


# Influence of Respiratory Muscle Training on Patients' Recovery after Lung Resection

## Authors

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## Key words

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## ABSTRACT

This prospective experimental study aimed to compare effects of 3 different home-based postoperative respiratory muscle training protocols – inspiratory, expiratory and combined, in the patients' postoperative recovery, regarding safety and respiratory muscle function, pulmonary function, physical fitness, physical activity (PA), dyspnoea and quality of life (QoL). Patients were divided in four groups Usual Care (UCare), inspiratory (IMT), expiratory (EMT) or combined muscle training (CombT) according to group allocation. Significant treatment \* time interactions were found for maximal inspiratory pressure (MIP) ( $p = 0.014$ ), sedentary PA (SEDPA) ( $p = 0.003$ ), light PA (LIGPA) ( $p = 0.045$ ) and total PA ( $p = 0.035$ ). Improvements were observed for MIP in CombT ( $p = 0.001$ ), IMT ( $p = 0.001$ ), EMT ( $p = 0.050$ ). SEDPA reduced in EMT ( $p = 0.001$ ) and IMT ( $p = 0.006$ ), while LIGPA increased in both groups ( $p = 0.001$ ), as well as Total PA ( $p = 0.005$  and  $p = 0.001$ , respectively). In UCare, CombT, and EMT, QoL improved only for Usual Activities. In conclusion, the addition of respiratory muscle training to physiotherapy usual care is safe and effective to increase MIP and contribute to improve physical activity. The CombT showed greater improvement on MIP, while IMT compared to EMT, was more effective to improve physical activity.

## Introduction

Pulmonary surgical resection is the gold standard treatment for the early stages of lung cancer [1, 2].

After surgery, lung function and exercise capacity decline, adversely affecting quality of life (QoL) [3–5]. Surgery induce impairments of respiratory muscles which are related to the type of surgical incision, age and patients preoperative condition [6, 7]. Despite the increasing use of video-assisted thoracic surgery, posterolateral

thoracotomy still is a common surgical incision, leading to a higher impairment of pulmonary function and slower recovery [6, 8].

In chronic obstructive pulmonary disease (COPD) patients there is evidence that inspiratory muscle training (IMT) may improve inspiratory muscle strength and endurance, exercise capacity, dyspnoea and QoL [9, 10].

Few studies have evaluated the effect of IMT after pulmonary surgery in reducing postoperative pulmonary complications and

recovery of lung function, which may be due to concerns about the postoperative safety of IMT [2, 11]. Brocki et al. [2] examined the additive effect of usual physiotherapy care plus IMT, and despite the significant reduction in hypoxemia, no significant difference was observed in muscle strength, pulmonary volumes, physical performance, or dyspnoea. Nevertheless, in the former study the training load used after surgery was 15 % of the preoperative maximal inspiratory pressure (MIP), which raise the interrogation about the dose adequacy [2]. Moreover, few studies [12–14] assessed the effects of expiratory muscle training (EMT) in COPD patients. Despite this, it seems that both IMT and EMT, alone or combined, ameliorate i) physical fitness (PF) ii) resting and exertional dyspnoea symptoms; and iii) health-related quality of life. However, there are no studies conducted preoperatively or postoperatively, using EMT alone or combined with IMT in lung cancer surgical patients.

Therefore, this study aimed to compare the effects of 3 different home-based postoperative respiratory muscle training protocols – inspiratory, expiratory and inspiratory plus expiratory – regarding safety and respiratory muscle strength and endurance, in lung cancer patients submitted to pulmonary resection by thoracotomy.

Secondarily, this study aimed to assess the influence of the above-mentioned training protocols on patient's pulmonary function, daily physical activity (PA), PF, QoL, and dyspnoea.

## Materials and Methods

### Study design, recruitment, and data collection

This is a prospective experimental study approved by the Ethical Committee for Health of Hospital São João in October 19<sup>th</sup>, 2010, respecting the ethical standards of IJSM [15]. Patients were recruited between 2011–2015 at the Cardiothoracic Surgery Department, Hospital Centro Hospitalar de São João, Centre São João (Porto, Portugal). All patients diagnosed with lung cancer selected to any different pulmonary resections, except pneumonectomy, were invited to participate in the study during the first preoperative appointment (108 patients were contacted). The inclusion criterion were: i) adult patients, ii) selected for pulmonary resection by posterolateral thoracotomy. Exclusion criterion were i) patients selected for pneumonectomy ii) patients that underwent previous thoracic surgery; iii) mental disorders; iv) diagnostic of cardiac or neurologic diseases or renal failure; v) impaired autonomous deambulation. Eligible patients were randomly allocated using assignment by blocks. To generate random numbers, a randomizer form was programed for unsorted numbers with a range from 1 to 4 [representing the four conditions; IMT, EMT, combined training (CombT; IMT + EMT), and usual care (UsualC)].

All patients were treated by the same surgical team and received the same anaesthetic and analgesic protocol. During the hospital stay all patients received chest physiotherapy intervention twice a day.

In the first appointment after surgery an accelerometer was provided for the measurement of daily PA. Pulmonary function and PF were assessed, and instructions for respiratory muscle training were given.

Patients were instructed to report during the study period any adverse event as increased chest pain, alkalosis signs, perceived fatigue, respiratory discomfort or other pulmonary complications.

