

# Respiratory Muscle Endurance Training in Chronic Obstructive Pulmonary Disease

## Impact on Exercise Capacity, Dyspnea, and Quality of Life

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Inspiratory muscle training may have beneficial effects in certain patients with chronic obstructive pulmonary disease (COPD). Because of the lack of a home training device, normocapnic hyperpnea has rarely been used as a training mode for patients with COPD, and is generally considered unsuitable to large-scale application. To study the effects of hyperpnea training, we randomized 30 patients with COPD and ventilatory limitation to respiratory muscle training (RMT;  $n = 15$ ) with a new portable device or to breathing exercises with an incentive spirometer (controls;  $n = 15$ ). Both groups trained twice daily for 15 min for 5 d per week for 8 wk. Training-induced changes were significantly greater in the RMT than in the control group for the following variables: respiratory muscle endurance measured through sustained ventilation ( $+825 \pm 170$  s [mean  $\pm$  SEM] versus  $-27 \pm 61$  s,  $p < 0.001$ ), inspiratory muscle endurance measured through incremental inspiratory threshold loading ( $+58 \pm 10$  g versus  $+21.7 \pm 9.5$  g,  $p = 0.016$ ), maximal expiratory pressure ( $+20 \pm 7$  cm H<sub>2</sub>O versus  $-6 \pm 6$  cm H<sub>2</sub>O,  $p = 0.009$ ), 6-min walking distance ( $+58 \pm 11$  m versus  $+11 \pm 11$  m,  $p = 0.002$ ),  $\dot{V}_{O_{2peak}}$  ( $+2.5 \pm 0.6$  ml/kg/min versus  $-0.3 \pm 0.9$  ml/kg/min,  $p = 0.015$ ), and the SF-12 physical component score ( $+9.9 \pm 2.7$  versus  $+1.8 \pm 2.4$ ,  $p = 0.03$ ). Changes in dyspnea, maximal inspiratory pressure, treadmill endurance, and the SF-12 mental component score did not differ significantly between the RMT and control groups. In conclusion, home-based respiratory muscle endurance training with the new device used in this study is feasible and has beneficial effects in subjects with COPD and ventilatory limitation.

Many patients with chronic obstructive pulmonary disease (COPD) are limited in their physical activity by dyspnea. Lung hyperinflation, increased deadspace ventilation, and increased energy consumption during hyperpnea lead to decreased ventilatory reserve and dyspnea on exertion (1, 2). Some subjects with COPD show decreased maximal respiratory pressures (3, 4), which are indicative of respiratory muscle weakness and which may contribute to the perception of dyspnea.

Some studies have shown that the respiratory muscles can be trained if an adequate training stimulus is applied, and that exercise performance (5, 6) and dyspnea (6, 7) may improve as a result of such training. In most studies inspiratory muscle training has been done with resistive breathing or threshold loading (TL) (6–11). Few patients have been trained with normocapnic hyperpnea (5, 12, 13) because the complicated equipment needed to prevent hypocapnia has usually required a hospital facility or research laboratory, and has not been available for home training. Therefore, this training mode,

which imitates most closely the load on the respiratory muscles during exercise, was considered difficult to apply on a large scale (14). In only one study was home-based training applied in conjunction with a comprehensive rehabilitation program (15).

As compared with resistive breathing through a fixed orifice (0.5 cm) at a breathing rate of 15 breaths/min, or TL with a threshold pressure of 30% of maximum inspiratory pressure ( $P_{I_{max}}$ ) at a breathing rate of 15 breaths/min, normocapnic hyperpnea at a target minute ventilation ( $\dot{V}_E$ ) of 75% of maximal voluntary ventilation (MVV) generates the greatest work of breathing (16). Prior work in subjects with COPD showed that training with normocapnic hyperpnea improves respiratory muscle endurance and exercise performance (5, 15). The effects of such training on dyspnea and quality of life, important outcome variables for patient compliance and well-being, have not been yet studied.

A recently developed training device allows respiratory muscle training (RMT) with normocapnic hyperpnea at home. Studies with healthy subjects using this device resulted in increased cycling endurance (17) and decreased perceived respiratory exertion during exercise (18). On the basis of these results, we wanted to test the feasibility and effectiveness of home training with this device in a randomized, controlled study of subjects with COPD. The aim was not only to assess the effects on respiratory muscle and exercise performance, but also to include the important variables of dyspnea and health-related quality of life.

