Exercise Performance Improves in Patients With COPD due to Respiratory Muscle Endurance Training*

Ralph J. H. Koppers, MD; Petra J. E. Vos, MD, PhD; Cecile R. L. Boot, PhD; and Hans Th. M. Folgering, MD, PhD

Background: Impaired exercise tolerance is frequently observed in patients with COPD. Respiratory muscle endurance training (RMET) by means of normocapnic hyperpnea can be used to improve respiratory muscle function and probably exercise capacity. RMET is not applied on a large scale because complicated equipment is needed to maintain carbon dioxide homeostasis during hyperpnea, which can also be done by enlarging the dead space of the ventilatory system by breathing through a tube. Therefore, tube breathing might be a new, inexpensive method for home-based RMET. The aim of this study was to assess whether home-based RMET by means of tube breathing improves endurance exercise performance in patients with COPD.

Methods: We randomized 36 patients with moderate-to-severe COPD to RMET by paced tube breathing (n = 18) or sham training (control, n = 18). Both groups trained twice daily for 15 min, 7 days per week, for 5 weeks.

Results: Patients receiving RMET showed significant improvements in endurance exercise capacity (constant-load exercise on cycle ergometry; 18 min vs 28 min, p < 0.001), in perception of dyspnea (Borg score; 8.4 vs 5.4, p < 0.001), and respiratory muscle endurance capacity (sustainable inspiratory pressure; 25 cm H2O vs 31 cm H2O, p = 0.005). Quality of life (chronic respiratory disease questionnaire) also improved (78.7 to 86.6, p = 0.001). The control group showed no significant changes.

Conclusion: Home-based RMET by means of tube breathing leads to a significant improvement of endurance exercise capacity, a reduction in perception of dyspnea, and an improvement in quality of life in patients with moderate-to-severe COPD. (CHEST 2006; 129:886–892)

Key words: breathing exercises; dyspnea; exercise tolerance; quality of life

Abbreviations: ANCOVA = analysis of covariance; BMI = body mass index; CLET = constant-load exercise test; CPET = cardiopulmonary exercise test; CRQ = chronic respiratory disease questionnaire; f = respiratory frequency; HET = hyperpnea endurance test; IVC = inspiratory vital capacity; MVV = maximum voluntary ventilation; PEmax = maximal expiratory mouth pressure; PImax = maximal inspiratory mouth pressure; Pifsmax = maximal sustainable inspiratory pressure; RMET = respiratory muscle endurance training; 6MWD = 6-min walking distance; VO2 = oxygen consumption; VO2peak = peak oxygen consumption; Wmax = maximal working capacity

Impaired exercise tolerance and diminished ventilatory efficiency are frequently observed in patients with COPD. Airflow limitation leads to altered ventilation/perfusion matching and hyperinflation, which decreases effective alveolar ventilation and reduces ventilatory efficiency. Increased airway resistance also leads to increased work of breathing.1 In COPD patients, low maximal respiratory pres-
tures have been observed. This is indicative of
diminished respiratory muscle function due to respi-
ratory muscle weakness, hyperinflation, or a combi-
nation of these factors, which contributes to im-
paired exercise tolerance and dyspnea.

Several forms of respiratory muscle training have
been applied in patients with COPD to improve
respiratory muscle function and, to some extent,
dyspnea and exercise performance. Most of these
studies used respiratory muscle strength training and
showed inconsistent results regarding improvements
doing the informed consent form were randomly assigned
to an RMET group or a control group (sham training). The study
protocol was approved by the Ethics Committee of the University
Hypoxemia at rest or during exercise; (2) cardiac or
orthopedic disease; and (3) body mass index (BMI) > 30 kg/m².

All patients on the waiting list for pulmonary rehabilitation
(n = 92) were screened between July 2001 and November 2002.
Three patients refused to participate, and 50 patients met the
exclusion criteria (FEV₁ < 30% of predicted and/or hypoxemia at
rest or during exercise, n = 46; BMI > 30, n = 3; and orthopedic
disease, n = 1). Initially, 39 patients were included in the study.
Three patients dropped out of the study (severe exacerbation
requiring hospitalization: two control subjects and one patient in
the study group). Thirty-six patients completed the study.