### Intervention

After hospital discharge all patients received outpatient physiotherapy, encompassing pulmonary expansion exercises, bronchial clearance and general exercises – usual care [5]. Adding to the usual care the intervention groups received home-based respiratory muscle training program, which last for eight weeks: IMT group receive inspiratory muscle training; EMT group received expiratory muscle training; CombT group received inspiratory muscle training plus expiratory muscle training. The usual care group (UCare) did not received any type of respiratory muscle training. Respiratory muscle training was performed six days a week, for fifteen minutes each session, at a pace of one breathing effort and one resting cycle, and supervised once a week. Adherence was self-reported.

### Inspiratory muscle training

Patients in IMT group received a Threshold IMT (Philips, Respironics), and during the first week exercised at 25 % of MIP, with a load increment of 5 % each week, until reaching 60 % of MIP. Patients were instructed to exercise from residual volume to the maximal tolerable inspiratory volume against the inspiratory resistance. Training was performed in a seated position, and wearing a nose clip.

### Expiratory muscle training

The EMT patients received a Threshold PEP (Philips Respironics), and were instructed to exercise from total lung capacity until maximal tolerable expiratory volume against the expiratory resistance to nearby residual volume, the training load and conditions were as described in the IMT.

### Combined training

Patients received both Threshold IMT and Threshold PEP. The training loads and procedures were the same as for IMT and EMT, with the exception for training volume, since IMT was performed during 15 min, and EMT for 15 min.

### Assessments

Clinical data included information about smoking habits. Anthropometrics included measurements of height, and weight, and body mass index (BMI) was calculated.

Dyspnoea was assessed with the Medical Research Council Dyspnoea Questionnaire (MRC) [16, 17].

The Portuguese version of EuroQoL (EQ-5D-3L) was used to assess QoL [18]. The EQ-5D-3L questionnaire encompasses five dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression [19, 20]. Pulmonary and respiratory muscles function tests were conducted according to the ATS/ERS guidelines using body plethysmography (MasterScreen™; Jaeger, Germany) [21, 22]. The measurements included forced vital capacity (FVC), forced expiratory volume in the first second (FEV<sub>1</sub>), Tiffeneau index (TI), peak expiratory flow (PEF), total lung capacity (TLC), diffusing capacity of the lung for carbon monoxide (DLCO), diffusing capacity of the lung for carbon monoxide per unit of alveolar volume

(DLCO/VA), respiratory muscle function [maximum voluntary ventilation (MVV), maximal inspiratory pressure (MIP) and maximal expiratory pressure (MEP)].

Physical fitness was assessed by the six minutes' walk distance test (6-MWD), according to the American Thoracic Society (ATS) guidelines [23]. During the test heart rate and oxygen saturation were monitored using the PULSO X-3i (Konica Minolta).

Daily PA was measured by accelerometry [Actigraph GT1M (ActiGraph, LLC, Pensacola, FL, USA)] during 7 consecutive days, with a minimum of 8-hours/day (480min/day), and at least four-week days and one weekend day [24]. The standard software ActiLife (version 6.13.2, ActiGraph, LLC, Pensacola, FL, USA) was used for data analysis.

The reduced data was: total time of recording, total PA (total PA), time in sedentary PA [(SEDPA) (0–99 cpm)], light PA [(LIGPA) (100–2019 cpm)], moderate to vigorous PA [(MVPA) ( $\geq$  2020 cpm)], and the ratio of time spent in each intensity was calculated, and expressed as a percentage (SEDPA%; LIGPA%; MVPA%) [25].

### Statistical analysis

At baseline, between-treatment comparisons were carried out through One-way Analysis of Variance (one-way ANOVA), with Bonferroni post hoc tests for continuous variables, and Chi-square test for categorical data. To analyse the effectiveness of the home-based respiratory muscle training in the dependent variables, General Linear Model (GLM) – Repeated Measures ANOVA with Bonfer-