## METHODS

The study protocol was approved by the ethics committee of the Triemli Hospital, Zurich.

### Subjects

Subjects were recruited from the outpatient clinic of the Pulmonary Division of the Triemli Hospital. Consecutive patients were screened by reviewing their charts and by interview. Those who met the inclusion criteria, agreed to participate, and had signed the informed consent form were randomly assigned to an RMT group or a control group, according to a computer-generated randomization table. Inclusion criteria were chronic airflow obstruction ( $FEV_1 < 70\%$  predicted,  $FEV_1/FVC < 70\%$  predicted,  $< 15\%$  improvement in  $FEV_1$  after bronchodilation with 200  $\mu$ g of albuterol inhaled from a pressurized metered-dose inhaler with a spacer), an age of 20 to 80 yr, and a stable clinical condition for at least 1 mo. The patients' physical activity had to be limited by pulmonary dyspnea only. In case of any possibility that cardiac disease limited physical performance, patients underwent cardiopulmonary exercise testing and echocardiography before inclusion in the study. Patients with dyspnea at rest, cardiac disease, poor compliance, drug or alcohol abuse, pregnancy or lactation, a requirement for supplemental oxygen, CO<sub>2</sub> retention, or use of any mechanical ventilatory support were excluded.

Forty-nine patients were initially screened for the study. Ten patients refused to participate and five met one or more exclusion criteria. Thirty-four subjects were initially included. One patient assigned

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to RMT withdrew during the initial testing and one control subject withdrew during Week 2 of the study. One patient in the RMT and one in the control group had to be excluded after traumatic hip and rib fractures. Thirty subjects completed the study.

Baseline characteristics of the study population are outlined in Table 1. The age range of the study population was 46 to 80 yr. No significant differences existed between the two study groups. During the study, subjects in the RMT group experienced  $1.1 \pm 0.2$  (mean  $\pm$  SEM) intercurrent illnesses, had  $1.1 \pm 0.2$  medication changes, and had  $1.3 \pm 0.5$  missed training days per patient, versus  $1.0 \pm 0.2$  intercurrent illnesses,  $1.1 \pm 0.2$  medication changes, and  $0.7 \pm 0.3$  missed training days per patient, respectively, in the control group (no significant differences existed between the RMT and control groups in these variables).

### Study Protocol

All tests were performed in a standardized manner and sequence before starting the training and 1 wk after its completion. Care was given that subjects were familiarized with the different tests and devices used. Throughout the study period, subjects documented their training, their pulmonary and other physical symptoms, physical activity, and any medication change in a diary, which, in addition to interviews of the subjects and evaluation of their training progress, served as a control for compliance with the training program. The study was conducted in a single-blind manner (i.e., subjects of both groups were told that they were undergoing respiratory muscle training, and that two different devices for this were being compared). The subjects in one group were not informed about the device or training of the other group.

### Testing

The sequence of testing was as follows:

*Day 1.* On Day 1 of the study, subjects were given pulmonary function tests (PFTs), had their 12-s MVV, maximal inspiratory and expi-

ratory pressures ( $P_{i\max}$  and  $P_{E\max}$ ) measured at the mouth, and were given a dyspnea questionnaire (baseline or transition dyspnea index), 6-min walking test, 20-min rest period, respiratory muscle endurance test (sustained ventilation), and health questionnaire, and underwent measurement of peak oxygen consumption ( $\dot{V}O_{2\max}$ ), had a 20-min rest period, testing of inspiratory muscle endurance (TL), a third 20-min rest period, and an endurance test on a treadmill.

*Day 2.* On Day 2 of the study the subjects had a 6-min walking test, 20-min rest period, inspiratory muscle endurance test (TL), 20-min rest period, 6-min walking test, 20-min rest period, and second inspiratory muscle endurance test (TL).

Pulmonary function tests were done according to American Thoracic Society criteria (19, 20), with measurement of slow VC, tidal volume ( $V_T$ ), FVC, FEV<sub>1</sub>, peak expiratory flow (PEF), and 12-s MVV, with the Medical Graphics CPX/D System (Medical Graphics Corporation, St. Paul, MN). Reference normal values were taken from the European Community for Steel and Coal (21).

