



# Effects of Unsupported Upper Extremity Exercise Training in Patients With COPD

## A Randomized Clinical Trial

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**Background:** Current guidelines on pulmonary rehabilitation (PR) recommend upper extremity exercise training (UEET) in patients with COPD. However, the literature still questions the effectiveness of systematic UEET in this population. We studied the effects of 15 sessions of unsupported UEET on functional exercise capacity, the ability to perform activities of daily living (ADL), and symptoms perceived during activities involving arms in patients with COPD.

**Methods:** We conducted a randomized trial that consisted of 3 weeks of inpatient PR, comparing the short-term effects of unsupported UEET plus PR (intervention group) to those of PR alone (control group). A change in the 6-min ring test (6MRT) was the primary outcome; the ADL field test (four shuttle stations), the dyspnea score as assessed by the Medical Research Council scale, the London Chest Activity of Daily Living scale (LCADL), and the distance walked in 6 min served as secondary outcomes of the study. At the 6-month follow-up, we repeated the 6MRT and the LCADL.

**Results:** Fifty patients with COPD were randomly assigned to the two groups and completed the study. At the end of the study period, patients in the intervention group improved in the 6MRT and ADL field test compared with those patients in the control group ( $p = 0.018$  and  $p = 0.010$ , respectively) with reduced perception of fatigue ( $p \leq 0.006$ ). At the 6-month follow-up, 6MRT ( $p = 0.001$ ) and LCADL ( $p = 0.039$ ) scores were still significantly better in the intervention group compared with the control group.

**Conclusions:** Our trial corroborates the effectiveness of unsupported UEET in specifically improving functional exercise capacity of patients with COPD. Moreover, it also provides evidence that this training modality may ameliorate and maintain the patients' autonomy over and above standard PR.

**Trial registration:** ClinicalTrials.gov Identifier: NCT00825032 (CHEST 2009; 136:387–395)

**Abbreviations:** ADL = activities of daily living; HR = heart rate; LCADL = London Chest Activity of Daily Living scale; MRC = Medical Research Council; PR = pulmonary rehabilitation; RR = respiratory rate; RV = residual volume; 6MRT = 6-min ring test; 6MWT = 6-min walking test; SpO<sub>2</sub> = pulse oximetric saturation; Tend = completion of pulmonary rehabilitation; TLC = total lung capacity; T0 = before pulmonary rehabilitation; UE = upper extremity; UEET = upper extremity exercise training

COPD leads to important systemic clinical effects of which the loss of lean body mass and muscle deconditioning are markers of worsening.<sup>1</sup> A recent guideline<sup>2</sup> aimed at COPD treatment emphasizes the role of physical exercise in breaking the vicious circle of deconditioning.

The most up-to-date guideline on pulmonary rehabilitation (PR)<sup>3</sup> recommends the inclusion of exercise training targeted at the muscles of the upper extremities (UEs) in the physical therapy programs

specific to patients with COPD, as suggested by results from previous randomized trials<sup>4–7</sup> or observational trials.<sup>8–12</sup>

Aerobic training of the lower extremities is able to contrast the atrophy of the skeletal muscles, partially reestablishing the normal muscle metabolism and morphology.<sup>13,14</sup> This leads to improvement of symptoms, quality of life, and exercise capacity.<sup>15</sup>

The rationale supporting the inclusion of UE exercise training (UEET) in PR for patients with

COPD is the competitive dual role of a number of UE muscles that sustain the upper girdle but also act as accessory respiratory muscles. During inspiration, these muscles are usually inactive in healthy and resting people, but operate during physical effort,<sup>16-18</sup> and even at rest in patients who have COPD with diaphragmatic dysfunction.<sup>19</sup> Thus, during activities involving the UEs, respiration becomes ineffective because the accessory respiratory muscles work to sustain the shoulder girdle. This leads to the functional overload of the diaphragm,<sup>19</sup> thus triggering the premature appearance of dyspnea and fatigue.