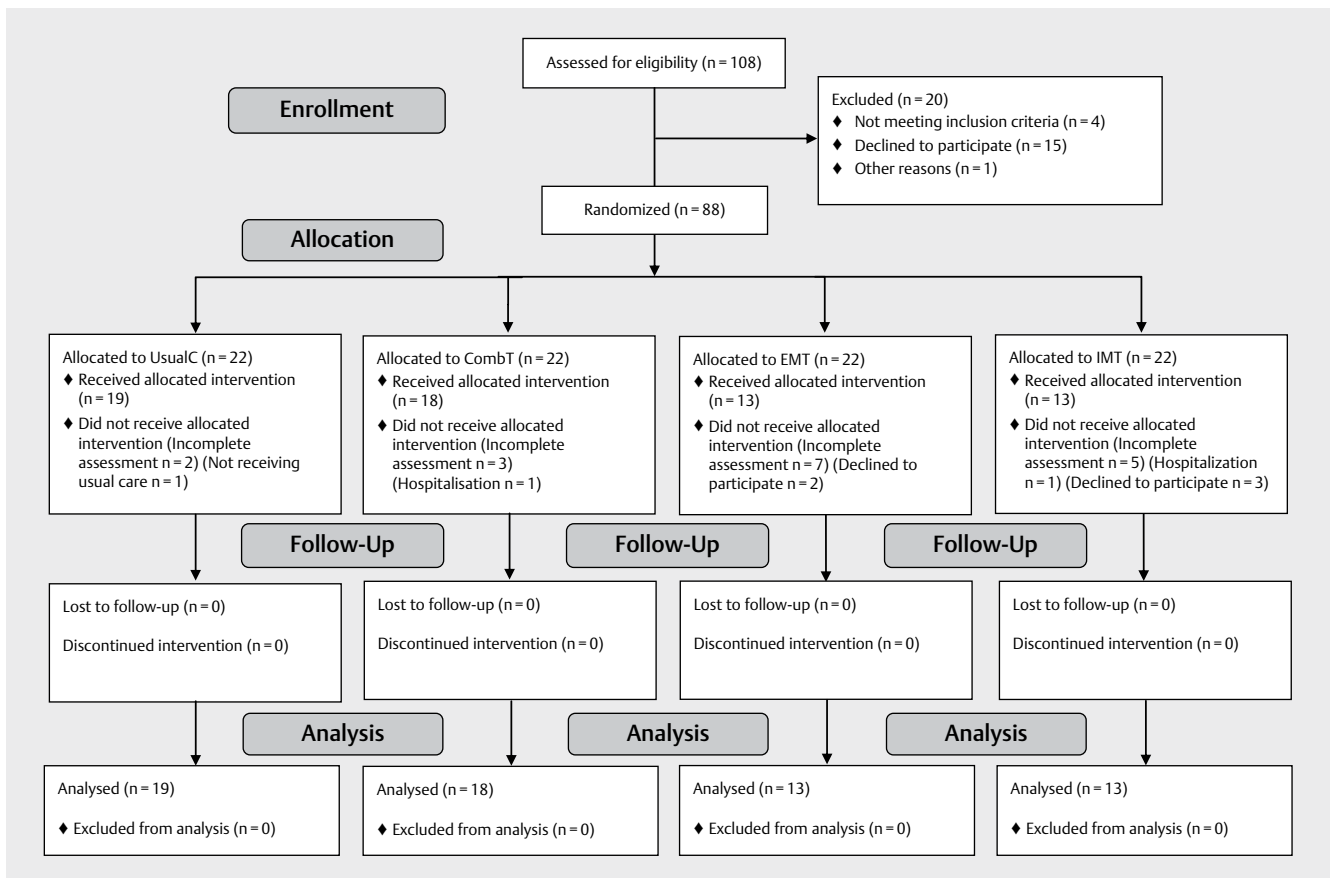
roni corrections were carried out for each outcome. As recommended elsewhere, [26–28] the effectiveness of the intervention was assumed if treatment \* time interactions were significant. When a significant treatment \* time interaction was observed, a Univariate GLM ANOVA with Bonferroni post hoc tests was performed with treatment as the fixed factor to ascertain the differences between groups (IMT, EMT, CombT and UCare) at the final assessment. Partial eta-squared ( $\eta^2_p$ ) was reported as the effect size. For analysis of QoL dimensions, excepting health state, non-parametric methods were used. The Kruskal–Wallis test by ranks was used for between groups comparisons of changes between baseline and final assessment. The Wilcoxon signed-rank test was used to for comparisons within groups. Statistical significance was set at  $p < 0.05$ . All analyses were carried out in SPSS 21.0 (SPSS Inc., Chigago, IL, USA).

### Results

From the 108 patients assessed for eligibility, 63 patients completed the training protocol (UCare,  $n = 19$ ; CombT,  $n = 18$ ; IMT,  $n = 13$ ; EMT,  $n = 13$ ) (► **Fig. 1**).

At baseline there were no differences between groups regarding age, sex, and clinical data (► **Table 1**). Moreover, no group effect was detected at baseline for indicators of physical fitness, physical activity or quality of life.

There were no adverse events during the study period.



► **Fig. 1** Flow diagram of patients.

► **Table 1** Baseline patients characteristics, and between groups comparisons [data is presented as mean (SD) or n (%)].

	UCare (n=19)	CombT (n=18)	EMT (n=13)	IMT (n=13)	Statistic	p-value
	mean (SD)	mean (SD)	mean (SD)	mean (SD)		
Age (years)	63.42 (9.38)	64.06 (5.81)	60.00 (13.02)	62.31 (8.66)	F=0.540	0.657
Height (cm)	165.11 (6.74)	165.17 (8.01)	162.77 (12.34)	167.77 (9.27)	F=0.672	0.573
Weight (kg)	69.32 (10.10)	71.67 (10.60)	66.08 (11.93)	72.42 (14.23)	F=0.836	0.480
BMI (Kg/m <sup>2</sup> )	25.38 (2.92)	26.15 (2.31)	24.92 (3.41)	25.59 (3.49)	F=0.455	0.715
Cigarettes peck-year	40.58 (36.69)	52.47 (50.82)	30.58 (27.01)	33.42 (36.70)	F=0.953	0.421
Postoperative hospital stay (days)	7.11 (5.55)	7.28 (2.97)	7.54 (3.41)	10.31 (10.43)	F=0.879	0.457
	n (%)	n (%)	n (%)	n (%)		
<b>Sex</b>					$\chi^2=2.338$	0.505
Woman	7 (36.8)	9 (50)	5 (38.5)	3 (23.1)		
Men	12 (63.2)	9 (50)	8 (61.5)	10 (76.9)		
<b>Smoking relapse</b>					$\chi^2=1.544$	0.672
No	17 (89.5)	16 (88.9)	13 (100)	12 (92.3)		
Yes	2 (10.5)	2 (11.1)	0 (0)	1 (7.7)		
<b>Neoadjuvant therapy</b>					$\chi^2=4.192$	0.651
No	17 (89.5)	15 (83.3)	12 (92.3)	10 (76.9)		
Chemotherapy	2 (10.5)	2 (11.1)	1 (7.7)	3 (23.1)		
Chemotherapy + radiotherapy	0 (0)	1 (5.6)	0 (0)	0 (0)		
<b>Coadjuvant treatment</b>					$\chi^2=7.883$	0.247
No	12 (63.2)	10 (55.6)	6 (46.2)	10 (76.9)		
Chemotherapy	7 (36.8)	6 (33.3)	7 (53.8)	3 (23.1)		
Chemotherapy + radiotherapy	0 (0)	2 (11.1)	0 (0)	0 (0)		
<b>Surgery</b>					$\chi^2=5.388$	0.495
Low lob	7 (36.8)	8 (44.4)	3 (23.1)	6 (46.2)		
Superior Lob	9 (47.4)	9 (50)	9 (69.2)	4 (30.8)		
Others	3 (15.8)	1 (5.6)	1 (7.7)	3 (23.1)		
<b>Bronchodilators</b>					$\chi^2=2.034$	0.565
no	17 (89.5)	13 (72.2)	11 (84.6)	10 (76.9)		
yes	2 (10.5)	5 (27.8)	2 (15.4)	3 (23.1)		
<b>Corticoids</b>					$\chi^2=5.227$	0.156
no	18 (94.7)	13 (72.2)	12 (92.3)	12 (92.3)		
yes	1 (5.3)	5 (27.8)	1 (7.7)	1 (7.7)		

