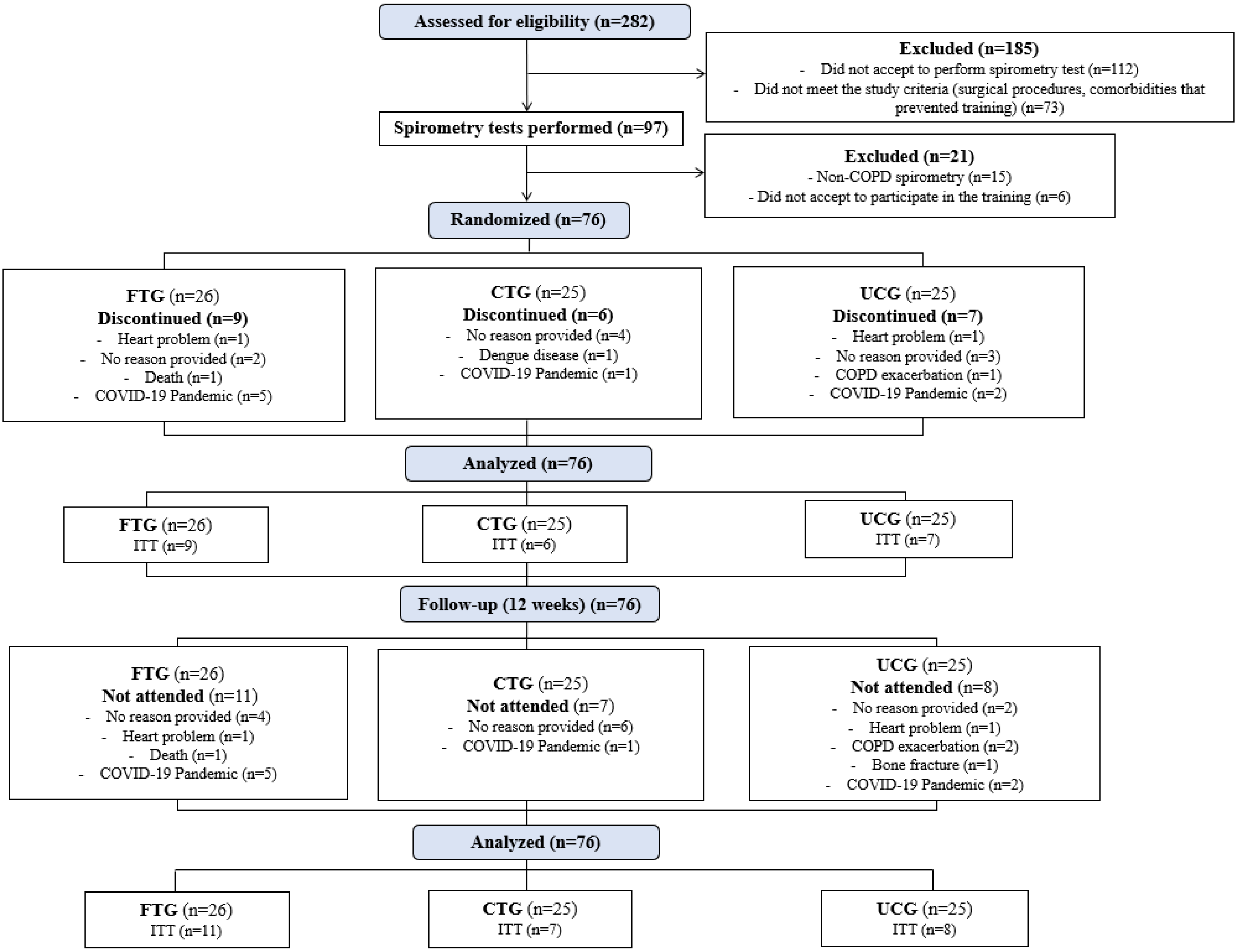

Figure 1: Flowchart of sample selection and participation. FTG: Functional circuit training group; CTG: Conventional training group; UCG: Usual care group; ITT: Intention-to-treat analysis.

Table 1 shows the baseline characteristics of the groups. Only for PADL (activity monitoring) one patient in UCG was missed due to technical failure (n=24 for this variable in this group). There were no differences in baseline characteristics between groups.

Table 1. Baseline characteristics of the groups.