This phenomenon underscores the clinical importance of the UEET in patients with COPD. A systematic review of the literature carried out by our staff<sup>20</sup> revealed that the clinical trials carried out up to now to verify the effectiveness of UEET are of poor methodological quality: none of these trials was powered to give conclusive results and the potential sources of bias detected compromised both the internal validity and generalizability of their results. We began this randomized, controlled clinical trial for the following purposes: (1) to determine the short-term effect of unsupported UEET on the exercise capacity of the UEs in patients with COPD; (2) to verify any possible advantages of unsupported UEET over standard PR on the ability to perform activities of daily living (ADL), on the degree of perceived dyspnea during these activities, and on general exercise capacity; and (3) to study the specific long-term (6 months) effects of UEET in this population.

## MATERIALS AND METHODS

### *Population*

We recruited inpatients with stable COPD who were referred for the inpatient PR program at the regional center of Villa Pineta Hospital, Pavullo, Italy. Patients were asked to participate in the study if they fulfilled the following criteria: diagnosis of COPD confirmed by clinical examination and a pulmonary function test;

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a degree of COPD severity equal to or above grade 2 (moderate) on the basis of the Global Initiative for Chronic Obstructive Pulmonary Disease classification<sup>21</sup>; clinical stability for a minimum of 4 weeks; and a degree of chronic dyspnea equal to or above grade 2 on the Medical Research Council (MRC) dyspnea scale.<sup>22</sup>

Patients were excluded from the study if they had muscular-skeletal abnormalities limiting the shoulder girdle functionality, cognitive impairment limiting participation, had been included within the last 3 years in UEET programs, or had concomitant malignancies. Age, gender, anthropometry, respiratory function, comorbidities, and global function as assessed by the body mass, airflow obstruction, dyspnea, and exercise capacity (or BODE) index<sup>23</sup> were collected in all patients (Table 1). The local ethics committee and the hospital board for clinical trials approved the study.

### *Study Protocol*

After the initial screening for inclusion/exclusion criteria, patients who gave their informed consent to participate were included in a parallel-group, single-blind clinical trial. Using a computer-generated randomization list that was drawn up by a researcher not directly involved in the trial procedures, patients were consecutively allocated into the intervention or control groups. To allow for a concealed allocation into groups, the code was revealed to the researcher responsible for the recruitment after the initial screening was complete.

Patients randomly assigned to the control group undertook an inpatient comprehensive PR program that consisted of a minimum of 15 consecutive sessions of specific training for the lower extremities and general exercises. General training was performed on a cycle ergometer once a day up to 30 min while the load was progressively increased starting from 50% of the patients' maximal exercise capacity as shown at baseline. In addition, patients performed whole-body calisthenics and resistance exercises on a daily basis. The program details have been described elsewhere.<sup>24</sup> The whole program lasted 3 weeks and complied with the recommendations made by the American Thoracic Society and the European Respiratory Society.<sup>4</sup>

During the 3-week PR program, subjects randomly assigned to the intervention group also participated in an experimental program of unsupported UEET in addition to the standard PR program. Both programs were carried out by the same skilled staff members.

### *Experimental UEET*

The UEET involved 15 sessions of resistance exercises specific to five different muscular groups, which were performed by using dumbbells. This training consisted of five movements that specifically require the activation of muscles that may be involved in respiration and/or in the support of the shoulder girdle during the ADL performed with unsupported arms (see Appendix for details). Patients performed the training in a standing posture with slight hip abduction and knee flexion, without the support of the UEs.

Patients were initially submitted to the "one repetition maximum" test<sup>25</sup> to determine the maximal force expressed by any of the five muscular groups. Afterward, the daily training consisted of asking the patient to perform the same movements against a resistance that was initially set at 50% of the patient's maximal force for each muscular group. The training was composed of three series of 10 repetitions for each of the five movements specific to the muscular group trained. At the end of the three series, patients were asked to rate the perceived dyspnea and arm