$P_{i\max}$  and  $P_{E\max}$  were measured from RV and TLC, respectively, with a handheld device (Micro M.P.M.; Micro Medical Ltd., Rochester, UK) that has a built-in small air leak to prevent pressure generation by glottis closure. The highest pressure from among 10 measurements was recorded. Reference normal values were taken from Black and Hyatt (22).

Endurance of the respiratory muscles was measured in two ways, as follows:

1. With the respiratory muscle endurance test to assess performance of the inspiratory and expiratory muscles. This test was based on the 12-s MVV, which was performed three times. The highest MVV was recorded. Respiratory muscle endurance was measured as sustained ventilation at 66% of each subject's highest MVV. The time during which subjects were able to sustain this target ventilation was recorded. If a subject surpassed 15 min of breathing at this level, the test was repeated on the following day at 75% of MVV. Subjects were not coached and breathing was not paced. To assure normocapnia, the training device (described subsequently), connected to the metabolic cart (CPX/D system; Medical Graphics), was used. Patients had visual feedback of their  $\dot{V}_E$ .  $\dot{V}_E$ , end-tidal carbon dioxide pressure ( $P_{ETCO_2}$ ), and  $Sa_{O_2}$  (Minolta Pulsox 5; Minolta Switzerland, Dietikon, Switzerland) were measured continuously.
2. With the inspiratory muscle endurance test to assess performance of the inspiratory muscles. This test was done with an inspiratory TL device built according to the specifications of Nickerson and Keens (23). The inspiratory threshold pressure was varied with weights that were attached to a plunger, which closed the inspiratory valve. The initial threshold pressure was set to about 20% of  $P_{i\max}$ . The weight was increased every 2 min by 50% of the initial weight until the subject was unable to continue breathing. The greatest weight the subject was able to sustain for at least 1 min was taken as the measure for inspiratory muscle endurance. The test was performed three times, and the greatest weight the subject endured was recorded. Results were compared with normal reference values established by Johnson and coworkers (24).

Exercise performance was tested with a 6-min walking test and a treadmill endurance test. The 6-min walking test was performed in a corridor of 90 m length. The subjects were instructed to cover as much distance as possible during 6 min. They were not verbally coached, but a person was walking about 1 m behind them. The test was repeated three times, and the longest distance walked was recorded. Results were compared with normal reference values established by Troosters and coworkers in healthy elderly subjects (25).

The endurance test on the treadmill was performed at a submaximal workload (see the subsequent discussion), and subjects were not encouraged during this test. To determine the level of the submaximal workload used in the test, peak power output and  $\dot{V}O_{2\text{peak}}$  were measured with an incremental treadmill test by first gradually adjusting the treadmill speed until the subject walked comfortably. The inclination of the treadmill was then increased by 2.5% in 2-min intervals until the subject was exhausted. Normal reference values for  $\dot{V}O_{2\text{peak}}$  were taken from Hansen and coworkers (26). To determine treadmill endurance, the treadmill was set to 80% of the inclination and to 100% of the speed reached at  $\dot{V}O_{2\text{peak}}$ . For subjects unable to walk