Table 1 shows the baseline characteristics of the subjects.
There were no significant differences between the groups. Age
ranged from 38 to 73 years (mean ± SD, 56 ± 8 years). All
patients used bronchodilators (long-acting β-agonists and short-
or long-acting anticholinergics). Inhaled corticosteroids were

**Table 1—Baseline Characteristics**

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>RMET</th>
<th>Control Group</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subjects, No.</td>
<td>18</td>
<td>18</td>
<td></td>
</tr>
<tr>
<td>Age, yr</td>
<td>54.4 (7.7)</td>
<td>57.0 (8.5)</td>
<td>0.35</td>
</tr>
<tr>
<td>Male/female gender, No.</td>
<td>8/10</td>
<td>9/9</td>
<td>0.75</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>26.7 (5.0)</td>
<td>27.5 (3.3)</td>
<td>0.61</td>
</tr>
<tr>
<td>FEV₁, L</td>
<td>1.5 (0.4)</td>
<td>1.7 (0.5)</td>
<td>0.15</td>
</tr>
<tr>
<td>FEV₁, % predicted</td>
<td>50 (14)</td>
<td>58 (15)</td>
<td>0.10</td>
</tr>
<tr>
<td>FEV₁/IVC ratio</td>
<td>46 (13)</td>
<td>50 (14)</td>
<td>0.47</td>
</tr>
<tr>
<td>Residual volume, % predicted</td>
<td>137 (38)</td>
<td>127 (26)</td>
<td>0.36</td>
</tr>
<tr>
<td>Pimax, cm H₂O</td>
<td>69 (29)</td>
<td>72 (23)</td>
<td>0.69</td>
</tr>
<tr>
<td>Pimax, % predicted</td>
<td>89 (34)</td>
<td>93 (28)</td>
<td>0.73</td>
</tr>
<tr>
<td>HET, s</td>
<td>534 (349)</td>
<td>389 (265)</td>
<td>0.17</td>
</tr>
<tr>
<td>Pimax, cm H₂O</td>
<td>25 (6)</td>
<td>29 (12)</td>
<td>0.37</td>
</tr>
<tr>
<td>Wmax, CPET</td>
<td>111 (33)</td>
<td>123 (35)</td>
<td>0.29</td>
</tr>
<tr>
<td>Wmax, % predicted CPET</td>
<td>65 (16)</td>
<td>67 (15)</td>
<td>0.66</td>
</tr>
<tr>
<td>VO₂peak, mL/min/kg</td>
<td>19.6 (4.5)</td>
<td>19.3 (4.0)</td>
<td>0.85</td>
</tr>
<tr>
<td>6MWD, m</td>
<td>519 (89)</td>
<td>559 (75)</td>
<td>0.27</td>
</tr>
<tr>
<td>6MWD, % predicted</td>
<td>92 (15)</td>
<td>100 (12)</td>
<td>0.09</td>
</tr>
<tr>
<td>CLET min</td>
<td>17 (10)</td>
<td>16 (15)</td>
<td>0.75</td>
</tr>
<tr>
<td>Borg dyspnea CLET (isocapnic time 80%)</td>
<td>8.4 (1.9)</td>
<td>8.3 (1.7)</td>
<td>0.78</td>
</tr>
<tr>
<td>CRQ</td>
<td>78.7 (20.6)</td>
<td>82.4 (14.7)</td>
<td>0.5</td>
</tr>
</tbody>
</table>

*Data are expressed as mean (SD) unless otherwise indicated.*
used by 13 patients in the RMET group vs 12 patients in the control group, and aminophylline was used by 2 patients in both groups. The use of medication did not differ significantly between groups. Medication was not changed during the study period. None of the patients had participated in a previous rehabilitation program.