UCare – usual care; CombT – combined respiratory muscle training; IMT – inspiratory muscle training; EMT – expiratory muscle training; BMI – Body mass index.

The between-treatment comparisons (treatment \* time interaction) for pulmonary function, PF, PA and perceived health status, is presented in ► **Table 2**.

Significant treatment \* time interactions were found for MIP, MIP%, SEDPA, SEDPA%, LIGPA%, Total PA.

The analysis of mean differences between final assessment and baseline (► **Table 3**), showed significant improvements of MIP and MIP% in CombT, EMT, and IMT groups, with the largest effect sizes achieved by CombT group, followed by IMT and EMT groups, respectively. The SEDPA, SEDPA%, LIGPA%, and Total PA, improved significantly in the EMT and IMT groups (► **Table 3**), with largest effect sizes favouring the IMT group.

The possible bias related to the seasonality on physical activity behaviors was checked and the proportion of physical activity measurements at spring, summer, autumn or winter was similar across groups ( $\chi^2=7.783$ ,  $p=0.556$ ).

No differences between groups were found at baseline for QoL.

As can be observed in ► **Table 2**, no significant treatment \* time interaction was observed for perceived health state. Regarding the five dimensions of QoL there was no significant differences between groups from baseline to final assessment. However, comparisons within groups (baseline *versus* final assessment) shown significant improvements in usual activities for UCare ( $z=-2,496$ ;  $p=0.013$ ), CombT ( $z=-3.000$ ;  $p=0.003$ ), and EMT ( $z=-2,646$ ;  $p=0.008$ ). No differences were observed in the other QoL dimensions.

## Discussion

This study compared 3 different home-based postoperative respiratory muscle training protocols – inspiratory, expiratory and inspiratory plus expiratory – regarding safety and respiratory muscle function, in patients submitted to pulmonary resection by thoracotomy. Secondly, this study aimed to examine the influence of

► **Table 2** Changes in pulmonary function, fitness, physical activity and quality of life across groups, and between-treatment comparison (treatment\* time interaction).