**Table 1—Baseline Characteristics of the Sample Studied**

Characteristics	All Patients (n = 50)	Intervention Group (n = 25)	Control Group (n = 25)	p Value
Gender				0.370
Male	33	18	15	
Female	17	7	10	
Age, yr	69.5 ± 8.9	68.6 ± 10.4	70.4 ± 7.2	0.462
BMI, kg/m <sup>2</sup>	26.0 ± 4.1	26.1 ± 3.8	26.0 ± 4.5	0.891
BODE index score	4.6 ± 1.4	4.3 ± 1.6	5.0 ± 1.3	0.108
FEV <sub>1</sub> , L	1.02 ± 0.41	1.09 ± 0.49	0.96 ± 0.29	0.272
FEV <sub>1</sub> , % predicted	40.9 ± 15.5	41.3 ± 16.8	40.6 ± 14.4	0.865
FVC, L	2.21 ± 0.72	2.29 ± 0.82	2.12 ± 0.60	0.398
FVC, % predicted	73.3 ± 23.1	73.2 ± 24.4	73.4 ± 22.4	0.976
FEV <sub>1</sub> /FVC, %	46.8 ± 10.6	46.8 ± 9.8	46.9 ± 11.7	0.969
TLC, L	7.24 ± 2.07	7.06 ± 1.78	7.42 ± 2.35	0.536
TLC, % predicted	123.5 ± 27.2	120.0 ± 29.0	127.0 ± 25.4	0.367
RV, L	4.66 ± 1.83	4.59 ± 1.56	4.72 ± 2.10	0.811
RV, % predicted	198.9 ± 69.9	197.8 ± 65.0	200.0 ± 75.8	0.914
Charlson index score	4.18 ± 1.13	3.96 ± 1.20	4.40 ± 1.04	0.174

Results are presented as the mean ± SD, unless otherwise indicated. BODE = body-mass, airflow obstruction, dyspnea, and exercise capacity index.

muscular fatigue by using a modified Borg scale.<sup>26</sup> If these ratings were ≤ 3 on that scale, the following day the attending physiotherapist increased the number of repetitions in that series from 10 to 12 and, successively, from 12 to 15. Once the patient reached 15 repetitions per movement, with a rate of perceived dyspnea and arm fatigue ≤ 3 on the modified Borg scale, the physiotherapist increased the resistance by 500g and set back to 10 the number of repetitions in that series. Patients rested 30 s between series and 1 min between different movements. During activities, patients receiving long-term oxygen therapy used a standardized flow (3 L/min) of supplemental oxygen.

### Outcomes

Measurements were taken in both groups before PR (T0) and at the completion of PR (Tend). One physiotherapist who was unaware of the patient's group allocation was specifically in charge for the following assessments.

**6-Min Ring Test:** The 6-min ring test (6MRT) was performed as originally described by Celli et al.<sup>27</sup> Before testing, subjects were allowed to practice the exercise in order to familiarize themselves with the procedure. Subjects were permitted to stop and rest during the test if they needed to and then to resume the test once they could. The test was monitored throughout by means of a transcutaneous oximeter (Pulsox 5; Minolta; Tokyo, Japan) to deliver heart rate (HR) and pulse oximetric saturation (SpO<sub>2</sub>) data. The total number of rings moved during the 6-min period, the pretest-posttest HR, the SpO<sub>2</sub>, the respiratory rate (RR), and the patient's perceived dyspnea and arm fatigue ascertained by the modified Borg scale score<sup>26</sup> were recorded as outcomes.

**ADL Field Test:** This test was similar to the one used by Ries and coworkers<sup>5</sup> in order to objectively assess the ability to perform some ADL that involve the UEs and the level of dyspnea perceived during these activities. Patients were asked to repeatedly perform a circuit of four simulated activities (shuttle) that required the elevation of the unsupported UE above the shoulder level. These activities (Fig 1) were as follows: (1) to wipe a wavy-shaped drawing off from a blackboard, simulating the action of window-cleaning; (2) to screw in and then to unscrew three light bulbs positioned on a board above the head of the patient; (3) to dry 10 dishes completely and to put them on a shelf fixed

above shoulder level; and (4) to put a number of groceries on a shelf, lifting each pack of about 500 to 1,000 g (*eg*, salt, sugar, or pasta) from a lower to an upper shelf, the latter fixed above shoulder level.

