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Peer-reviewed author version

DOI: 10.1080/09593985.2022.2148146
Handle: http://hdl.handle.net/1942/39186

COMBINING FUNCTIONAL EXERCISES WITH EXERCISE TRAINING IN COPD: A RANDOMIZED CONTROLLED TRIAL

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ABSTRACT

Introduction: Increasing physical activity in daily life (PADL) in COPD, mainly in short-term training programs, is still a challenge. The combination of functional exercises with aerobic and resistance training may be a strategy to improve PADL and limitations in activities of daily living (ADL) in COPD. **Objective:** To evaluated the short and medium-term effects of the combination of functional exercises with aerobic and resistance training. **Methods**: 76 patients were randomized into: Functional Training Group (FTG) who performed resistance and aerobic and functional exercises or; Conventional Training Group (CTG) who performed resistance and aerobic exercise or; Usual Care Group (UCG) who performed respiratory physiotherapy. Patients were evaluated about: PADL (activity monitor), ADL limitations (London Chest Activity of Daily Living scale- LCADL), functional exercise capacity (6-minute walk test 6MWT), and peripheral muscle strength before and after eight weeks. Medium-term effects were evaluated 12 weeks after the training. **Results:** There were no changes or differences between groups in PADL and in 6MWT post-intervention and 12 weeks post-training. Only CTG showed reduction in the total score on LCADL scale after the intervention and increase at follow-up (score: 20±8; 17±6; 19±8, pre, post-intervention, and 12 weeks post-training, respectively) ($p=0.001$), without differences between groups ($p=0.375$). There were increases in the muscle strength of knee flexors ($p=0.016$) and extensors ($p<0.001$) after the intervention only in CTG. **Conclusions:** Combined aerobic and resistance training with functional exercises failed to improve PADL and ADL limitations in COPD. Eight weeks of conventional training improved ADL. This, however, was not superior to the results from the other groups and was not sustained at medium-term 12 weeks post-training.

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

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

INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD) is a preventable disease characterized by persistent respiratory symptoms and airflow limitation. The disease is a public health challenge, and one of the leading causes of chronic morbidity and mortality (GOLD, 2020), being responsible for approximately 6% of total deaths worldwide (World Health Organization, 2018). Although COPD has primarily respiratory characteristics, patients also present significant extrapulmonary consequences, including skeletal muscle dysfunction, contributing to exercise intolerance (GOLD, 2020). These patients are less physically active than age-matched healthy individuals (Pitta et al, 2005; Vorrink, Kort, Troosters and Lammers, 2011), and lower levels of physical activity in daily life (PADL) are associated with hospitalizations (Garcia-Aymerich et al, 2006), worse prognosis (Gimeno-Santos et al, 2014), disease progression (Waschki et al, 2015), and an increased risk of premature death in COPD (Waschki et al, 2011).

Pulmonary rehabilitation (PR) is well established as an essential and integral part of the care of patients with COPD (McCarthy et al, 2015). Exercise training is considered the cornerstone of PR (Alison et al, 2017; Spruit et al, 2013), and aerobic and resistance training have been commonly proposed for these patients, showing promising results when combined (Bernard et al, 1999). In addition, it is recommended by international guidelines (Bolton et al, 2013; Ries et al, 2007). Although PR programs improve the functional exercise capacity in this population (McCarthy et al, 2015; Spruit et al, 2013), evidence on increased PADL in patients with COPD is contradictory and inconsistent (Garcia-Aymerich and Pitta, 2014; Spruit et al, 2013), suggesting a small effect on PADL and inconsistent translation of functional gain into increased PADL (Cindy Ng, Mackney, Jenkins and Hill, 2012). Furthermore, exercise training has demonstrated better results on PADL in long-term rehabilitation programs (Pitta, Troosters, et al, 2008). Thus strategies are necessary to improve PADL in a short term program.