**Study Protocol**

Standardized tests were performed before the start (baseline) and in the last week of the training period. Baseline testing was performed by the investigator. All other tests were performed by a doctor and physiotherapist who were not aware of baseline results nor of the training device that was used by the patient.

Pulmonary function testing, measurement of peak oxygen consumption (VO₂peak), maximal respiratory muscle strength, and BMI were performed during the screening for pulmonary rehabilitation. If patients were suitable for participation, supplementary tests were performed within 1 week.

On the first day of the study, patients performed an inspiratory muscle endurance test (incremental threshold loading). After 30 min of rest, a hyperpnea endurance test (HET) was done. After another 30 min of rest, a 6-min walking distance (6MWD) test was performed. The chronic respiratory disease questionnaire (CRQ) for measurement of health-related quality of life was completed.

On the second day, incremental threshold loading (30 min of rest), HET (30 min of rest), and 6MWD test were repeated followed by (30 min of rest) an endurance test on a cycle ergometer. The best results were taken for analysis. Patients of both groups were told that they were undergoing respiratory muscle exercises and that two different devices were being compared for this purpose.

**Testing**

**Pulmonary Function Testing:** A complete pulmonary function study was performed according to the statement of the European Respiratory Society.

**Measurement of Respiratory Muscle Performance:** Maximal inspiratory pressure (Pmax) and maximal expiratory pressure (Pmax) were measured in sitting position at residual volume and total lung capacity, respectively, using a flanged mouthpiece with a small air leak. The pressure was measured with a transducer (Validyne DP103–32, Validyne Engineering, Northridge, CA) and recorded (BD 101; Kipp & Zonen, Delft, the Netherlands). Measurements of plateau values were taken. Reference normal values were taken from Wilson et al. Inspiratory muscle endurance was measured by incremental threshold loading. Patients inspired against a weighted inspiratory valve, of which the load was increased at regular intervals. The pressure was measured with a transducer (Validyne DP103–32). The pressure achieved during the heaviest load tolerated for at least 45 s was defined as the maximal sustainable inspiratory pressure (P(tmax)).

An HET was used to assess endurance performance of respiratory muscles. Subjects wearing a nose clip breathed in a closed spirometer circuit (Godart; Billhoven, the Netherlands), in which the soda lime absorber could be partially bypassed to maintain an isocapnic situation during the test. Oxygen was supplemented. End-tidal carbon dioxide pressure was measured at the mouth (Type 8290000; Drager), and oxygen saturation was monitored with a pulse oximeter. Patients breathed with a fixed respiratory frequency (f) of 30 breaths/min, inspiratory time/total time of one respiratory cycle ratio of 1.3, using an electronic metronome (Qwik Time QT5), and with a tidal volume of 45% of vital capacity. The subjects had visual feedback of their tidal volumes on the spirometer and were not encouraged during the test. The test was terminated when the patient could no longer sustain the f or tidal volume during three consecutive breaths or after a maximum of 20 min, and this time was recorded.

**Exercise Testing:** Maximal incremental cardiopulmonary exercise testing (CPET) was performed on an electrically braked cycle ergometer (Lode; Groningen, the Netherlands). During this symptom-limited test, the work rate increased every 30 s by 5% of the predicted maximal workload, and pedaling rate was set at approximately 60 revolutions per minute. Ventilatory parameters were measured at the mouth (Vmax 29; Sensor-Medics; Yorba Linda, CA). Arterial blood samples were obtained at regular intervals. Heart rate was monitored by ECG recording. At the end of the test, VO₂peak and maximal working capacity (Wmax) were recorded. Results were compared (before and after training) at identical levels of exercise: isocapnic workload. Wmax of the first CPET was set at 100%.