	UCare		CombT		EMT		IMT		Treatment* time interaction	
	Baseline	Final	Baseline	Final	Baseline	Final	Baseline	Final	F	p-value
<b>Clinical data and respiratory function</b>										
Pain	2.8 (2.1)	1.1 (1.6)	3.6 (1.6)	1.8 (2.3)	2.7 (1.7)	1.2 (2.2)	2.1 (1.7)	0.5 (0.9)	0.049	0.986
Dyspnoea	2.3 (0.9)	1.9 (0.7)	2.4 (0.6)	1.9 (0.7)	2.3 (0.5)	1.5 (0.5)	2.4 (0.7)	1.5 (0.7)	1.580	0.204
FVC (L)	2.8 (0.8)	2.9 (0.8)	2.6 (0.7)	3.0 (0.7)	2.8 (0.7)	3.1 (0.8)	3.1 (0.9)	3.3 (0.9)	1.486	0.228
FVC (%)	84.5 (14.2)	91.1 (15.8)	86.9 (17.5)	97.9 (17.3)	92.4 (17.4)	100.2 (16.8)	88.0 (20.4)	94.6 (20.0)	1.522	0.218
FEV <sub>1</sub> (L)	1.8 (0.5)	2.0 (0.6)	1.9 (0.5)	2.0 (0.5)	2.1 (0.6)	2.2 (0.7)	2.3 (0.7)	2.4 (0.7)	0.090	0.965
FEV <sub>1</sub> (%)	69.9 (14.6)	76.3 (17.9)	77.5 (16.9)	81.9 (15.5)	83.8 (17.1)	90.6 (19.9)	80.6 (17.3)	85.9 (18.0)	0.428	0.734
PEF (L/s)	4.9 (1.7)	5.2 (1.7)	5.2 (1.4)	5.6 (1.2)	5.0 (1.8)	5.6 (1.3)	6.4 (2.2)	6.7 (2.1)	0.273	0.845
PEF (%)	69.3 (21.0)	73.7 (19.6)	78.5 (17.2)	84.8 (18.2)	77.3 (14.2)	81.3 (12.0)	85.2 (22.0)	89.7 (19.7)	0.111	0.953
IT	66.2 (8.9)	66.7 (9.4)	72.3 (12.8)	68.2 (10.1)	73.2 (8.6)	72.7 (8.7)	73.6 (10.1)	71.9 (8.3)	2.317	0.085
MVV (L/min)	73.5 (22.3)	81.1 (27.7)	68.8 (15.6)	80.1 (17.0)	87.8 (30.7)	92.7 (29.3)	94.7 (29.4)	100.5 (34.5)	0.613	0.609
MVV (%)	72.2 (17.1)	79.7 (22.3)	71.1 (15.1)	82.1 (14.0)	87.7 (23.4)	91.6 (14.8)	87.4 (20.9)	92.3 (24.5)	0.883	0.455
MIP (cmH <sub>2</sub> O)	75.3 (23.4)	79.6 (31.4)	67.5 (21.4)	87.1 (22.1)	79.0 (21.8)	86.9 (17.1)	92.9 (24.1)	106.2 (30.1)	3.853	0.014*
MIP%	70.4 (22.1)	73.3 (28.9)	62.7 (20.1)	80.7 (20.5)	73.1 (20.4)	80.4 (16.3)	88.4 (25.1)	101.8 (29.7)	5.271	0.003*
MEP (cmH <sub>2</sub> O)	87.2 (22.5)	92.6 (24.5)	87.9 (24.6)	100.5 (24.0)	86.5 (29.6)	93.6 (23.3)	95.7 (27.7)	101.4 (33.4)	0.620	0.605
MEP%	84.9 (19.6)	90.6 (22.7)	93.1 (30.6)	105.5 (27.7)	83.0 (28.1)	90.9 (28.9)	83.0 (20.6)	90.3 (37.9)	0.327	0.806
TLC (L)	5.3 (1.1)	5.2 (1.1)	5.2 (1.2)	5.3 (0.8)	5.5 (1.1)	5.7 (1.1)	5.5 (0.8)	6.1 (1.0)	2.214	0.096
TLC (%)	93.5 (13.8)	97.3 (10.5)	96.7 (12.6)	96.7 (11.2)	101.4 (13.1)	103.0 (8.2)	93.3 (12.7)	102.0 (14.3)	1.854	0.147
DICO (mmol/min/kPa)	5.2 (1.7)	5.3 (1.9)	4.5 (1.3)	5.0 (0.9)	4.8 (1.2)	5.0 (1.7)	4.9 (1.1)	5.4 (1.2)	0.644	0.590
DICO (%)	64.4 (16.5)	64.8 (19.0)	57.7 (11.3)	63.9 (9.6)	62.6 (16.7)	63.4 (15.4)	60.0 (13.0)	64.6 (11.6)	0.786	0.506
DICO/VA (mmol/min/kPa/L)	1.2 (0.3)	1.2 (0.4)	1.1 (0.2)	1.1 (0.2)	1.1 (0.2)	1.1 (0.2)	1.1 (0.3)	1.1 (0.3)	1.091	0.360
DICO/VA (%)	82.5 (21.2)	83.0 (20.9)	73.8 (14.9)	79.0 (11.4)	78.5 (20.5)	74.1 (16.9)	80.4 (17.9)	81.1 (20.7)	1.123	0.347
<b>Physical activity, Physical fitness and Quality of life</b>										
6-MWD (m)	442.9 (72.4)	482.9 (63.1)	425.2 (54.4)	462.7 (38.1)	429.2 (56.0)	442.7 (74.1)	462.5 (63.3)	469.6 (64.1)	1.949	0.132
Total rec. time (min/day)	702.1 (85.6)	728.7 (82.4)	739.0 (92.3)	806.0 (99.1)	742.3 (79.8)	732.8 (82.5)	744.1 (36.5)	743.7 (65.9)	2.545	0.065
SEDPA (min/day)	472.2 (72.4)	475.9 (71.1)	485.8 (96.1)	516.3 (112.2)	537.7 (73.4)	484.6 (66.6)	532.8 (74.3)	474.4 (74.4)	5.329	0.003*
SEDPA (%)	67.3 (7.0)	65.7 (9.4)	65.6 (9.1)	63.7 (9.1)	72.4 (5.9)	66.3 (8.1)	71.6 (9.3)	63.8 (8.0)	4.195	0.009*
LIGPA (min/day)	211.2 (51.6)	230.1 (76.1)	237.3 (68.2)	272.2 (68.0)	191.6 (45.2)	230.3 (65.5)	197.8 (63.2)	243.5 (58.3)	0.799	0.499
LIGPA (%)	30.0 (6.3)	31.3 (8.7)	32.2 (8.9)	34.0 (8.6)	25.9 (5.3)	31.3 (7.3)	26.6 (8.7)	32.7 (7.4)	2.851	0.045*
MVPA (min/day)	18.7 (20.0)	22.7 (19.2)	15.9 (16.6)	17.6 (15.3)	13.0 (8.6)	18.0 (13.8)	13.6 (9.9)	25.8 (15.5)	2.290	0.088
MVPA (%)	2.7 (2.7)	3.1 (2.6)	2.2 (2.4)	2.3 (2.1)	1.7 (1.0)	2.4 (1.8)	1.8 (1.3)	3.6 (2.4)	2.623	0.059
Total PA (counts/min)	241.4 (117.3)	270.9 (135.0)	227.2 (93.8)	245.5 (103.0)	178.4 (54.2)	239.0 (95.1)	194.7 (84.8)	289.5 (115.9)	3.061	0.035*
QoL(perceived health state)	69.0 (20.1)	77.9 (15.4)	70.4 (19.8)	73.9 (14.4)	75.0 (17.8)	83.9 (12.6)	72.3 (15.1)	80.8 (15.5)	0.320	0.811