	FTG (n=26)	CTG (n=25)	UCG (n=25)	p
Male/Female n (%)	12 (46.15) /14 (53.8)	13 (52) / 12 (48)	14 (56)/ 11 (44)	0.673
Age (years)	68.2±7.4	68.5±6.0	71.1±7.2	0.271
BMI (kg/m^2)	24.9±5.1	27.0±4.9	25.5±4.9	0.321
Lung function				
FEV_1 (L)	1.31 [1.17 – 1.71]	1.21 [0.97 – 1.78]	1.14 [0.84 – 1.37]	0.156
FEV_1(% of predicted)	55.34±19.42	52.04±17.01	44.24±15.50	0.073
FVC (L)	2.28 [1.89 – 3.35]	2.20 [1.88 – 3.08]	2.36 [2.04 – 2.69]	0.888
FEV_1/FVC (%)	55.75±12.67	54.69±8.48	48.72±13.74	0.083
PADL				
Steps per Day	4704 [2755 – 6357]	4356 [3733 – 6272]	4226 [2011 – 5398]	0.280
MVPA (%)	0.54 [0.21 – 1.56]	0.99 [0.28 – 1.59]	0.37 [0.17 – 1.80]	0.456
ADL Limitations (LCADL)				
Total Score	20 [14– 25]	17 [15– 25]	21 [16– 29]	0.616
Functional Capacity (6MWT)				
Distance (m)	458.5±102.1	478.6±75.0	422.4±120.1	0.143
% of Predicted	85.8±18.7	90.8±14.7	78.9±22.6	0.093
Muscle Strength				
Elbow Flexion (N)	85.2±31.0	95.4±35.1	98.2±36.1	0.365
Knee Flexion (N)	114.2±29.3	113.5±34.7	115.5±45.1	0.982
Knee Extension (N)	164.3±53.9	190.9±56.9	171.6±52.1	0.205

Data expressed as frequency (%), mean ±SD or median [IQR 25-75%].FTG: Functional circuit training group; CTG: Conventional training group; UCG: Usual care group; %: percentage; BMI: Body Mass Index; Kg/ m^2: kilograms per square meter; FEV_1: Forced expiratory volume in the first second; L, Liters; FVC: forced vital capacity; PADL: physical activity in daily life; MVPA: Moderate to vigorous physical activity; ADL: Activities of daily living; LCADL: London Chest Activity of Daily Living scale; 6MWT: 6-minute walk test; m:meters; N: Newton.

Comparisons of PADL and ADL limitations at baseline, 8 weeks, and follow-up are described in table 2.Sendentary time analyses showed no diferrence between groups, and any changes at 8-weeks and at 12-weeks follow-up (Baseline (%): FTG:64±12; CTG: 65±12; UCG: 69±11; 8-weeks: FTG: 65±13; CTG: 64±11; UCG: 69±12; 12-weeks follow-up: FTG:66±13; CTG: 64±12; UCG: 69±11 (P>0.05). FTG showed improvement only for the LCADL leisure activities domain after training (p=0.048). CTG showed improvement after training in self-care (p=0.014), physical activity (p=0.014) (worsening at follow-up (p<0.001) and leisure activities (p=0.009) domains. Total score improved only in CTG after the intervention (p=0.001), worsening at follow-up (p=0.022) (Table 2 and Figure 2). Between groups difference was found only between CTG and UCG to physical activity domain of the LCADL Comparing Follow up-8weeks deltas (p=0.016).

Table 2. Physical activity in daily life and ADL limitations comparisons.