Endurance test or constant-load exercise testing (CLET) was performed on the same cycle ergometer. Patients exercised at a work rate of 50% of the individual Wmax, with pedaling rate at 60 revolutions per minute. They were not encouraged during the test. The test was terminated when patients indicated that they were exhausted and were unable to maintain a pedaling frequency of 60 revolutions per minute. This time was recorded as cycle endurance time. Ventilatory parameters were measured. Perception of dyspnea was measured by Borg scores at regular intervals. Results (before and after training) were compared at identical time points of exercise: isocapnic workload. The endurance time of the first CLET was set at 100%. The 6MWD test was performed in a standardized way in a corridor of 50 m in length.

**Endurance Respiratory Muscle Training and Sham Training**

RMET: RMET was performed by means of tube breathing. A tube (internal diameter, 3 cm) connected to a mouthpiece was added to the respiratory system to rebreathe exhaled carbon dioxide. Maximum ventilatory capacity that can be sustained for 15 min is approximately 60% of maximum voluntary ventilation (MVV). Therefore, the aimed level of ventilation during training was set at 60% of MVV, which was calculated from 35 times FEV₁ (60% MVV = 0.6 × 35 × FEV₁). The dead space was adjusted to 60% of the patients inspiratory vital capacity (IVC) plus the resting tidal volume because during exercise, when minute ventilation rises, tidal volume increases to approximately 60% of vital capacity and remains constant thereafter. f was calculated: 60% MVV = f × (0.6 × IVC + resting tidal volume) and was increased during training to a maximum of 20 breaths/min. f was imposed by an electronic metronome: inspiratory time/total time of one respiratory cycle ratio of 0.33 (Qwik Time QT5). Patients wore a nose clip and were instructed to take deep breaths. End-tidal carbon dioxide pressure was analyzed with a sampling capnograph (Type 8290000; Drager) that was connected to the mouthpiece.

Sham Training: Sham training was performed by breathing six to seven times per minute through an incentive flowmeter (Inspirx; Respcare Medical; the Hague, the Netherlands). Airflow resistance was set at ± 5% Pmax.

Training Intensity: Patients in both groups trained twice daily for 15 min, 7 days a week, for 5 weeks. All patients were seen weekly at the pulmonary laboratory to check whether training was performed correctly. Furthermore, patients completed a diary in which they reported the training regimen.
Statistical Analysis

Data are reported as mean ± SD. Training-induced changes (after training minus before training values) were compared between groups using analysis of covariance (ANCOVA) with baseline as covariable. The Student t test for paired samples was used to evaluate differences within groups (before vs after training). Significance was set at p ≤ 0.05. Statistical software was used for analysis (SPSS 10.0 for Windows; SPSS; Chicago, IL).

Results

Respiratory Muscle Performance

Table 2 shows the effects of 5 weeks of home-based RMET on respiratory muscle performance. HET and Ptsmax significantly increased in the RMET group. The control group showed a decrease of these parameters. Pimax and Peimax showed no significant changes. Subset analysis of patients with a low Pmax (< 75% predicted, n = 6 in RMET group; and n = 5 in control group), as indicative of respiratory muscle weakness, showed the same results in HET and Ptsmax; moreover, Pmax increased significantly in the RMET group, from 39 cm H2O (54% of predicted) to 58 cm H2O (80% of predicted), p = 0.049. No changes occurred in the control group.

Exercise Performance and Quality of Life

The effects of home-based RMET on exercise performance and quality of life are shown in Table 2. CLET significantly increased by 58% in the RMET group, whereas no change was found in the control group. 6MWD and quality of life also showed a significant increase in the RMET group, without a change in the control group.

At an isocapnic work time of 80% of the initial endurance time, there were significant changes in the RMET group for the following variables (Table 3): ventilation decreased from 42.8 ± 10.5 to 39.6 ± 10.0 L/min, p = 0.034; f decreased from 37 ± 7 to 30 ± 7 breaths/min, p < 0.001; and tidal volume increased from 1.2 ± 0.3 to 1.4 ± 0.5 L; p = 0.035. Borg score for exercise dyspnea at isocapnic work time significantly decreased in the RMET group, from 8.4 ± 1.9 to 5.4 ± 1.3, p < 0.001. In the control group, there were no significant changes for these parameters.