Patients were asked to perform the shuttles as quickly as possible during a period of 10 min. Again, patients were allowed to stop and rest if they needed to, and to resume the activities once they could. The number of shuttles completed at the end of 10 min, the pretest-posttest HR, the SpO<sub>2</sub>, the RR, and the patient's perceived dyspnea and arm fatigue ascertained by the modified Borg scale score<sup>26</sup> were recorded for analysis.

**London Chest Activity of Daily Living Scale:** The London Chest Activity of Daily Living (LCADL) scale was designed and validated to assess dyspnea during daily activities in patients with severe COPD.<sup>28</sup> The items included in the domains of "self-care" and "domestic" require the activity of UEs and are concerned with activities that patients need to perform on a daily basis.

**Distance Walked in 6 Min:** The 6-min walking test (6MWT) is a measure of general exercise capacity that is widely used in PR and according to the American Thoracic Society/European Respiratory Society guidelines.<sup>29</sup>

**MRC Dyspnea Scale:** This scale measures the effect of breathlessness on daily activities as previously reported in patients with COPD.<sup>22</sup>

To verify whether the experimental training leads to long-term results on the functional arm exercise capacity, the 6MRT and the LCADL were repeated after 6 months as the latest follow-up (*ie*, after the conclusion of the treatment period).

### Data Analysis

Based on the estimated training effect on the rings moved at the 6MRT (primary outcome measure), to gain a power of 90% with a type I error ≤ 5%, we sought to recruit and obtain complete data from 22 patients per group. Statistical analysis was performed using a specific software package (SPSS, version 8.0 for Windows; SPSS; Chicago, IL). Results are presented as the mean ± SD or frequencies, as appropriate.

We followed an intention-to-treat approach, in which we included in the analysis all participants with evaluable data for the outcome measure under consideration. An analysis of variance model, using repeated measures, was used to compare changes in



FIGURE 1. Activities performed in the shuttle during the ADL field test were to wipe a wavy-shaped drawing off from a blackboard (A), to screw in and then to unscrew three light bulbs (B), to dry dishes completely and to put them on a shelf (C), and to put a number of groceries on a shelf (D).

physiologic measures over the trial period and between groups. All statistics were two tailed, and significance was set at  $p < 0.05$ .

## RESULTS

From March to September 2007, 350 patients were referred to the PR hospital program. One hundred fifty-five of them were eligible for the study protocol. Fifty of them (17 female patients) fulfilled all the inclusion/exclusion criteria and were then recruited. All the patients completed the treatment period and data were collected from all of them at Tend. After 6 months, we collected data from 46 patients (23 in each group) since 4 patients did not attend follow-up because of logistical motivations (Fig 2).

Groups were similar at baseline, as described in Table 1. Patients were in stage II or III according to the Global Initiative for Chronic Obstructive Pulmonary Disease classification<sup>21</sup>; they presented signs of lung hyperinflation, as shown by the increase in mean total lung capacity (TLC) [ $123.5 \pm 27.2\%$ ] and mean residual volume (RV) [ $198.9 \pm 69.9\%$ ] with respect to the predicted values.

Table 2 reports the results of all the outcomes measured throughout the PR in both groups. At T0, patients in the intervention group showed a reduced perception of fatigue during exercise.

At Tend, the between-group comparison was in favor of the intervention group in the number of rings moved ( $202.8 \pm 36.5$  vs  $172.8 \pm 28.8$ , respectively), in the arm fatigue during the 6MRT ( $1.58 \pm 1.30$  vs  $2.50 \pm 1.52$ , respectively), in the number of shuttles completed ( $18.0 \pm 6.2$  vs  $12.6 \pm 4.3$ , respectively), and in arm fatigue during the ADL field test ( $1.24 \pm 1.44$  vs  $2.68 \pm 1.13$ , respectively). None of the cardiorespiratory parameters ( $SpO_2$ , RR, and HR) measured during the 6MRT or the ADL field test changed significantly at this stage. The distance walked during the 6MWT and the MRC score similarly changed in both groups, while the LCADL score significantly improved in the intervention group but not in the control group at Tend.