In older adults, functional exercise training improves performance in activities of daily living (ADL), and mobility (de Bruin and Murer, 2007; Liu, Shiroy, Jones and Clark, 2014). This training involves coordinated patterns of multi-joint movements and dynamic tasks (Liu, Shiroy, Jones and Clark, 2014). When combined with another exercise modality, functional exercise training has demonstrated positive effects for patients with COPD (Sewell et al, 2005). However, despite the benefits obtained in 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 (short-term) of the training program (Sewell et al, 2005). Thus, it is not possible to know if the effects were maintained in medium-term after the program. Furthermore, the training protocol did not include progressive resistance training (Sewell et al, 2005), an essential component related to improvements in ADL performance in patients with COPD (O'Shea, Taylor and Paratz, 2009).

Thus, the present study evaluated the short term (8 weeks) and medium-term (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 was expected that the inclusion of functional training would promote behavioral change by improving ADL limitations, PADL, and exercise tolerance in patients with COPD.

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) (GOLD, 2020); 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; not participating in another structured exercise program. Exclusion criteria to consider dropouts were: 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 (FCT/UNESP), Presidente Prudente, Brazil (#77909317.2.0000.5402) and participants provided written informed consent. Specific details of the methods have been previously reported (de Lima et al, 2019).

Study design

A randomized controlled trial was conducted at the Center for Studies and Care in Physical Therapy and Rehabilitation of the FCT/UNESP, Presidente Prudente, Brazil. Participants underwent an initial assessment which included: anamnesis, lung function (spirometry) (Miller et al, 2005; Neder, Andreoni, Castelo-Filho and Nery, 1999); ADL limitations, functional exercise capacity, peripheral muscle strength, and PADL. Subsequently, 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 opaque envelopes. All evaluators were trained to carry out the evaluations and blinded to the allocation of participants to interventions. FTG performed resistance, aerobic, and functional exercise training; CTG performed aerobic and resistance exercise training, and UCG performed respiratory physiotherapy techniques. After eight weeks of training, the initial assessments were repeated. 12-weeks after the end of the training program, PADL, ADL limitations, functional exercise

capacity, and muscle strength were reassessed (follow-up after completion of the training program). Patients did not receive recommendations to continue exercise or physical activity during the follow-up period after the end of the intervention.

Intervention protocol

The exercise training program lasted 8 weeks, with a frequency of three sessions per week of approximately 60 minutes each session, totalizing 24 sessions. The sessions started with general dynamic stretching; the aerobic training was performed on a treadmill (Movement LX170/LX 3.0, Brazil) for 30 minutes starting with an intensity of 80% of the average speed reached in the six minute walk test (6MWT) and the progression was based on the subjective sensation of dyspnea of the individuals (4 – 6 on the Borg scale) (Garvey et al, 2016), thus, when the individual reports a dyspnea sensation with values between 4 and 6 on the Borg scale, the intensity was maintained, this being considered an adequate training intensity, however, when the intensity was less than 4, there was a 5% increase in training intensity. For the resistance training prescription, a 1-repetition maximum test (1RM) was performed of the following muscle groups: elbow flexors, and knee extensors and flexors. The resistance training was performed using weight machines (Ipiranga® - Brazil): 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 test, 3 sets of 10 repetitions and two-minute intervals between sets. The load increase was performed every four stimuli (sessions), with a 5% increase in the intensity of the 1RM test until reaching 80%. These dynamics were performed by both FTG and CTG, except for the third weekly session in which FTG performed the functional training in a circuit format instead of aerobic training. The functional circuit training was composed of 12 exercises (stations) that simulate ADL: Exercise 1: Simulate drying the back; Exercise 2: Simulate sweeping the floor; Exercise 3: Simulate Tying Shoes; Exercise 4: Simulate passing a squeegee on the floor; Exercise 5: Simulate bath movements to wash the

hair; Exercise 6: Simulate picking up objects in high and low places; Exercise 7: Simulate squatting; Exercise 8: Simulate walking on uneven ground using ramps and stairs; Exercise 9: Simulate standing up and sitting in a chair; Exercise 10: Simulate changing clothes; Exercise 11: Simulate the avoidance of obstacles during gait; Exercise 12: Simulate picking up objects. 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, thus, 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, measured using the Borg scale (4 – 6 on the Borg scale) (Borg, 1998). The UCG performed only respiratory physiotherapy including inhalation therapy, pulmonary deflation techniques, diaphragmatic awareness, and inspiratory muscle exercises, twice a week. Details of the training protocol, as well as the functional training, were described previously (de Lima et al, 2019).