CPET showed a significant increase in maximal workload in the RMET group (Table 2). VO2peak did not change. At an isocapnic workload of 80%, the following changes were observed in the RMET group: minute ventilation, f, oxygen consumption (VO2), and heart rate all significantly decreased. No significant changes were observed in the control group (Table 4).

Discussion

The present study shows that home-based RMET by means of tube breathing leads to a substantial

| Table 2—Pretraining and Posttraining Values and Significance of Training-Induced Changes* |
|----------------------------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| **Pulmonary function tests**     | **RMET**        | **Control Group** |
|                                 | Before | After | p Value, Within Group | Before | After | p Value, Within Group | pΔ |
| FEV1, L                         | 1.5 (0.4) | 1.6 (0.5) | 0.12 | 1.7 (0.5) | 1.8 (0.5) | 0.18 | 0.84 |
| IVC, L                          | 3.3 (0.7) | 3.3 (0.7) | 0.26 | 3.6 (0.9) | 3.7 (0.9) | 0.10 | 0.52 |
| **Respiratory muscle performance** |     |     |     |     |     |     |     |
| Pimax, cm H2O                   | 66 (29) | 73 (28) | 0.10 | 72 (23) | 75 (30) | 0.72 | 0.53 |
| HET, s                          | 534 (349) | 833 (348) | < 0.001 | 389 (265) | 343 (259) | 0.05 | < 0.001 |
| Pmax, cm H2O                    | 25 (89) | 31 (14) | 0.005 | 29 (12) | 26 (12) | 0.04 | < 0.001 |
| **Exercise performance and CRQ** |     |     |     |     |     |     |     |
| CLET (min)                      | < 0.001 | 0.85 | < 0.001 |
| s                               | 17 (10) | 28 (14) | 16 (15) | 16 (14) |
| 6MWD, m                         | 512 (86) | 535 (77) | 0.007 | 549 (75) | 544 (85) | 0.48 | 0.02 |
| VO2peak, mL/min/kg              | 19.6 (4.5) | 19.9 (4.7) | 0.33 | 19.3 (4.0) | 19.9 (5.1) | 0.51 | 0.93 |
| CRQ                             | 78.7 (20.6) | 86.6 (18.4) | 0.001 | 82.4 (14.7) | 85.0 (15.0) | 0.2 | 0.07 |

*Data are expressed as mean (SD). pΔ = significance of training-induced changes (after minus before training values) between groups by ANCOVA.
improvement of endurance exercise capacity by 58%, an improvement in quality of life, and a reduction in the perception of dyspnea in patients with moderate-to-severe COPD. These findings suggest that this inexpensive technique can be a clinically relevant and easily applicable training intervention for COPD patients.

To our knowledge, this is the first study using tube breathing as home-based RMET in COPD patients. We found an improvement in exercise endurance capacity of 58%. One other study showed an increase of 54% in submaximal cycling endurance exercise after RMET in COPD patients. However, RMET was not performed in a home-based setting, and that study had no control group. Another study, performing home-based RMET in patients with COPD, with a specially developed, expensive electromechanical device reported an increase in submaximal treadmill exercise in the study group compared to the control group that did not reach statistical significance. Furthermore, submaximal exercise on a treadmill has never been validated in COPD, whereas CLET on cycle ergometry has been proven to be a reproducible, reliable, and valid method to assess endurance exercise capacity in patients with COPD. CLET can be used to measure endurance exercise time as well as to compare ventilatory and metabolic parameters at the same work rate, before and after intervention, the latter being an effort-independent measurement of training effects. Our study shows a change in breathing pattern after RMET. We found a lower minute ventilation, a lower f, and a larger tidal volume during CLET at isocapnic work time of 80%. This change of breathing pattern has two major advantages. First, the ratio of dead space to tidal volume decreases, which leads to an increase in effective alveolar ventilation. Second, it diminishes the work of breathing. It also indicates that respiratory muscle fatigue leading to a rapid, shallow breathing pattern is delayed. These observations are supported by the finding that Borg scores were significantly lower in the RMET group at isocapnic time during CLET. This can be an additional explanation for the better performance during endurance exercise.