		n	Baseline	8-weeks	Follow-up	Δ (8weeks-Baseline)	p	Δ (Follow up-8weeks)	p	Effect	P
PADL											
	FTG	26	4982±2270	4792±2776	4868±2822	-189 (-567, 187)		76 (-330, 782)		Group	0.207
Steps Day	**CTG**	25	5848±4121	6143±4249	5771±4277	294 (-147, 736)	0.347	-371 (-981, 238)	0.412	Time	0.547
	UCG	24	4121±2708	4378±2928	4284±2862	256 (-90, 603)		-94 (-666, 477)		Group x Time	0.458
	FTG	26	0.54 [0.21 – 1.56]	0.80 [0.27 – 1.43]	0.69 [0.21 – 1.33]	0.04 (-0.22, 0.31)		-0.05 (-0.22, 0.10)		Group	0.078
MVPA (%)	**CTG**	25	0.99 [0.28 – 1.59]	0.98 [0.27 – 2.69]	0.98 [0.27 – 2.10]	0.42 (-0.21, 1.06)	0.608	-0.16 (-0.91, 0.59)	0.240	Time	0.544
	UCG	24	0.37 [0.17 – 1.80]	0.40 [0.23 – 1.41]	0.37 [0.13 – 1.71]	-0.04 (-0.36, 0.28)		0.02 (-0.55, 0.59)		Group x Time	0.573
ADL Limitations (LCADL)											
	FTG	26	5 [4 – 7]	4.5 [4 – 7]	4.5 [4 – 7]	-0.19 (-0.62, 0.23)		0.19 (-0.13, 0.51)		Group	0.664
Self-care	**CTG**	25	5 [4 – 7]	4 [4 – 5]*	4 [4 – 6]	-0.92 (-1.69, -0.14)	0.212	0.52 (-0.20, 1.24)	0.921	Time	0.005
	UCG	25	6 [4 – 8]	5 [4 – 7]	5 [4 – 7.5]	-0.48 (-1.17, 0.21)		0.28 (-0.21, 0.77)		Group x Time	0.484
	FTG	26	7 [5 – 10]	7 [4.7 – 10]	7.5 [5 – 10]	-0.19 (-1.05, 0.67)		0.19 (-0.69, 1.07)		Group	0.685
Household Activities	**CTG**	25	6 [4 – 9]	5 [4 – 7.5]	6 [4 – 8]	-0.88 (-1.99, 0.23)	0.538	0.56 (-0.33, 1.45)	0.629	Time	0.321
	UCG	25	6 [5 – 10]	7 [5 – 9]	7 [4– 10]	-0.12 (-0.92, 0.68)		0.24 (-0.95, 1.43)		Group x Time	0.828
	FTG	26	3 [1.7 – 4]	3 [1 – 3.2]	3 [1.7 – 4]	-0.38 (-0.79, 0.02)		0.30 (0.01, 0.60)		Group	0.192
Physical Activity	**CTG**	25	2 [2 – 4]	2 [1 – 2]*	2 [2 – 4]¥	-0.80 (-1.48, -0.11)	0.556	0.88 (0.31, 1.44)#	0.016	Time	0.004
	UCG	25	3 [2 – 5]	3 [2 – 5]	3 [2 – 4.5]	-0.20 (-0.75, 0.35)		-0.04 (-0.38, 0.30)		Group x Time	0.132
	FTG	26	4 [3 – 6]	4 [3 – 5]*	3.5 [3 – 5]	-0.53 (-0.88, -0.19)		0.07 (-0.11, 0.27)		Group	0.265
Leisure Activities	**CTG**	25	4 [3 – 5]	4 [3 – 4]*	4 [3 – 4.5]	-0.68 (-1.27, -0.08)	0.150	0.32 (-0.13, 0.77)	0.215	Time	0.001
	UCG	25	5 [3 – 6]	5 [4 – 5]	4 [3 – 6]	-0.12 (-0.52, 0.28)		-0.20 (-0.49, 0.09)		Group x Time	0.292
	FTG	26	20 [15 – 25]	18 [14 – 24]	18.5 [15– 25]	-1.30 (-2.53, -0.07)		0.76 (-0.46, 2.00)		Group	0.375
Total Score	**CTG**	25	17 [14– 25]	16 [13 – 18]*	16 [14 – 23]¥	-3.28 (-5.36, -1.19)	0.092	2.12 (0.19, 4.04)	0.154	Time	0.001
	UCG	25	21 [16 – 29]	19 [15– 26]	18 [15– 26]	-0.92 (-2.91, 1.07)		0.28 (-1.24, 1.80)		Group x Time	0.256

Data expressed as mean and ±SD, median [IQR 25-75%] or mean (95% CI); FTG: Functional circuit training group; CTG: Conventional training group; UCG: Usual care group; PADL: physical activity in daily life; MVPA: Moderate to vigorous physical activity; %: percentual; ADL: Activities of daily living; LCADL: London Chest Activity of Daily Living scale; *: p<0.05 compared to baseline; ¥: p<0.05 compared to the 8-weeks moment;#:p<0.05compared toUCG.

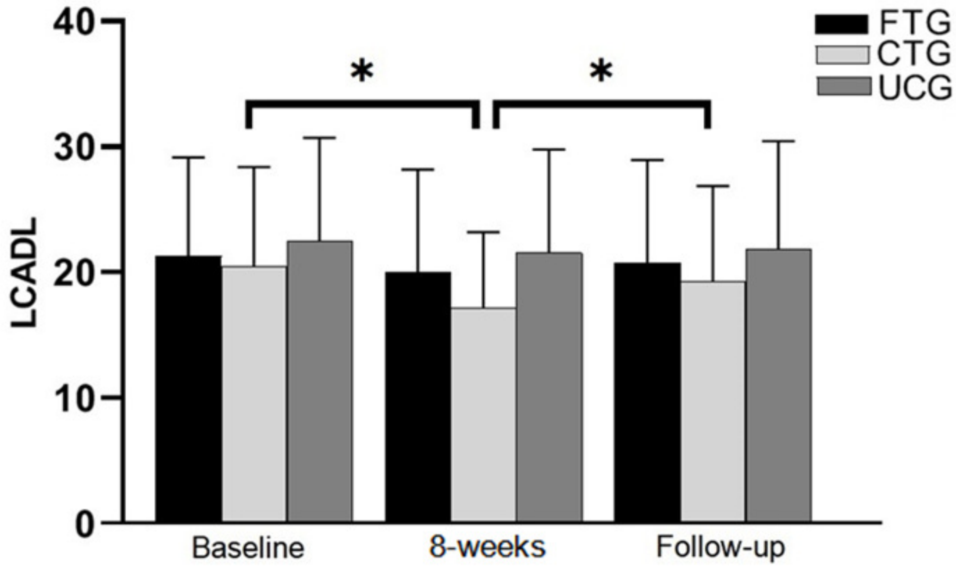

Figure 2: Activities of Daily Living limitations; Data expressed as mean ±SD; LCADL: London Chest Activity of Daily Living; FTG: Functional circuit training group; CTG: Conventional training group; UCG: Usual care group. *: p<0.05.