PADL and ADL Limitation Measurements

The PADL was the primary outcome, and was assessed using an activity monitor (Actigraph-GT3X, Actigraph LLC, Pensacola, FL/USA). Participants were instructed to use the device for seven days. Specific software was used for data analysis (ActiLife5 – Data Analysis Software by Actigraph) Patients with at least 3 days of use (Pitta, Troosters, et al, 2008; Pitta et al, 2005), and at least 8 hours each day, were included in the analysis (Demeyer et al, 2014). Perceived ADL limitations were evaluated by the *London Chest Activity of Daily Living* scale (LCADL) (Garrod et al, 2000), validated for use in Brazilian patients with COPD (Carpes et al, 2008; Pitta, Probst, et al, 2008). The total score can vary from 0 to 75 points, and the higher the score, the greater the limitation in ADL (Carpes et al, 2008).

Functional Exercise Capacity and Muscle Strength Measurements

Functional exercise capacity was evaluated by the 6MWT, performed according to an international guideline (Holland et al, 2014). Muscle strength was evaluated using a digital dynamometer (Force Gauge®, model FG-100kg) and the results were expressed in Newtons (N). The muscle groups evaluated were: elbow flexors, knee flexors, and knee extensors.

Statistical analysis

The sample size determination was performed based on the PADL (Cruz, Brooks and Marques, 2016). 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 the 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, 8-weeks, and 12-week follow-up moments. The Bonferroni post-test was used to identify specific differences. The level of significance adopted was 5%. As established in the study protocol (de Lima et al, 2019), an intention-to-treat (ITT) analysis was carried out including all participants. In case of absence of data (i.e. attrition) the results of the last available assessment were carried forward.

RESULTS

The study flow is described in figure 1. Due to the dropout rates, per-protocol analyses (two-way ANOVA) were also performed, but the differences found were similar to those of the ITT analyses, thus the ITT analyses were maintained, as established in the previously published study protocol (de Lima et al, 2019).

Figure 1

Table 1 shows the baseline characteristics of the groups. 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

Comparisons of PADL and ADL limitations at baseline, 8 weeks, and follow-up are described in table 2. Sedentary time analyses showed no differences between groups, and no changes at 8-weeks and at the 12-week 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. 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). A between group difference was found only between CTG and UCG for the physical activity domain of the LCADL when comparing follow up and 8-week changes ($p=0.016$).

Table 2

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 the intervention only in CTG and maintenance of knee extensors strength ($p=0.005$ compared to baseline) at follow-up. Between group differences were found comparing knee extensor strength between CTG and FTG at 8-week ($p=0.030$) and follow-up ($p=0.023$) moments, as well as, comparing 8-week and baseline changes of knee flexors values between CTG and UCG ($p=0.044$) and between CTG and FTG ($p=0.049$). Showing superiority in strength gain in favor of CTG.

Table 3

DISCUSSION

The results of this randomized controlled trial showed that an 8-week exercise training program with functional exercises added to traditional aerobic and resistance training was not able to improve PADL and perceived ADL limitations in patients with COPD. Conventional (aerobic and resistance combined) training led to improvements in lower limb muscle strength of knee extensors compared to FTG and of knee flexors compared to FTG and 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 limb muscle strength in conventional training, as well as for the sustained effects in medium-term on knee extension strength. Considering that the functional training involved different activities and did not focus only on lower limbs, it can be suggested that the addition of functional training could cause better responses if added on different days to conventional training and not through replacement of the aerobic training.

Regarding the PADL, none of the groups presented modifications post-training or at the 12 week post-training follow-up. Indeed, exercise training has demonstrated a small effect on PADL in patients with COPD (Cindy Ng, Mackney, Jenkins and Hill, 2012), presenting better results in long-term rehabilitation programs (Pitta, Troosters, et al, 2008). The inclusion of the functional training failed to increase PADL in a short 8-week training protocol for these patients. As previously suggested, only the replacement of the third session of aerobic training may not have been sufficient to promote behavioral change in these patients. It is suggested that to achieve changes on PADL in these patients, interventions should include specific strategies

that focus on behavioral change to increase PADL, through increased motivation and self-efficacy to perform physical activity (Mantoani et al, 2016).