Group comparison between changes detected for all the outcomes measured is displayed in Table 3. Changes in the rings moved during the 6MRT ( $+ 24.8 \pm 18.4$  vs  $+ 5.2 \pm 21.5$ ) [the primary outcome of this study] as well as in the number of shuttles completed ( $+ 4.04 \pm 3.4$  vs  $+ 0.28 \pm 1.2$ ) and the arm fatigue during the ADL field test ( $- 0.74 \pm 0.9$  vs  $- 0.08 \pm 1.2$ ) were in favor of the intervention group. This group also demonstrated a significantly greater benefit in the number of meters walked during the 6MWT ( $+ 74.4 \pm 41.4$  vs  $+ 24.2 \pm 31.8$ ) and the MRC dyspnea score ( $- 1.04 \pm 0.07$  vs  $- 0.48 \pm 0.5$ ).

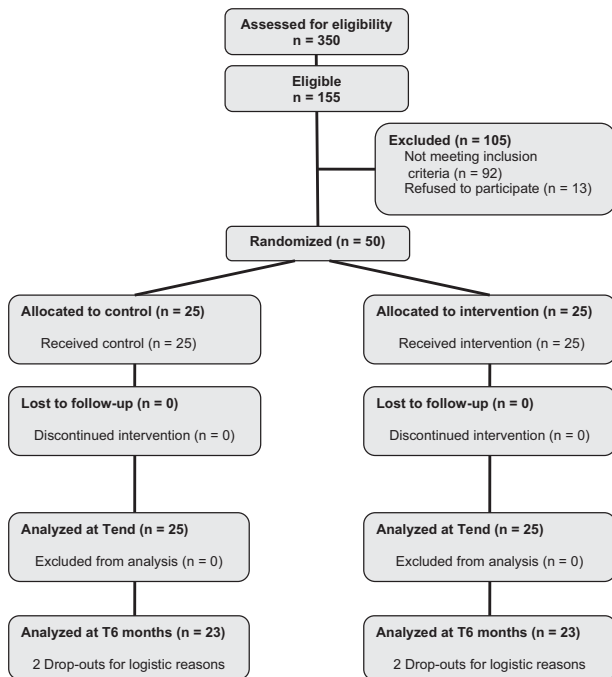


FIGURE 2. Flowchart of participant in this study.

Figure 3 shows the course of UE functionality in terms of both rings moved during the 6MRT and LCADL at the latest follow-up in the two groups. The improved number of rings moved during the 6MRT at T end was maintained ( $p = 0.001$ ), whereas the LCADL score was still significantly greater in the intervention group with respect to the control group ( $p = 0.039$ ) at 6 months.

## DISCUSSION

This study corroborates the efficacy of unsupported UEET, over and above standard PR, in improving the exercise capacity of the UEs in patients with COPD. Moreover, this trial provides new and relevant data regarding the benefits of this specific training on clinically important outcomes, such as the ability to perform ADL that involve the UEs and the fatigue related to these activities. Interestingly enough, the benefits demonstrated in exercise capacity and in dyspnea during daily activities were still sustained after 6 months in those patients who received UEET.

In patients with COPD, where the diaphragm is functionally compromised, the ventilatory constraints may determine a progressive restriction of the participation in activities performed with the arms, due to the involvement during inspiration of a number of muscles that are competitively involved in both inspiration and the support of the shoulder girdle. In

this population, activities performed with unsupported arms are perceived as particularly fatiguing by patients,<sup>19</sup> who in turn progressively dismiss activities that cause fatigue and experience a loss of performance in ADL carried out with their arms. Therefore, the recovery of UE capacity is probably as important as the recovery of lower extremity functional ability for this population.

Several trials<sup>7–11</sup> were previously designed to verify the efficacy of UEET over and/or above standard PR programs in patients with COPD. Overall, results show that UEET, when applied in the unsupported modality, improves both functional<sup>8,11</sup> and maximal<sup>7</sup> exercise capacity of the UEs more than nonspecific training alone. Notwithstanding, those studies were not powered to provide definitive conclusions on the effects of UEET, and the results were inconclusive regarding the effects of this experimental intervention on symptoms, health-related quality of life, and specific ability to perform ADL.<sup>20</sup> This study clearly demonstrated that the addition of site-specific training to general PR improves exercise capacity and fatigue of UEs without placing additional stress on the cardiovascular system.