Table 3 describes the comparisons of functional exercise capacity (6MWT) and muscle strength at the evaluated moments. There were increases in the muscle strength of knee flexors (p=0.005) and extensors (p<0.001) after intervention only in CTGand maintenance of knee extensors strength (p=0.005 compared to baseline) at follow-up. Between groups differences were found comparing knee extensors strength between CTG and FTG at 8-weeks (p=0.030) and follow-up (p=0.023) moments, as well as, comparing 8weeks-Baseline deltas of knee flexors values between CTG and UCG (p=0.020). Showing superiority in strength gain in favor of CTG.

Table 3. Functional exercise capacity and muscle strength comparisons.

		n	Baseline	8-weeks	Follow-up	Δ (8 weeks-Baseline)	p	Δ (Follow up-8 weeks)	p	Effect	p
Functional exercise Capacity											
Distance (m)	**FTG**	26	458.5±102.1	456.8±101.5	463.6±107.6	-1.7 (-12.8, 9.4)		6.8 (-6.6, 20.2)		Group	0.078
	CTG	25	478.6±75.0	480.2±73.5	479.1±71.0	1.6 (-18.6, 21.7)	0.539	-1.1 (-15.9, 13.7)	0.320	Time	0.583
	UCG	25	422.4±120.1	420.0±127.8	404.1±127.5	-2.4 (-15.1, 10.3)		-15.9 (-34.0, 2.1)		Group x Time	0.145
% of Predicted	**FTG**	26	85.8±18.7	85.4±18.9	86.8±19.4	-0.4 (-2.8, 2.0)		1.4 (-0.9, 3.7)		Group	0.057
	CTG	25	90.8±14.7	91.4±13.2	91.2±12.7	0.5 (-3.6, 4.6)	0.438	-0.2 (-2.7, 2.6)	0.175	Time	0.646
	UCG	25	78.9±22.6	79.8±24.5	76.1±23.8	0.8 (-2.2, 3.8)		-3.6 (-7.2, 0.0)		Group x Time	0.169
Muscle Strength											
Elbow Flexion (N)	**FTG**	26	85.3±31.0	89.6±30.4	87.5±30.8	4.3 (-1.3, 10.0)		-2.1 (-7.5, 3.4)		Group	0.404
	CTG	25	95.4±35.1	102.4±33.8	96.9±32.6	7.0 (0.1, 13.9)	0.300	-5.5 (-11.2, 0.3)	0.695	Time	0.016$^{\#}$
	UCG	25	98.2±36.1	100.6±35.0	94.9±37.8	2.4 (-3.8, 8.5)		-5.6 (-12.5, 1.3)		Group x Time	0.632
Knee Flexion (N)	**FTG**	26	114.2±29.3	122.2±39.9	115.0±32.4	7.9 (-3.8, 19.7)		-7.1 (-19.0, 4.8)		Group	0.727
	CTG	25	113.5±34.7	131.2±31.2*	119.9±33.4	17.7 (11.2, 24.2)$^{§¥}$	0.020	-11.2 (-20.0, -2.4)	0.083	Time	0.016
	UCG	25	115.5±45.1	114.2±37.3	112.5±43.1	-1.3 (-15.1, 12.6)		-1.7 (-11.6, 8.1)		Group x Time	0.157
Knee Extension (N)	**FTG**	26	164.3±53.9	178.7±62.3	170.0±47.5	14.4 (-2.8, 31.7)		-8.7 (-20.8, 3.4)		Group	0.034
	CTG	25	190.9±56.9	223.1±59.6*§	216.7±72.5*§	32.3 (18.0, 46.5)	0.116	-6.4 (-27.2, 14.3)	0.674	Time	<0.001
	UCG	25	171.6±52.1	187.9±57.6	186.2±60.4	16.3 (3.4, 29.2)		-1.7 (-13.5, 10.1)		Group x Time	0.302

Data expressed as mean and ±SD, median [IQR 25-75%] or mean (95% CI); 6MWT: 6-minute walk test; m:meters; FTG: Functional circuit training group; CTG: Conventional training group; UCG: Usual care group; %: percentual; N: Newton; $^{\#}$p<0.05 Comparing baseline, final and follow-up moments (without difference identified for the groups in the Bonferroni post-test); *: p<0.05 compared to baseline. §: p<0.05 Compared to FTG; $^{¥}$: p<0.05 Compared to UCG.

5.4. DISCUSSION

This randomized controlled trial showed that an 8-week exercise training program that added functional exercises on top of traditional aerobic and resistance training could not improve PADL and perceived ADL limitations in patients with COPD. Conventional (aerobic and resistance) training showed better improvement in lower limbs muscle strength of knee extensors compared to FTG and of knee flexors compared to UCG.