TABLE 1

BASELINE CHARACTERISTICS OF THE GROUP ASSIGNED TO RESPIRATORY MUSCLE TRAINING AND CONTROL GROUPS

	RMT Group	Control Group	p Value
n	15	15	
Age, yr	66.9 $\pm$ 2.4	71.0 $\pm$ 1.2	0.18
Sex, M/F	9 / 6	10 / 5	0.77
BMI	23.8 $\pm$ 0.8	25.9 $\pm$ 0.9	0.19
FEV <sub>1</sub> , %pred	50.2 $\pm$ 4.4	52.3 $\pm$ 3.5	0.46
FVC, %pred	86.8 $\pm$ 3.9	89.0 $\pm$ 4.7	0.97
$P_{i\max}$ , cm H <sub>2</sub> O	66.5 $\pm$ 9.2	70.3 $\pm$ 6.5	0.51
$P_{E\max}$ , %pred	70.0 $\pm$ 12.1	67.4 $\pm$ 6.2	0.59
$P_{E\max}$ , cm H <sub>2</sub> O	94.2 $\pm$ 8.1	109.7 $\pm$ 11.2	0.37
$P_{E\max}$ , %pred	90.1 $\pm$ 6.9	106.9 $\pm$ 14.6	0.59
MVV, L/min	50.3 $\pm$ 4.7	47.9 $\pm$ 4.3	0.81
MVV, %pred	49.7 $\pm$ 4.2	46.0 $\pm$ 4.1	0.51
RET, s	320.3 $\pm$ 48.6	400.2 $\pm$ 68.0	0.37
TL, g	106.3 $\pm$ 26.6	117.8 $\pm$ 22.7	0.59
TL, %pred	59.1 $\pm$ 4.8	61.0 $\pm$ 4.6	0.68
6-min WD, m	615.7 $\pm$ 36.0	664.3 $\pm$ 37.4	0.16
6-min WD, %pred	95.7 $\pm$ 6.1	105.1 $\pm$ 6.1	0.25
$\dot{V}O_{2\text{peak}}$ , ml/kg/min	14.0 $\pm$ 1.3	16.6 $\pm$ 1.2	0.14
$\dot{V}O_{2\text{peak}}$ , %pred	63.8 $\pm$ 7.7	74.2 $\pm$ 5.6	0.13
$\dot{V}_E$ /MVV	82.3 $\pm$ 3.6	88.4 $\pm$ 3.8	0.17
TM, s	460.8 $\pm$ 65.7	596.3 $\pm$ 79.1	0.25
BDI	5.7 $\pm$ 0.4	6.3 $\pm$ 0.5	0.41
SF-12 P score	34.3 $\pm$ 2.2	39.4 $\pm$ 2.3	0.14
SF-12 M score	53.0 $\pm$ 3.6	53.9 $\pm$ 1.8	0.46

*Definition of abbreviations:* BDI = Baseline Dyspnea Index; BMI = body mass index; MVV = 12-s maximal voluntary ventilation;  $P_{E\max}$  = maximal expiratory pressure;  $P_{i\max}$  = maximal inspiratory pressure; PEF = peak expiratory flow; RET = respiratory muscle endurance measured as sustained ventilation; RMT = respiratory muscle training; SF-12 P = score on physical component of the SF-12 health questionnaire; SF-12 M = score on mental component of the SF-12 questionnaire; TL = inspiratory muscle endurance measuring with threshold loading device; TM = endurance on treadmill;  $\dot{V}_E$ /MVV = minute ventilation at  $\dot{V}O_{2\text{peak}}$  as a percentage of MVV;  $\dot{V}O_{2\text{peak}}$  = maximal oxygen consumption; WD = walking distance.

with an inclination, the  $\dot{V}_{O_{2peak}}$  speed was reduced by 20%. The test was terminated when subjects indicated that they were exhausted and unable to keep up with the speed of the treadmill. The time during which a subject was able to walk at the preset load was recorded as treadmill endurance.

Before training, dyspnea in daily activities was assessed with Mahler's Baseline Dyspnea Index, and the change after training was assessed with Mahler's Transition Dyspnea Index (TDI) (27, 28). Health-related quality of life was tested with the SF-12 health questionnaire (acute form), issued by the Medical Outcomes Trust (Boston, MA), which consists of a physical (SF-12 P) and a mental component (SF-12 M) score. Because both questionnaires were originally written in English, three persons fluent in English translated the questionnaires independently into German, and one bilingual person translated the German versions back into English. All translations were compared, discussed, and adjusted to the most correct version.