A secondary objective of our trial was to verify the effects of unsupported UEET on the patients' ability to perform ADL and, from our encouraging results, we would suggest the introduction of this specific and practical training in the standard programs for patients with COPD. Moreover, the improvement in the perceived fatigue during effort is likely to determine a better performance, while reducing limitations in the residual ability. It is worth noting that Ries and coworkers<sup>5</sup> already assessed ADL performance objectively by using a similar field test, but they were not able to show any benefit in favor of the unsupported UEET in patients with COPD, probably because their trial was not powered to detect a meaningful difference for any specific measure of ADL functionality; furthermore, there was an important number of patients lost to follow-up, which detracts from their findings. Our findings encourage more research on this crucial end point from the patients' perspective.

Unexpected data emerged from our trial regarding the improvement of general exercise capacity, which is the most fundamental outcome measure in any PR program and is frequently quantified by means of the 6MWT. Although we have recorded a statistically significant improvement of the distance walked for both groups, as an expected effect of standard PR, when we have looked at the group comparison of changes obtained, the patients trained with unsupported UEET showed an improvement in the number of meters walked that was significantly greater than that in control patients. Moreover, only in the intervention group did this improvement reach the minimal clinical

**Table 2—Within-Group Comparison (Tend vs T0) and Between-Group Comparison for the Variables Assessed**

Variables	Intervention (n = 25)			Control (n = 25)			p Value*
	T0	Tend	p Value	T0	Tend	p Value	
<b>6MRT</b>							
Rings moved, No.	178.0 ± 31.5	202.8 ± 36.5	< 0.001	167.6 ± 25.7	172.8 ± 28.8	0.239	0.018
Dyspnea Borg score	2.42 ± 1.40	1.72 ± 1.13	0.007	3.00 ± 1.72	2.66 ± 1.85	0.124	0.070
Fatigue Borg score	1.74 ± 1.59	1.58 ± 1.30	0.620	2.98 ± 1.56	2.50 ± 1.52	0.030	0.006
RR, breaths/min	21.9 ± 4.13	20.9 ± 3.87	0.081	20.4 ± 3.05	21.2 ± 2.30	0.153	0.476
HR, beats/min	80.4 ± 15.1	79.7 ± 15.0	0.646	78.9 ± 11.3	79.6 ± 12.0	0.649	0.840
SpO <sub>2</sub> , %	92.2 ± 2.4	92.5 ± 1.7	0.364	91.3 ± 2.3	91.5 ± 2.4	0.346	0.126
SpO <sub>2</sub> nadir, %	90.2 ± 3.4	91.0 ± 2.5	0.145	89.2 ± 3.0	89.5 ± 3.1	0.442	0.139
<b>ADL field test</b>							
Shuttles completed, No.	13.9 ± 3.8	18.0 ± 6.2	< 0.001	12.3 ± 4.2	12.6 ± 4.3	0.283	0.010
Dyspnea Borg score	3.80 ± 1.86	2.56 ± 2.10	0.003	4.00 ± 1.25	3.49 ± 1.72	0.035	0.209
Fatigue Borg score	1.98 ± 1.56	1.24 ± 1.44	< 0.001	2.76 ± 1.32	2.68 ± 1.13	0.745	0.003
RR, breaths/min	21.8 ± 4.14	21.1 ± 4.42	0.201	20.7 ± 2.44	21.0 ± 2.38	0.294	0.492
HR, beats/min	93.6 ± 11.4	92.2 ± 11.6	0.309	91.4 ± 11.4	92.9 ± 12.9	0.322	0.815
SpO <sub>2</sub> , %	90.6 ± 2.74	91.0 ± 2.64	0.176	90.4 ± 3.16	90.8 ± 3.07	0.199	0.803
SpO <sub>2</sub> nadir, %	86.9 ± 4.07	87.8 ± 3.59	0.055	86.8 ± 4.6	87.5 ± 3.8	0.103	0.858
6MWT, m	341.6 ± 77.3	416.0 ± 76.3	< 0.001	333.6 ± 69.4	357.8 ± 73.0	0.001	0.110
MRC dyspnea scale score	2.36 ± 0.86	1.32 ± 0.98	< 0.001	2.36 ± 0.63	1.88 ± 0.72	< 0.001	0.189
LCADL score	18.8 ± 6.6	14.7 ± 5.6	0.048	22.0 ± 10.6	20.8 ± 10.5	0.194	0.065