We highlight that the only difference between the two exercise training groups (FTG and CTG) was the replacement of aerobic training by the functional exercise training in the third weekly session in FTG. Thus, it is suggested that the third weekly session of treadmill aerobic training was a determining factor for the improvement in lower limbs muscle strength in conventional training, as well as for the sustained effects on knee extension strength. Considering that functional training involved different activities and did not focus only on lower limbs. Thus, it can be suggested that the addition of functional training could cause better responses if added on different days than conventional training and not replacing the aerobic training.

Regarding the PADL, none of the groups presented modifications post-training, as well as, at 12 weeks post-training follow-up. Indeed, exercise training has demonstrated an small effect on PADL in patients with COPD[20], presenting better results in long-term rehabilitation programs[32]. The inclusion of the functional training failed in increase the PADL in a short time 8-weeks training for these patients. As previously suggested, only the replacement of the third section of aerobic training may not have been sufficient to promote behavioral change for these patients.

Improvement in ADL limitations was observed only in conventional (aerobic and resistance) training, with both statically significant, and minimal important difference[38]. However, the improvement in ADL limitations was lost at 12 weeks post-training follow-up. Improvements in lower limbs muscle strength was observed only in conventional training as well. In addition, the improvement in knee extension strength was sustained at 12 weeks post-training follow-up. The importance of improvement in ADL limitations in conventional training, reaching the minimal important difference, is related to the fact that this difference reflects improvements in dyspnea, health-related quality of life and the BODE index after an exercise training program[38]. Indeed, short term PR programs can improve ADL limitations in patients with COPD[24, 38, 39], however, it should be noted the loss of this improvement at 12 weeks post-training follow-up, observed in the present study, which suggests training to be continued during longer durations.

Maintained effects over a period after pulmonary rehabilitation have been demonstrated in long (six monthts)[40] and short term (seven weeks)[41] programs. Short-term training program was able to increase quadriceps strength and maintain for six months without a formal maintenance program[41]. The present study corroborates these findings, demonstrating sustained knee extension strength improvement at 12 weeks post-training follow-up in conventional training. However, the sustained effect in lower limb strength was not accompanied by sustained improvement in ADL Limitations.

Both exercise training programs were not sufficient to promote changes on functional exercise capacity. However, it is noteworthy that these individuals already had good functional exercise capacity at baseline, observed by the distance of the predicted (85.8% and 90.8% for FTG and CTG, respectively). It is known that not all patients with COPD are able to achieve the benefits of treatment, while those with greater functional impairment respond better to treatment[42].

The fact that the study was performed with patients of only one center can be considered a limitation, as well as the inability to blind the therapists and patients to the training protocol. However, assessors were blinded as to the allocation of participants to interventions. Another limitation was sample loss, largely due to the COVID-19 pandemic, however ITT analyses was conducted.

Conventional training showed to be the best alternative in a short term program to this patients. As future perspectives, it is suggested to carry out studies with the insertion of functional training in long training periods, as well as, with greater weekly frequency to assess whether there will be better responses in the evaluated outcomes.

5.5. CONCLUSIONS

In conclusion, combined aerobic and resistance training with functional exercises failed to improve the physical activity in daily life and activities of daily living limitations in patients with COPD. Eight weeks of conventional training (resistance and aerobic exercise) improved lower limbs muscle strength and limitations in activities of daily life, however, improvement in limitations in activities of daily life was not superior to the results from the other groups. Furthermore, improvement was sustained only in knee extension strength at 12-weeks post-training follow-up.

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Competing interests

The authors declare that they have no competing interests.

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6. FINAL CONCLUSIONS

The studies presented in this thesis allowed improving the knowledge regarding elastic resistance in patients with COPD. In addition, it was possible to evaluate the effects of the association of a functional exercise protocol with aerobic and resistance training in this population.

Regarding Lemgruber® elastic tubes,theycan be safely stretched up to 8 times in length. Resistance from individual tubes varies from 3N to 537N depending on elongation. Reference equations for resistance and elongation are provided, and the results offer increased knowledge of LET for its use in clinical practice.

The systematic review and meta-analysis showed that elastic resistance training can increase muscle strength in patients with COPD. Further, compared to resistance training using weight machines, elastic resistance training demonstrated similar effects on muscle strength, functional exercise capacity, HRQoL and dyspnea. The findings suggest elastic resistance as a potential alternative to conventional resistance training using weight machines in patients with COPD.

Finally, the randomized clinical trial showed that a short term (8-weeks) combination of a functional exercise training program, with an aerobic and resistance exercise training protocol, could not improve PADL and ADL limitations in patients with COPD. Improvement in ADL limitations was observed only in conventional (aerobic and resistance) training. This, however, was not superior to the results from the other groups. The improvement in ADL limitations was lost at 12 weeks post-training follow-up, which suggests training to be continued during longer durations.