## RMT

Respiratory muscle endurance training was done with a device that we developed, consisting of tubing (I.D. = 19 mm) that connects a rebreathing bag with a mouthpiece in a 90-degree angle. A sideport (of the same diameter as the tube) is inserted in the middle of this connecting piece. This sideport contains a 6-mm hole that allows inspiration from and expiration to fresh air, and also contains a valve. Subjects fill and empty the rebreathing bag completely during inspiration and expiration, while also inhaling additional fresh air through the sideport during inspiration and breathing partly out through the sideport during expiration. To assure a constant  $V_T$ , the valve inserted in the sideport closes when subjects have emptied the bag during inspiration. In our study the size of the bag was adjusted to 50 to 60% of the subject's VC, and the breathing frequency chosen was such that  $\dot{V}_E$  corresponded to 60% of MVV (monitored while the training device was connected to the metabolic cart). Correct performance was checked by analyzing  $P_{ETCO_2}$  with the metabolic cart and  $Sa_{O_2}$  with the pulse oximeter. If  $P_{ETCO_2}$  deviated from normal baseline values during the 10- to 15-min trial run,  $V_T$  was adjusted by changing the size of the rebreathing bag and breathing frequency was changed accordingly to keep  $\dot{V}_E$  at 60% of MVV. Values of training  $P_{ETCO_2}$  ranged from  $33.1 \pm 1.1$  mm Hg to  $38.5 \pm 1.3$  mm Hg. Hypocapnia during training was corrected by increasing the size of the rebreathing bag, and hypercapnia was corrected by decreasing the size of the bag. Hypoxemia was never observed.

While performing the breathing exercises, subjects wore a nose clip to ensure breathing exclusively through the training device. The exercises were performed twice daily for 15 min on 5 d per week for 8 wk. Splitting the exercise into 5-min sessions was allowed if the subject was unable to train for 15 min without interruption. Inspiration and expiration were paced by an electronic metronome (Seiko Digital Metronome; Seiko Corp., Tokyo, Japan).

Before the 8-wk training period and once every week during the training,  $Sa_{O_2}$ ,  $P_{ETCO_2}$ , breathing rate, and  $V_T$  were monitored in the pulmonary laboratory while subjects performed the breathing exer-

cises. This was done by connecting the training device to the metabolic cart and attaching a pulse oximeter to the subject's finger. During these weekly control sessions, breathing frequency was increased whenever possible in order to increase  $\dot{V}_E$  during training, so as to reach a maximal training stimulus. Three subjects complained of dyspnea or dizziness during training. They were immediately called to the laboratory to monitor training instrument settings,  $Sa_{O_2}$ , and  $P_{ETCO_2}$ . In the cases of two patients, settings had to be adjusted to correct for hyper- and hypoventilation.

The mean respiratory rate (RR) increased by 29% during the training period ( $p < 0.001$ ; Week 1:  $26.3 \pm 1.0$  breaths/min; Week 2:  $28.6 \pm 1.5$  breaths/min; Week 3:  $29.1 \pm 1.2$  breaths/min; Week 4:  $30.9 \pm 1.5$  breaths/min; Week 6:  $32.6 \pm 1.8$  breaths/min; Week 7:  $33.5 \pm 2.1$  breaths/min; and Week 8:  $33.9 \pm 2.0$  breaths/min).  $\dot{V}_T$  did not change significantly during training ( $1.07 \pm 0.06$  L at start of the training versus  $1.12 \pm 0.05$  L at the end;  $p = 0.50$ ).

## Breathing Exercises in the Control Group

Subjects in the control group were told that they were engaging in respiratory muscle training with an incentive spirometer (COACH 2 Volumetric Incentive Spirometer; DHD Healthcare, Canastota, NY). This device was chosen for the sham training to give the subjects the impression that they were undergoing training. Because airflow resistance through this device is minimal, and the RR during breathing exercises was kept at about 6 to 8 breaths/min, we assumed that no training effect would result. The target inspiratory  $V_T$  was set to 70% of each subject's VC. Subjects were instructed to breathe in slowly after a deep exhalation at a rate of 6 to 8 breaths/min, but their breathing was not paced. The exercises were performed twice daily for 15 min on 5 d per week for 8 wk. Splitting the exercises into 5-min sessions was allowed if the subject was unable to train for 15 min without interruption. The subjects also had weekly control sessions of their breathing exercises without a change in  $V_T$  or breathing rate.

Subjects in both the RMT and control groups who experienced acute breathing problems (e.g., due to an exacerbation of their COPD) were allowed to stop training for a maximum of 14 d. These subjects resumed their training from the same point at which they had stopped, in order to complete 40 training days.