Data are mean (SD); \* p<0.05. Legend: UCare – usual care; CombT – combined respiratory muscle training; IMT – inspiratory muscle training; EMT – expiratory muscle training; FVC – Forced Vital Capacity; FVC% – Forced Vital Capacity percent of predicted; FEV<sub>1</sub> – Forced Expiratory Volume in 1 second; FEV<sub>1</sub>% – Forced Expiratory Volume in 1 second percent of predicted; PEF – Peak Expiratory Flow; PEF% – Peak Expiratory Flow percent of predicted; TI – Tiffeneau Index; MVV – Maximal Voluntary Ventilation; MVV% – Maximal Voluntary Ventilation percent of predicted; MIP – Maximal Inspiratory Pressure; MIP% – Maximal Inspiratory Pressure percent of predicted; MEP – Maximal Expiratory Pressure; MEP% – Maximal Expiratory Pressure percent of predicted; TLC – Total Lung Capacity; TLC% – Total Lung Capacity percent of predicted; DICO – Diffusion Lung Capacity for Carbon Monoxide; DICO% – Diffusion Lung Capacity for Carbon Monoxide percent of predicted; DICO/VA – Diffusion Lung Capacity for Carbon Monoxide per unit alveolar volume; DICO/VA% – Diffusion Lung Capacity for Carbon Monoxide per unit alveolar volume percent of predicted; 6-MWD – Six-Minute Walking Distance Test; Total rec. time – Accelerometer total recording time; SEDPA – Sedentary Physical Activity; LIGPA – Light Physical Activity; MVPA – Moderate to Vigorous Physical Activity; Total PA (counts/min) – Total Physical Activity; QoL – Quality of Life.

► **Table 3** Mean differences between final assessment and baseline, and effect sizes in the treatment groups where a significant treatment \* time interaction was observed.

	CombT			EMT			IMT					
	Mean difference	F	p	Partial $\eta^2$	Mean difference	F	p	Partial $\eta^2$	Mean difference	F	p	Partial $\eta^2$
MIP (cmH <sub>2</sub> O)	19.593 (3.359)	0.634	0.001	0.366	7.898 (3.953)	0.937	0.050	0.063	13.295 (3.953)	0.839	0.001	0.161
MIP %	18.021 (2.881)	0.601	0.001	0.399	7.292 (3.390)	0.927	0.036	0.073	13.421 (3.390)	0.790	0.001	0.210
SEDPA (min/day)	-	-	-	-	-53.117 (20.466)	0.898	0.012	0.102	-58.382 (20.466)	0.879	0.006	0.121
SEDPA (%)	-	-	-	-	-6.084 (1.619)	14.122	0.001	0.193	-7.825 (1.619)	23.363	0.006	0.284
LIGPA (%)	-	-	-	-	5.381 (1.577)	11.645	0.001	0.165	6.067 (1.577)	14.801	0.001	0.201
Total PA (counts/min)	-	-	-	-	60.624 (21.016)	0.876	0.005	0.124	94.763 (2.016)	0.744	0.001	0.256

CombT – combined respiratory muscle training; EMT – expiratory muscle training; IMT – inspiratory muscle training; MIP % – percentage of maximal inspiratory pressure; SEDPA – time in sedentary physical activity; SEDPA (%) – time in sedentary physical activity as percentage of total wear time; LIGPA (%) – time in light physical activity as percentage of total wear time; Total PA – total physical activity.

training protocols, on patient's pulmonary function, daily PA, PF, QoL, and dyspnoea.

The main findings were i) the safety of training protocols, given that no recordings of adverse occurrences were observed, ii) the effectiveness of home-based training on the inspiratory muscles strength, and iii) the improvements on daily PA.

Regarding the training-induced improvement on MIP, changes were more noticeable in the CombT, followed by the IMT and the EMT, respectively. Two meta-analysis including studies enrolling COPD [9] and preoperative surgical [29] patients had showed that IMT is effective to improve respiratory muscle strength and endurance. Our findings agreed partly with these meta-analysis, since we didn't find any significant change on the maximum voluntary ventilation, whatever the training protocol used.

After lung resection respiratory muscle strength decrease, especially in thoracotomy, even 12 weeks after surgery [6], and it was expected that each training protocol lead to improvements of specific exercised muscles. Surprisingly, MEP didn't improve in the EMT group. This might be related to the used gadget that was built for PEP therapy, and not for EMT. Therefore, the training load range from 4 to 20 cm H<sub>2</sub>O, for some patients is not enough to reach the desirable training load. This can be considered a constraint in our study. Another possible reason for the lack of improvements on MEP, and also on maximum voluntary ventilation, might be related to training adhesion, which was self-reported, and therefore might be biased. To our best knowledge, beyond the impact of the type of surgical incision [6], there is no published data regarding the influence of the pulmonary resections extent on respiratory muscle function decline.

Notwithstanding, when EMT was combined to IMT, MIP improvements overcome the observed in the other training groups. A possible explanation for this finding might reside on training volume, as the CombT group practice IMT and EMT during 15 min/day each muscles, while the other groups practice only 15 min. This possibility might not be the main explanation for the higher MIP improvement on CombT group since the specific overload for each muscle was the same among groups, independently of the training volume. Another reason could be related to the fact that EMT mobilizes air from total lung capacity, which might contribute to the gain on MIP. Nevertheless, the most important contribution to explain this improvement might be the agonistic role of the trained expiratory muscles during inspiration, as suggested by the MIP improvement in the EMT group. A recent study report that during inspiration with expiratory load the individuals "at risk" of COPD showed a significant higher activation of the rectus abdominal, while in healthy group it was observed an increased activation of transversus, external and internal oblique muscles. It is possible that expiratory muscles reinforcement promoted by EMT, lead to better inspiration efficiency [30].