7. ACTIVITIES DEVELOPED IN THE PERIOD OF THE DOCTORATE

7.1. Internationalization

-Participated in the research development “The effects of elastic resistance training in people with Chronic Obstructive Pulmonary Disease: a systematic review with a meta-analysis”, in partnership with Curtin University, Perth / Australia in April 2019.

-Conducted a research internship at UHasselt - Diepenbeek - Belgium, from March to August 2020.

7.2. Production of complete articles published in journals

1. de Lima FF; Cavalheri, V; Grigoletto, I; Camillo, CA; Ramos, EMC. Author Response to Wewege et al. *Physical Therapy*. v.101, 2021.

2. **de Lima, FF**; Cavalheri, V; Silva, BSA; Grigoletto, I; Uzeloto, JS; Ramos, D; Camillo, CA; Ramos, EMC. Elastic Resistance Training Produces Benefits Similar to Conventional Resistance Training in People with Chronic Obstructive Pulmonary Disease: Systematic Review and Meta-Analysis. *Physical Therapy*. v.100, p.1891 - 1905, 2020.

3.Uzeloto, JS; de Toledo-Arruda, AC; Silva, BSA; Golim, MA; Braz, AMM; **Lima, FF**; Grigoletto, I; Ramos, EMC. Systemic Cytokine Profiles of CD4+ T Lymphocytes Correlate with Clinical Features and Functional Status in Stable COPD. *International Journal of Chronic Obstructive Pulmonary Disease*. , v.15, p.2931 - 2940, 2020.

4. Grigoletto, I; Cavalheri, V; **Lima, FF**; Ramos, EMC. Recovery after COVID-19: The potential role of pulmonary rehabilitation. *Brazilian Journal of Physical Therapy*. v.24, p.463 - 464, 2020.

5. Freire, APCF; Camillo, CA; De Alencar Silva, BS; Uzeloto, JS; **Lima, FF**; Gobbo, LA; Ramos, D; Ramos, EMC. Resistance training using different elastic components offers similar gains on muscle strength to weight machine equipment in Individuals

with COPD: A randomized controlled trial. *Physiotherapy Theory and Practice*. v.24, p 1-14, 2020.

6. **deLima, FF**; Camillo, CA; Silva, IG; Uzeloto, JS; Vanderlei, FM; Ramos, D; Ramos, EMC. Effects of combining functional exercises with exercise training on daily physical activities and functionality in patients with COPD: a protocol for a randomized clinical trial. *Trials*. v.20, p.680. 2019.

7. **Lima, FF**; Camillo, CA; Reis, EAP; Job, AE; Silva, BSA; Topalovic, M; Ramos, D; Ramos, EMC. Mechanical properties, safety and resistance values of Lemgruber® elastic tubing. *Brazilian Journal of Physical Therapy*. , v.23, p.41 - 47, 2019.

8. Silva, BSA; Ramos, D; Camillo, CA; Trevisan, IB; Arévalo, GA; Freire, APCF; Leite, MR; **Lima, FF**; Gobbo, LA; Ramos, EMC. Resistance Training With Elastic Tubing Improves Muscle Strength, Exercise Capacity, and Post-Exercise Creatine Kinase Clearance in Subjects With COPD. *Respiratory Care*. , v.64, p.respcare.05975 - 835, 2019.

9. Silva, IS; Silva, BSA; Freire, APCF; Santos, APS; **Lima, FF**; Ramos, D; Ramos, EMC. Functionality of patients with Chronic Obstructive Pulmonary Disease at 3 months follow-up after elastic resistance training: a randomized clinical trial. *Pulmonology*. , v.24, p.354 - 357, 2018.

10. **Lima, FF**; Camillo, CA.; Gobbo, LA.; Trevisan, IB.; Nascimento, WBBM.; Silva, BSA.; Lima, MCS; Ramos, D.; Ramos, EMC. Resistance training using low cost elastic tubing is equally effective to conventional weight machines in middle-aged to older healthy adults: a quasi-randomized controlled clinical trial. *Journal of Sports Science and Medicine*. , v.17, p.153 - 160, 2018.

11. Vanderlei, FM; Zandonadi, F; **Lima, FF**; Silva, BSA; Freire, APCF; Ramos, D; Ramos, EMC. Acute Effects of Different Types of Resistance Training on Cardiac Autonomic Modulation in COPD. *Respiratory Care*. , v.63, p.respcare.05898, 2018.

12. Silva, BSA.; Lira, F; Rossi, FE; Ramos, D; Uzeloto, JS; Freire, APCF; **Lima,**

FF;Gobbo, LA.; Ramos, EMC. Inflammatory and Metabolic Responses to Different Resistance Training on Chronic Obstructive Pulmonary Disease: A Randomized Control Trial. *Frontiers in Physiology*. v,9, p.262, 2018.