Results are presented as the mean ± SD, unless otherwise indicated. SpO<sub>2</sub> nadir = minimal observed value during pulse oximetric saturation. \*Between-group comparison by way of analysis of variance.

cally important difference (+ 54 m) established for this outcome in patients with COPD.<sup>30</sup> Because it is well known that the training effects are specific to the muscles trained, this result appears rather difficult to explain and merits further investigation.

Although it would be useful to verify the effects of UEET training alone, this study did not involve a third arm of study population. Lake and colleagues<sup>4</sup> performed this comparison and showed a benefit in the

exercise capacity of the UEs as a consequence of UEET, but this advantage was not extended to either general exercise capacity or the quality of life of patients with COPD.

Even if our findings add new perspectives to the clinical use of UEET in patients with COPD, they are still not fully informative about the selection of the ideal candidate to this additional training modality. The trial profile (Fig 2) informs the readers that,

**Table 3—Comparison Between the Changes Detected Within Each Group (Tend vs T0) for All the Outcomes Measured**

Variables	Intervention Group (n = 25)	Control Group (n = 25)	p Value
<b>6MRT</b>			
Rings moved, No.	24.8 ± 18.4	5.2 ± 21.5	0.001
Dyspnea Borg score	- 0.70 ± 1.1	- 0.34 ± 1.0	0.264
Fatigue Borg score	- 0.16 ± 1.5	- 0.50 ± 1.0	0.381
RR, breaths/min	- 1.04 ± 3.1	- 0.32 ± 2.8	0.403
HR, beats/min	- 0.64 ± 6.8	0.70 ± 7.5	0.516
SpO <sub>2</sub> , %	0.34 ± 1.8	0.20 ± 1.0	0.742
SpO <sub>2</sub> nadir, %	0.76 ± 2.5	0.24 ± 1.5	0.383
<b>ADL field test</b>			
Shuttles completed, No.	4.04 ± 3.4	0.28 ± 1.2	< 0.001
Dyspnea Borg score	- 1.24 ± 1.8	- 0.50 ± 1.1	0.099
Fatigue Borg score	- 0.74 ± 0.9	- 0.08 ± 1.2	0.035
RR, breaths/min	- 0.48 ± 3.1	0.96 ± 3.0	0.106
HR, beats/min	- 1.46 ± 7.0	1.52 ± 7.5	0.154
SpO <sub>2</sub> , %	0.42 ± 1.5	- 0.38 ± 1.4	0.924
SpO <sub>2</sub> nadir, %	0.88 ± 2.1	0.64 ± 1.8	0.680
6MWT meter	74.4 ± 41.4	24.2 ± 31.8	< 0.001
MRC dyspnea scale score	- 1.04 ± 0.7	- 0.48 ± 0.5	0.005
LCADL score	- 3.12 ± 4.6	- 1.16 ± 4.3	0.130

Values are given as the mean ± SD, unless otherwise indicated. See Table 2 for abbreviation not used in the text.