Future studies might ascertain if daily supervised training is more/as effective as home-based training on changing respiratory muscle function. According to the meta-analysis conducted by Kendall et al. [31], there are several issues that might empower inspiratory muscle training, as starting load < 30 % of MIP, with deliberated load increment, session duration > 15 min, training length > 2 weeks, and daily training supervision combined with exercise [31].

Regarding the secondary aims, total PA and light PA increased, and percentage of sedentary time diminished, both in IMT and EMT groups, being the effect size higher in the IMT group. After lung resection with or without adjuvant therapy patients experience reduced PA, persistent fatigue, exercise intolerance, depression and loss of QoL [32].

Granger et al. [33] analysed PA in patients with lung cancer, comparing surgical patients and non-surgical patients by the time of diagnoses and after treatment (8–10 weeks), and found that after surgery patients PA showed a significant reduction while in patients submitted to adjuvant therapy it remained unchanged. According to Novoa et al. [34], one month after lobectomy, patients reduce by 25% the total steps number, and by 28% the total walking distance. It is likely that the participants in the present study also experienced PA reductions after surgery, which were posteriorly reversed by IMT and EMT. However, we can't explain these PA changes since we don't observe changes in pulmonary function, dyspnoea, pain and PF, which might be plausible modulators of PA levels [9]. Furthermore, there is no explanation why PA was unchanged in CombT.

No significant changes were found in the other secondary outcomes, as pulmonary function, PF, dyspnoea, and QoL excepting usual activities.

Having into account that in the first month after surgery the pulmonary function recovers almost completely, it is plausible that when the interventions started there is little room to additional improvements on pulmonary function [5, 35].

Regarding PF, Cavalhieri et al. [36] highlighted that lung cancer might induce disruption in pulmonary mechanics and gas exchange, leading to weight loss, anorexia, anaemia, protein catabolism and muscle wasting. Moreover, dyspnoea and fatigue are associated to increased sedentary behaviours leading to skeletal muscle and cardiovascular deconditioning. According to Nagamatsu et al. [35] exercise intolerance is also attributed to the lung volume reduction accompanied by pulmonary vascular bed reduction, increased load on the right side of the heart, and therefore, compromising cardiovascular function. Moreover, complete recovery (95%) of exercise capacity usually takes place 1 year after surgery [35], which might explain the lack of significant changes in PF in our study.

Given that for COPD patients the recommended duration of rehabilitation programs should last 12 weeks [37], it is arguable that if the training protocol had exceeded 8 weeks, a greater effect on secondary outcomes would be expectable.

Regarding QoL, improvements were only significant for the usual activities. Interestingly, the changes were significantly higher in the UCare, as compared to CombT and EMT groups, respectively, and no significant changes in the IMT group.

Regarding other outcomes that did not changed, we assume that the physiotherapy usual care was effective to improve patient's recovery.

This study has several limitations. First, related to the small sample size, which could have limited the power to reach levels of significance in several outcomes. Moreover, the adequacy of expiratory muscle trainer would not be the best instrument to expiratory muscle training.

## Conclusions

After pulmonary resections, except pneumonectomy, respiratory muscle training combined with conventional physiotherapy is effective to ameliorate inspiratory muscle strength and contribute to increase daily PA. The combination of IMT plus EMT plus usual care showed better results to improve MIP, while IMT alone compared to EMT, was more effective to improve daily PA levels.

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## Conflict of Interest

The authors declare that there is no conflict of interest.

## References

- [1] Cukic V. Reduction of pulmonary function after surgical lung resections of different volume. *Med Arch* 2014; 68: 231–235
- [2] Brocki BC, Andreasen JJ, Langer D et al. Postoperative inspiratory muscle training in addition to breathing exercises and early mobilization improves oxygenation in high-risk patients after lung cancer surgery: a randomized controlled trial. *Eur J Cardiothorac Surg* 2016; 49: 1483–1491
- [3] Kwon S, Symons R, Yukawa M et al. Evaluating the association of preoperative functional status and postoperative functional decline in older patients undergoing major surgery. *Am Surg* 2012; 78: 1336–1344
- [4] Brunelli A. Risk assessment for pulmonary resection. *Semin Thorac Cardiovasc Surg* 2010; 22: 2–13
- [5] Kendall F, Abreu P, Pinho P et al. The role of physiotherapy in patients undergoing pulmonary surgery for lung cancer. A literature review. *Rev Port Pneumol (2006)* 2017; 23: 343–351
- [6] Nomori H, Horio H, Fuyuno G et al. Respiratory muscle strength after lung resection with special reference to age and procedures of thoracotomy. *Eur J Cardiothorac Surg* 1996; 10: 352–358
- [7] Qaseem A, Snow V, Fitterman N et al. Risk assessment for and strategies to reduce perioperative pulmonary complications for patients undergoing noncardiothoracic surgery: A guideline from the American College of Physicians. *Ann Intern Med* 2006; 144: 575–580
- [8] Nomori H, Ohtsuka T, Horio H et al. Difference in the impairment of vital capacity and 6-minute walking after a lobectomy performed by thoracoscopic surgery, an anterior limited thoracotomy, an anteroaxillary thoracotomy, and a posterolateral thoracotomy. *Surg Today* 2003; 33: 7–12
- [9] Gosselink R, De Vos J, van den Heuvel SP et al. Impact of inspiratory muscle training in patients with COPD: What is the evidence? *Eur Respir J* 2011; 37: 416–425