13. Leite, MR; Uzeloto, JS; De Alencar Silva, BS; Freire, APCF; **Lima, FF**; Campos, Eduardo Zapaterra; Christofaro, Diego Giulliano Destro; Kalva-Filho, Carlos Augusto; Ramos, Dionei; Ramos, Ercy Mara Cipulo. Critical Velocity Determined by a Non-Exhaustive Method in Subjects with COPD. *Respiratory Care*. , v.63, p.respcare.05637, 2017.

14. Bertolini, GN; Ramos, D; Leite, MR; Carvalho Junior, LCS; Freire, APCF; **Lima, FF**; Silva, BSA; Pastre, CM; Ramos, EMC. Effects of a home-based exercise program after supervised resistance training in patients with chronic obstructive pulmonary disease. *Medicina* (USP. FMRP). v.49, p.331, 2016.

7.3. Published book

1. TOLETO ARRUDA, Alessandra Choqueta de et al. Asthma in the COVID-19 pandemic scenario:guidance and exercises/Asma no cenário da pandemia da COVID-19: guia de orientações e exercícios. Rio de Janeiro: Universidade Federal do Rio de Janeiro, Laboratório de Investigação em Avaliação e Reabilitação Pulmonar, 2021. E-book. Available in: http://hdl.handle.net/11422/13601

7.4.Presentation of studies

1. **Lima, FF**; Cavalheri, V; Silva, BSA; Grigoletto, I; Uzeloto, JS; Ramos, D; Camillo, CA; Ramos, EMC. Elastic resistance training in people with COPD: a systematic review and meta-analysis.2020. (Congress, Study Presentation).

2. **Lima, FF**; Buzzachera, C; Grigoletto, I; Uzeloto, J; Gabardo, J; Ramos, D; Camillo, CA; Ramos, EMC. Muscle oxygenation and hemodynamics after submaximal exercise in different COPD severities.2019. (Congress, Study Presentation).

3. **Lima, FF**; Freire, APCF; Silva, BSA.; Manfrim, PB; Previatto, MB; Gomes, PR;

Lourenco, J; Zandonadi, F; Ramos, D; Gobbo, LA; Camillo, CA; Ramos, EMC. Effects of resistance training using elastic tube or bands on muscle function and body composition in COPD subjects, 2016. (Congress, Study Presentation).

4. **Lima, FF**; Arevalo, GA; Franco, MC; Pinto, RZ; Freire, APCF; Gomes, PR; Camillo, CA; Ramos, D; Ramos, EMC. Factors influencing participation and adherence to a pulmonary rehabilitation program in patients with COPD: A qualitative study.2016. (Congress, Study Presentation).

5. **Lima, FF**; Moseley, A; Uzeloto, JS; Elkins, M; Franco, MC; Pinto, RZ; Freire, APCF; Camillo, CA; Ramos, D; Ramos, EMC. The quality of evidence-based clinical practice guidelines for chronic respiratory diseases could be improved: An observational study.2016. (Congress, Study Presentation).

7.5. Participation in events

1.**European Respiratory Society-ERS International Congress**, 2020. (Congress)

2. **LFIP 25 ANOS: Simpósio Online de Fisioterapia e Pesquisa em Reabilitação Pulmonar**, 2020. (Symposium)

3. **European Respiratory Society-ERS International Congress**, 2019. (Congress)

4. **XXIII Mostra de Projetos e Trabalhos Científicos do Curso de Fisioterapia da FCT/UNESP**, 2019. (Congress)

5. **Meeting Imunologia e exercício**, 2018. (Meeting)

6. **Redação Científica**, 2018. (Meeting)

7. **Ventilação Mecânica Básica e Avançado**, 2018. (Meeting)

8. **XXII Mostra de Projetos e Trabalhos Científicos do Curso de Fisioterapia da FCT/UNESP**, 2018. (Congress)

9. **XXI Mostra de Projetos e Trabalhos Científicos - FCT/UNESP**, 2017. (Congress)

10. **Encontro Nacional de Ensino, Pesquisa e Extensão - ENEPE**, 2016. (Congress)

11. **European Respiratory Society-ERS International Congress,** 2016. (Congress)

12. **I Simpósio de Fisioterapia Baseada em Evidências da FCT/UNESP**, 2016. (Symposium)

13. **EPAFIR - Encontro Paranaense Cardiorrespiratória e Fisioterapia em terapia intensiva da ASSOBRAFIR**, 2016. (Congress)

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7.6.Participation in Board of completion of course study

1. **LIMA, FF**; GRIGOLETTO, I; FREIRE, APCF. Participation in Board of Andressa L. C. Da Silva Santos E Caroline A. F. Da Silva. Satisfação De Fisioterapeutas Frente Á Utilização De Um Software Para Reabilitação Cardiopulmonar. 2020 (Physiotherapy), Universidade Estadual Paulista Júlio de Mesquita Filho