Remarkably, W_max improved in the RMET group by 8%, without a change in VO_2peak. This can be explained by comparing parameters of CPET at isocapnic workload of 80%, showing that minute ventilation, f, VO_2, and heart rate are significantly less after training, as a result of a more efficient way of breathing and less work of breathing. The reduction of minute ventilation and f and their mutual relationship leads to an improvement of ventilation/perfusion. The decrease of VO_2 by 100 mL/min at

### Table 3—Pretraining and Posttraining Values and Significance of Training-Induced Changes*

<table>
<thead>
<tr>
<th>Variables</th>
<th>RMET</th>
<th>Control Group</th>
<th>p Value, Within Group</th>
<th>p Value, Within Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ventilation, L/min</td>
<td>Before 42.8 (10.5)</td>
<td>After 39.6 (10.0)</td>
<td>0.034</td>
<td>Before 40.9 (8.6)</td>
</tr>
<tr>
<td>f, breaths/min</td>
<td>37 (7)</td>
<td>30 (7)</td>
<td>&lt; 0.001</td>
<td>32 (6)</td>
</tr>
<tr>
<td>Tidal volume, L</td>
<td>1.2 (0.3)</td>
<td>1.4 (0.5)</td>
<td>0.035</td>
<td>1.3 (0.3)</td>
</tr>
<tr>
<td>Borg dyspnea</td>
<td>8.4 (1.9)</td>
<td>5.4 (1.3)</td>
<td>&lt; 0.001</td>
<td>8.3 (1.7)</td>
</tr>
</tbody>
</table>

*Data are expressed as mean (SD). See Table 1 for expansion of abbreviation.

### Table 4—Pretraining and Posttraining Values and Significance of Training-Induced Changes*

<table>
<thead>
<tr>
<th>Variables</th>
<th>RMET</th>
<th>Control Group</th>
<th>p Value, Within Group</th>
<th>p Value, Within Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ventilation, L/min</td>
<td>Before 53.5 (14.8)</td>
<td>After 47.9 (15.1)</td>
<td>0.01</td>
<td>Before 53.7 (10.4)</td>
</tr>
<tr>
<td>f, breaths/min</td>
<td>40 (7)</td>
<td>32 (5)</td>
<td>0.002</td>
<td>36 (5)</td>
</tr>
<tr>
<td>VO_2, L/min</td>
<td>1.52 (0.41)</td>
<td>1.42 (0.41)</td>
<td>0.01</td>
<td>1.52 (0.42)</td>
</tr>
<tr>
<td>Heart rate, beats/min</td>
<td>150 (17)</td>
<td>135 (16)</td>
<td>0.005</td>
<td>144 (17)</td>
</tr>
</tbody>
</table>

*Data are expressed as mean (SD). Maximal work load of first CPET = 100%. See Table 1 for expansion of abbreviation.
the same workload can be a result of a better trained respiratory system in terms of oxidative capacity, requiring less oxygen for the same amount of work and thus a lower heart rate. Translating these data to maximal exercise capacity leads to an improvement of workload at the same $V_{O_2}$. An increase in $V_{O_2\text{peak}}$ of 19% was found in the only other study on home-based RMET in COPD patients. However, they did not speculate on the mechanism explaining this increase. Thus, our results show effort-independent improvements in cardiocirculatory and ventilatory parameters as a result of RMET.

In accordance with improvements in endurance and maximal exercise capacity, patients in our RMET group significantly improved 6MWD by 5% (23 m). Other studies showed improvements of 8 to 12%. Although the improvement in 6MWD was statistically significant, a distance of 23 m does not seem to be clinically relevant. However, our patients had baseline values of 92% and 100% of reference values for 6MWD (RMET and control, respectively) and therefore great improvements were not expected. The fact that the RMET group, in contrast to the control group, significantly increased, in combination with significant training group changes, indicates a true training effect. Therefore, functional exercise capacity, a useful outcome in evaluating the effects of respiratory muscle training, improved as a result of home-based RMET.