## Statistics

The results of the study are presented as mean  $\pm$  SEM. Because the values were not normally distributed (normality of distribution was tested with the Shapiro-Wille's test), the nonparametric Mann-Whitney U test was used to compare baseline characteristics and training-related changes in the RMT and control groups, Wilcoxon's matched pairs test was used to assess training-induced changes within a particular group, and Friedman's analysis of variance with Kendall's concordance was used to assess weekly changes over the course of the training. A value of  $p < 0.05$  was considered significant. The Statistica for Windows software program (Statsoft Inc., Tulsa, OK) was used for all calculations. To achieve a difference in change in respiratory muscle endurance of 20% with an SD of 50 s and a statistical power of 80%, it was calculated that 12 to 15 patients had to be included in each study group. The primary endpoint of the study was respiratory muscle endurance; secondary endpoints were respiratory muscle strength, exercise performance, dyspnea, and health-related quality of life.

## RESULTS

Training-related changes in the RMT as compared with the control group are shown in Table 2 and Figures 1 through 6.

TABLE 2

TRAINING RELATED CHANGES IN THE GROUP ASSIGNED TO RESPIRATORY MUSCLE TRAINING AND IN THE CONTROL GROUP

	RMT Group	Control Group	p Value
n	15	15	
$\Delta FEV_1$ , %	$+0.6 \pm 5.3$	$+3.7 \pm 3.9$	0.84
$\Delta PEF$ , %	$-3.1 \pm 5.1$	$+10.9 \pm 8.0$	0.15
$\Delta FVC$ , %	$+0.3 \pm 3.9$	$+6.6 \pm 3.9$	0.32
$\Delta P_{I_{max}}$ , cm H <sub>2</sub> O	$+19.7 \pm 4.3$	$+12.3 \pm 3.7$	0.30
$\Delta P_{E_{max}}$ , cm H <sub>2</sub> O	$+20.3 \pm 7.0$	$-5.6 \pm 6.2$	0.009
$\Delta \dot{V}_{O_{2peak}}$ , ml/kg/min	$+2.5 \pm 0.6$	$-0.3 \pm 0.9$	0.015
$\Delta SF-12$ M score	$+1.0 \pm 3.6$	$+1.7 \pm 2.5$	0.71

Definition of abbreviations:  $\Delta FEV_1$  = change in forced expiratory volume in 1 s;  $\Delta FVC$  = change in FVC;  $\Delta P_{E_{max}}$  = change in maximal expiratory pressure;  $\Delta P_{I_{max}}$  = change in maximal inspiratory pressure;  $\Delta PEF$  = change in peak expiratory flow; RMT = respiratory muscle training;  $\Delta SF-12$  M = change in score on mental component of the SF-12 questionnaire;  $\Delta \dot{V}_{O_{2peak}}$  = change in maximal oxygen consumption.

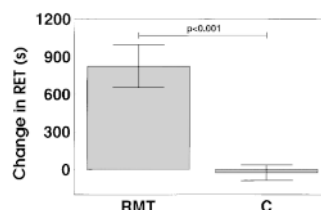
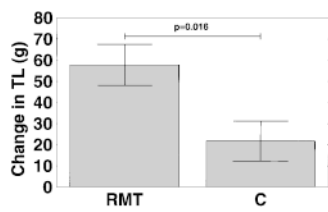


Figure 1. Change in respiratory muscle endurance (RET), measured as time of sustained ventilation. RMT = respiratory muscle training group; C = control group.



**Figure 2.** Change in inspiratory muscle endurance, measured with incremental threshold loading (TL). Results are presented as weight added to the plunger closing the inspiratory valve. RMT = respiratory muscle endurance training group; C = control group.

Improvement in respiratory muscle endurance measured as sustained ventilation (RMT group at  $69 \pm 7\%$  of MVV; control group at  $70 \pm 5\%$  of MVV) (Figure 1), and assessed with incremental TL (Figure 2), was significantly greater in the RMT group. Likewise, change in  $PE_{max}$  (but not in  $PI_{max}$ ), increase in 6-min walking distance (Figure 3),  $\dot{V}O_{2peak}$ , and the physical (Figure 4) (but not the mental) component of the SF-12 health survey were significantly greater in the RMT than in the control group. Both groups showed a decrease in dyspnea in daily activities, but the difference was not significant (Figure 5). Likewise, the change in treadmill endurance did not differ significantly between the two groups (Figure 6).