2. RAMOS, EMC; GRIGOLETTO, I; **LIMA, FF**. Participation in Board of Vittoria Raffaela Alves Formico. Identificação de Fatores que facilitam e dificultam a adesão de participantes a um programa de cessação tabagistica: um estudo qualitativo. 2019 (Physiotherapy), Universidade Estadual Paulista Júlio de Mesquita Filho

3. RAMOS, EMC; SILVA, RN; SANTOS, CP; **LIMA, FF**. Participation in Board of Taynara Veríssimo da Silva. Influência do tabagismo e do grau de dependência à nicotina na frequência cardíaca e em sintomas de dispneia e fadiga durante o exercício máximo, 2019 (Physiotherapy), Universidade Estadual Paulista Júlio de Mesquita Filho

4. RAMOS, EMC; **LIMA, FF**; UZELOTO, JS; GRIGOLETTO, I. Participation in Board of Ana Paula Rabelo Nespolo. Efeitos da inserção de um circuito funcional ao treinamento aeróbico e resistido na funcionalidade e dispneia de pacientes com DPOC: Um estudo clínico randomizado, 2018 (Physiotherapy)Universidade Estadual Paulista Júlio de Mesquita Filho

5. RAMOS, EMC; **LIMA, FF**; UZELOTO, JS; GRIGOLETTO, I. Participation in Board of Caio Marcelo Sereghetti da Silva. Efeitos da inserção de um circuito funcional ao

treinamento aeróbico e resistido na qualidade de vida e capacidade funcional de pacientes com DPOC: Um estudo clínico randomizado (TG I), 2018(Physiotherapy)Universidade Estadual Paulista Júlio de Mesquita Filho

6. RAMOS, EMC; UZELOTO, JS; SILVA, IG; **LIMA, FF**. Participation in Board of Vittoria Raffaela Alves Formico. Identificação de fatores que facilitam e dificultam a adesão de participantes a um programa de cessação tabagística: um estudo qualitativo, 2018(Physiotherapy) Universidade Estadual Paulista Júlio de Mesquita Filho

7. RAMOS, EMC; UZELOTO, JS; **LIMA, FF**. Participation in Board of Rafaela Simões de Camargo. Resposta metabólica de pacientes com DPOC submetidos a diferentes tipos de treinamento resistido: ensaio clínico randomizado, 2018 (Physiotherapy) Universidade Estadual Paulista Júlio de Mesquita Filho

8. RAMOS, EMC; **LIMA, FF**; TACAO, GY; UZELOTO, JS. Participation in Board of Ana Paula RabeloNespolo. Avaliação da aceitabilidade de pacientes com doença pulmonar obstrutiva crônica ao exercício físico em trilhas urbanas: um estudo qualiquantitativo (TG I - Co - orientador), 2017 (Physiotherapy) Universidade Estadual Paulista Júlio de Mesquita Filho

9. RAMOS, EMC; **LIMA, FF**; UZELOTO, JS. Participation in Board of Rafaela Simões de Camargo. Efeitos do treino resistido com tubos elásticos no perfil metabólicos de pacientes com DPOC, 2017(Physiotherapy) Universidade Estadual Paulista Júlio de Mesquita Filho

10. RAMOS, EMC; **LIMA, FF**; UZELOTO, JS. Participation in Board of Thais de Oliveira Souza. Influência de um feedback sobre os níveis de atividade física e seu impacto na capacidade funcional de Indivíduos tabagistas, 2017(Physiotherapy) Universidade Estadual Paulista Júlio de Mesquita Filho

11. RAMOS, D; GOUVEIA, TS; **LIMA, FF**; TACAO, GY. Participation in Board ofGiuliannaRibasMemoli. Síndrome de abstinência em tabagistas submetidos a um treino resistido com tubo elástico, 2017(Physiotherapy) Universidade Estadual

Paulista Júlio de Mesquita Filho

7.7. Participation in Board of judging committees

1.**XXIII Mostra de Projetos e Trabalhos Científicos do Curso de Fisioterapia da FCT/UNESP**, 2019 - Universidade Estadual Paulista Júlio de Mesquita Filho.

2. **XXII Mostra de Projetos e Trabalhos Científicos do Curso de Fisioterapia da FCT/UNESP**, 2018.- Universidade Estadual Paulista Júlio de Mesquita Filho.

3. **XXI Mostra de Projetos e Trabalhos Científicos do Curso de Fisioterapia - FCT/UNESP**, 2017 - Universidade Estadual Paulista Júlio de Mesquita Filho.

4. **Encontro Nacional de Ensino, Pesquisa e Extensão - ENEPE**, 2016. Universidade do Oeste Paulista – UNOESTE.

7.8. Citations

Web of Science: Total citations: 45; H Factor: 4; Date: 15/03/2021

SCOPUS: Total citations: 36; Date: 04/01/2021

Google Scholar: Total citations: 106; Date: 04/01/2021