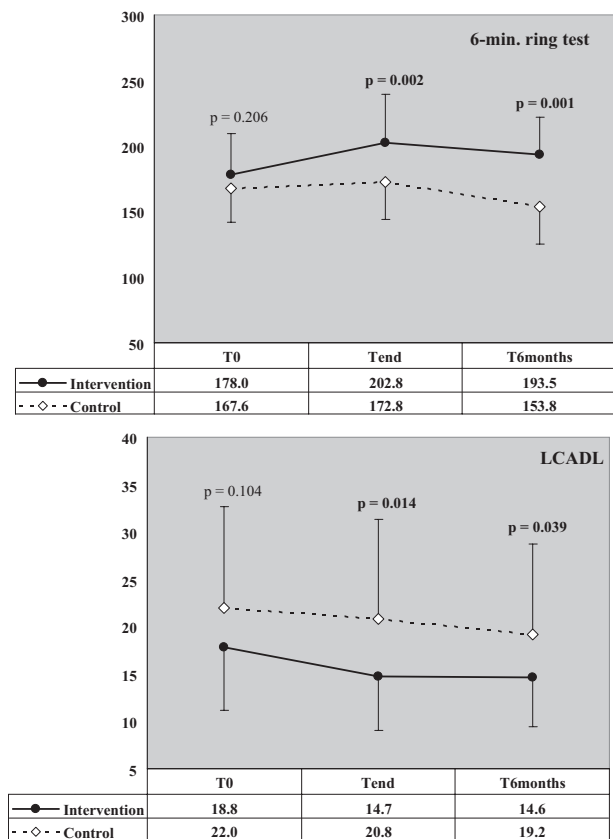


FIGURE 3. Time course of the UE functionality in terms of rings moved during the 6MRT (top) and LCADL score (bottom) at the latest follow-up in the two groups.

at the best of the study inclusion criteria, only about 30% of candidates may be effectively recruited to active UEET. Moreover, this study may suffer from a potential allocation bias; indeed, at baseline, patients in the intervention group had lower levels of fatigue perceived during the field tests when compared with patients in the control group. Notwithstanding, symptoms on effort during the 6MRT and the ADL field test were not considered as entry criteria. Additionally, in our opinion, and despite this, it is noteworthy that only the intervention group experienced a significant change in symptoms at the end of the study.

An important methodological limitation of our study is the lack of blindness in treatment allocation for both patients and physiotherapists who administered the training. Trials in the field of physical therapy are usually open labeled because it is impossible for the physiotherapists to be blind to the intervention and control programs. Regarding the patients recruited, it would be unethical to obtain consent to participate in the study without informing the patients about the nature of the intervention and control programs. However, the physiotherapist that

performed all of the assessments was blinded to the study purposes and to the allocation of patients into either group.

Another limitation of our study regards the ADL field test that we employed to objectively assess the UE performance in clinically meaningful tasks. Although a similar test had already been used for the same purpose,<sup>8</sup> it has not been standardized or validated in the population of interest. Nonetheless, to our knowledge, there is not a valid test with the same scope for patients with COPD. Because our ADL field test is cheap and simple to implement in any setting, we are now confident that future research should address its validity to provide an objective instrument to measure clinically relevant results in this population, and even to reinforce the guideline recommendations,<sup>6</sup> which the present study supports.

## CONCLUSIONS

This randomized trial underscores the true efficacy of unsupported UEET in improving the specific functional exercise capacity of the UEs in patients with COPD. It also adds evidence that this training modality may ameliorate the patients' general exercise capacity and autonomy, over and above standard PR.

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## APPENDIX

During UEET the following exercises were performed for each muscle group involved:

1. *Exercise I* (Pectoralis): Starting with shoulders at 90° of abduction on the coronal plane, elbows at 90° of flexion, palms holding the dumbbells facing forward, ask the patient to adduct the elbows on the horizontal plane and to return to the initial position.
2. *Exercise II* (Deltoids): Starting with the UEs extended and adducted in anatomical position, ask the patient to abduct both of them simultaneously on the scapular plane up to 100° while holding the dumbbells and to return to the initial position.
3. *Exercise III* (Triceps brachii): Starting with the right shoulder flexed at 180° on the sagittal plane with the elbow completely flexed, ask the patient to extend the right elbow while holding the dumbbell and to return to the initial position. The left arm rests in anatomical position. After the completion of three series, repeat the movement with the opposite arm.
4. *Exercise IV* (Trapezius and triceps brachii): Starting with shoulders at 90° of abduction on the coronal plane, elbows completely flexed and dumbbells resting on the shoulders, ask the patient to completely abduct shoulders while extending elbows to reach the 180° of arm abduction on the coronal plane and to return to the initial position.
5. *Exercise V* (Biceps brachii): Starting with UEs extended and adducted in anatomical position and shoulders externally rotated, ask the patient to flex the elbows simultaneously maintaining them close to the thorax while holding the dumbbells and to return to the initial position.

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