Improvement in ADL limitations was observed only in conventional (aerobic and resistance combined) training, with both statistical significance and reaching the minimum clinically important difference (MCID) (Almeida Gulart et al, 2020). However, the improvement in ADL limitations was not sustained at medium-term 12 week post-training follow-up. Improvements in lower limb muscle strength were also observed only in conventional training. The improvement in knee extension strength was sustained at the 12 week post-training follow-up. The importance of improvement in ADL limitations in conventional training, reaching the MCID, 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 (Almeida Gulart et al, 2020). Indeed, short term PR programs can improve ADL limitations in patients with COPD (Almeida Gulart et al, 2020; Sewell et al, 2005; Vaes et al, 2019), however, the loss of this improvement at the 12 week post-training follow-up, observed in the present study, suggests that training protocol should be continued over a longer period.

Maintained effects after pulmonary rehabilitation have been demonstrated in long (six months) (Troosters, Gosselink and Decramer, 2000) and short term (seven weeks) (Houchen et al, 2011) programs. A short-term training program was able to increase quadriceps strength, which was maintained for six months without a formal maintenance program (Houchen et al, 2011). The present study corroborates these findings, demonstrating sustained knee extension strength improvement at medium-term 12-week post-training follow-up after the conventional training. However, the sustained effect in lower limb strength was not accompanied by sustained improvement in ADL.

Neither of the exercise training programs were sufficient to promote changes in functional exercise capacity. However, it is noteworthy that these individuals already had good functional

exercise capacity at baseline, observed by the predicted distances (85.8% and 90.8% for FTG and CTG, respectively). It is known that not all patients with COPD are able to achieve benefits from treatment, while those with greater functional impairment respond better to treatment (Spruit et al, 2015).

The fact that this study was performed with patients from a single health center can be considered as a limitation, as well as the inability to blind the therapists and patients to the training protocol. However, assessors were blinded with respect to the allocation of participants to the interventions. Another limitation was sample loss, largely due to the COVID-19 pandemic, however ITT and per-protocol analyses demonstrated similar results.

Conventional training demonstrated to be the best alternative for a short-term program in these patients. The findings of this study showed that aerobic and resistance exercise training for at least 3 sessions per week for 8 weeks was necessary to demonstrate a significant effect on knee muscle strength, and that one session per week of functional task training was insufficient to demonstrate any effect on PADL Thus, it is suggested that at least three conventional training sessions are necessary to obtain better results for these patients. Furthermore, as future perspectives, it is suggested that studies are carried out including functional training in long training periods, as well as with a greater weekly frequency, to assess whether this leads to better responses in the evaluated outcomes.

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

extension strength was sustained. Based on these findings, conventional training is recommended, performed at least 3 times a week for these patients.

ACKNOWLEDGEMENTS

Funding: This work was supported by the São Paulo Research Foundation - FAPESP under Grants [number #2018/04871-0 #2017/10145-7]; and Coordenação de Aperfeiçoamento de Pessoal de Nível Superior - Brasil (CAPES) under Grant [Finance Code #001].

Disclosure statement: The authors report there are no competing interests to declare.

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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 (Steps/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 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; Total score LCADL: means of the total scores of the London Chest Activity of Daily Living scale; 6MWT: 6-minute walk test; m: Meters; N: Newtons.

Table 2. Comparisons of physical activity in daily life and ADL limitations.

		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 per 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 training group; CTG: Conventional training group; UCG: Usual care group; PADL: Physical activity in daily life; MVPA: Moderate to vigorous physical activity; %: Percentage; 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-week moment; #:$p<0.05$compared to UCG.

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											
	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
6MWTdistance (m)	**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
	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
6MWT% of Predicted	**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											
	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
Elbow Flexion (N)	**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
	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
Knee Flexion (N)	**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
	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
Knee Extension (N)	**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 training group; CTG: Conventional training group; UCG: Usual care group; %: Percentage; 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.

Figure captions

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