- [10] Charususin N, Gosselink R, McConnell A et al. Inspiratory muscle training improves breathing pattern during exercise in COPD patients. *Eur Respir J* 2016; 47: 1261–1264
- [11] Weiner P, Man A, Weiner M et al. The effect of incentive spirometry and inspiratory muscle training on pulmonary function after lung resection. *J Thorac Cardiovasc Surg* 1997; 113: 552–557
- [12] Mota S, Guell R, Barreiro E et al. Clinical outcomes of expiratory muscle training in severe COPD patients. *Respir Med* 2007; 101: 516–524
- [13] Neves LF, Reis MH, Plentz RDM et al. Expiratory and expiratory plus inspiratory muscle training improves respiratory muscle strength in subjects with COPD: Systematic review. *Respir Care* 2014; 59: 1381
- [14] Petrovic M, Reiter M, Zipko H et al. Effects of inspiratory muscle training on dynamic hyperinflation in patients with COPD. *Int J Chron Obstruct Pulmon Dis* 2012; 7: 797–805
- [15] Harriss DJ, MacSween A, Atkinson G. Ethical standards in sport and exercise science research: 2020 update. *Int J Sports Med* 2019; 40: 813–817
- [16] Kovelis D, Segretti NO, Probst VS et al. Validation of the Modified Pulmonary Functional Status and Dyspnea Questionnaire and the Medical Research Council scale for use in Brazilian patients with chronic obstructive pulmonary disease. *J Bras Pneumol* 2008; 34: 1008–1018
- [17] Bestall JC, Paul EA, Garrod R et al. Usefulness of the Medical Research Council (MRC) dyspnoea scale as a measure of disability in patients with chronic obstructive pulmonary disease. *Thorax* 1999; 54: 581–586
- [18] Ferreira PL, Ferreira LN, Pereira LN. Contribution for the validation of the Portuguese version of EQ-5D. *Acta Med Port* 2013; 26: 664–675
- [19] Brooks R. EuroQol: The current state of play. *Health Policy* 1996; 37: 53
- [20] Rabin R, Gudex C, Selai C et al. Preference-based assessments: From translation to version management: A history and review of methods for the cultural adaptation of the EuroQol five-dimensional questionnaire. *Value Health* 2014; 17: 70–76
- [21] Miller MR, Hankinson J, Brusasco V et al. Standardisation of spirometry. *Eur Respir J* 2005; 26: 319–338
- [22] American Thoracic Society/European Respiratory Society/ATS/ERS Statement on respiratory muscle testing. *Am J Respir Crit Care Med* 2002; 166: 518–624
- [23] Laboratories ATSCoPSfCPF. ATS statement: guidelines for the six-minute walk test. *Am J Respir Crit Care Med* 2002; 166: 111–117
- [24] Trost SG, McIver KL, Pate RR. Conducting accelerometer-based activity assessments in field-based research. *Med Sci Sports Exerc* 2005; 37: S531–S543
- [25] Troiano RP, Berrigan D, Dodd KW et al. Physical activity in the United States measured by accelerometer. *Med Sci Sports Exerc* 2008; 40: 181–188
- [26] Estellat C, Torgerson DJ, Ravaud P. How to perform a critical analysis of a randomised controlled trial. *Best Pract Res Clin Rheumatol* 2009; 23: 291–303
- [27] Rothwell PM. Treating individuals 2. Subgroup analysis in randomised controlled trials: Importance, indications, and interpretation. *Lancet* 2005; 365: 176–186
- [28] VanderWeele TJ, Knol MJ. Interpretation of subgroup analyses in randomized trials: heterogeneity versus secondary interventions. *Ann Intern Med* 2011; 154: 680–683
- [29] Mans CM, Reeve JC, Elkins MR. Postoperative outcomes following preoperative inspiratory muscle training in patients undergoing cardiothoracic or upper abdominal surgery: A systematic review and meta analysis. *Clin Rehabil* 2015; 29: 426–438
- [30] Mesquita Montes A, Crasto C, de Melo CA et al. The effect of inspiratory and expiratory loads on abdominal muscle activity during breathing in subjects “at risk” for the development of chronic obstructive pulmonary disease and healthy. *J Electromyogr Kinesiol* 2017; 34: 50–57
- [31] Kendall F, Oliveira J, Peleteiro B et al. Inspiratory muscle training is effective to reduce postoperative pulmonary complications and length of hospital stay: a systematic review and meta-analysis. *Disabil Rehabil* 2018; 40: 864–882
- [32] Janssen SM, Abbink JJ, Lindeboom R et al. Outcomes of pulmonary rehabilitation after treatment for non-small cell lung cancer stages I to IIIa: An observational study. *J Cardiopulm Rehabil Prev* 2017; 37: 65–71
- [33] Granger CL, Parry SM, Edbrooke L et al. Deterioration in physical activity and function differs according to treatment type in non-small cell lung cancer – future directions for physiotherapy management. *Physiotherapy* 2016; 102: 256–263
- [34] Novoa N, Varela G, Jimenez MF et al. Influence of major pulmonary resection on postoperative daily ambulatory activity of the patients. *Interact Cardiovasc Thorac Surg* 2009; 9: 934–938
- [35] Nagamatsu Y, Maeshiro K, Kimura NY et al. Long-term recovery of exercise capacity and pulmonary function after lobectomy. *J Thorac Cardiovasc Surg* 2007; 134: 1273–1278
- [36] Cavalheri V, Tahirah F, Nonoyama M et al. Exercise training for people following lung resection for non-small cell lung cancer – a Cochrane systematic review. *Cancer Treat Rev* 2014; 40: 585–594
- [37] Ries AL, Bauldoff GS, Carlin BW et al. Pulmonary Rehabilitation: Joint ACCP/AACVPR Evidence-Based Clinical Practice Guidelines. *Chest* 2007; 131: 4S–42S