Improvements in exercise capacity can, in part, be explained by improved respiratory muscle function. Indeed, respiratory muscle endurance, measured by HET, significantly improved by 56% in the RMET group. Previous studies using endurance respiratory muscle training as a training mode in patients with COPD showed improvements in maximal sustained ventilatory capacity of 29% to 47%. Our results are comparable with these studies. Scherer et al reported an increase of 258% in sustained ventilation using a different protocol. We terminated the RMET after 20 min because we were looking for improvements in respiratory muscle endurance capacity and not for maximal results. The improvement in HET was confirmed by a significant improvement in incremental threshold loading. Therefore, RMET by means of tube breathing leads to an improvement in respiratory muscle function.

General exercise training, compared to isolated respiratory muscle training, is another way to train the respiratory muscles in a very specific way. General exercise training during 6 weeks indeed showed an improvement of exercise performance and respiratory muscle function. However, our study showed that training of the respiratory muscles without any other intervention leads to an improvement of exercise capacity and respiratory muscle endurance performance. RMET can be performed in a home-based setting with minimal supervision, whereas general exercise training has to be performed in an institute. Furthermore, RMET can be seen as an add-on therapy to general exercise training. Ries and Moser showed that adding RMET to a rehabilitation program leads to an improvement in exercise capacity compared to a control group receiving general exercise training only. Future investigations are needed to evaluate whether starting RMET before the start of general exercise training or pulmonary rehabilitation leads to better outcomes of these programs in terms of exercise performance.

One of the limitations of this study is the possibility of introducing bias because patients included in our study were selected on the basis of an intended rehabilitation treatment for COPD: Global Initiative for Chronic obstructive Lung Disease stages II and III. This means that these patients were highly motivated to improve their health status. However, motivation to perform this time- and energy-consuming training is very important. Furthermore, neither respiratory muscle weakness nor ventilatory limitation were inclusion criteria. Analysis of our data shows only a slightly lowered $P_{\text{max}}$ compared to reference values. However, other studies even found improvements of respiratory muscle function and exercise capacity in normal sedentary subjects and in normal trained subjects after endurance training of the respiratory muscles. Therefore RMET is also useful in subjects with normal respiratory muscle performance.

The results of this study may have important clinical implications for the treatment of COPD patients. This easy applicable and inexpensive technique can be applied on a large scale. In this light, it can be added to the nonpharmacologic therapeutic interventions in COPD, whereas respiratory muscle training until now is indicated, only along with a pulmonary rehabilitation program for selected patients with decreased respiratory muscle strength. Furthermore, when pulmonary rehabilitation or even general exercise training is not available, home-based RMET by means of tube breathing can be a good alternative. In addition, home-based RMET resulted in a significant improvement in health-related quality of life, especially the domain dyspnea, an important clinical outcome parameter in COPD patients.

In conclusion, the results of this study show that home-based RMET by means of tube breathing substantially improves endurance exercise capacity. It also improves quality of life and leads to a decrease of dyspnea in patients with moderate-to-severe COPD. Future investigations are needed to determine the effects of RMET in patients with very severe COPD.
structive Lung Disease stage IV. Furthermore, it will be interesting to find out whether adding RMET to a pulmonary rehabilitation program might result in improvements of the outcomes of such a program.

ACKNOWLEDGMENT: The authors thank T. de Boo PhD, Department of Biostatistics, University of Nijmegen, and W. Hop PhD, Department of Biostatistics, Erasmus Medical Center Rotterdam, for statistical advice.

REFERENCES

34. Polkey MI, Meadham J. Improvement in volitional tests of muscle function alone may not be adequate evidence that inspiratory muscle training is effective. Eur Respir J 2004; 23:5–6