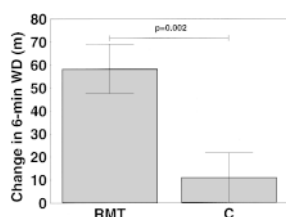
## DISCUSSION

Our results in subjects with COPD and ventilatory limitation show that home-based RMT with normocapnic hyperpnea improved respiratory muscle endurance, exercise performance, health-related quality of life, and dyspnea in daily activities, whereas pulmonary function did not change significantly. Baseline characteristics, incidences of intercurrent illnesses, and medication changes were comparable in the RMT and control groups in the study.

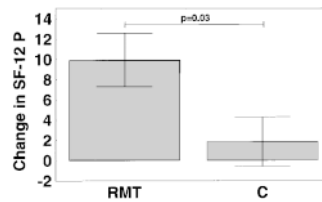
The inclusion criteria for the study were directed to chronic airflow limitation and limitation in physical activity by pulmonary dyspnea. Respiratory muscle weakness and/or ventilatory limitation of physical activity were not prerequisites to study inclusion. Analysis of our data show, however, that ventilatory limitation, reflected by high ventilation at  $\dot{V}O_{2peak}$  ( $\dot{V}_E$ /MVV of 85%), was clearly present. As compared with a healthy control population, our study subjects also had some weakness of their respiratory muscles, as expressed by their low  $PI_{max}$ , MVV, and TL. These findings probably had an effect on our results, and support the view that subjects with COPD, respiratory muscle weakness, and ventilatory limitation may benefit from RMT.

The hyperpnea training in our study was usually well tolerated. Only three patients called because they experienced adverse effects, and their problems were readily solved.

In RMT, the increase in respiratory muscle endurance, measured as sustained ventilation, was large (258%). Previous studies, using normocapnic hyperpnea as a training mode in subjects with COPD, had already demonstrated the beneficial effects of this training mode on respiratory muscle endurance. Using maximal sustained ventilatory capacity (MSVC) as a measure of respiratory muscle endurance, Belman and Mittman (5) reported an increase from 32 to 42 L/min (+31%),



**Figure 3.** Change in 6-min walking distance (6-min WD). RMT = respiratory muscle endurance training group; C = control group.

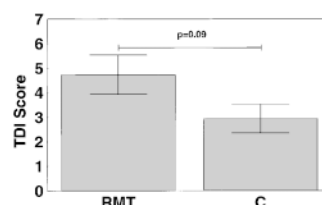


**Figure 4.** Change in score of the physical component of the SF-12 health questionnaire (SF-12 P). RMT = respiratory muscle endurance training group; C = control group.

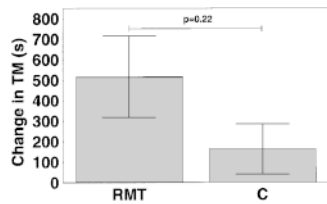
Keens and coworkers (12) found an increase from 74 to 109 L/min (+47%), and Levine and coworkers (13) found an increase from 56 to 79 L/min (+41%) in MSVC. We are aware of only one study that evaluated home-based training (15). The investigators in this study achieved an increase from 34 to 44 L/min (+29%) in MSVC.

Subjects in the present study also increased their exercise performance as a result of RMT. Their 6-min walking distance increased by 10% and  $\dot{V}O_{2peak}$  increased by 19%. These changes were significantly larger in the RMT than in the control group. The 58-m increase in 6-min walking distance in the RMT group was large enough to be considered clinically relevant (29). Belman and Mittman (5) reported comparable results. A 6-wk period of training increased the 12-min walking distance from 1,058 m to 1,188 m (+12%). Ries and Moser (15), who applied home-based respiratory muscle endurance training in conjunction with pulmonary rehabilitation, observed significant improvements in  $\dot{V}O_{2max}$ , from 15.1 ml/kg/min to 16.4 ml/kg/min (+9%), and in 12-min walking distance, from 943 m to 1,020 m (+8%), which are also in the range of our training-induced changes. Although the training-related increase in treadmill endurance was considerably greater in the RMT group in our study, the changes did not differ significantly between the two study groups. One reason for this insignificant difference may be that the individual improvements varied widely. The sample size was too small to reliably exclude a difference in treadmill endurance, and a type II error therefore cannot be excluded.

The increased exercise performance with RMT is important for patients with COPD, since it may help in their daily activities. It is unclear, however, how this translates into an improvement in dyspnea and quality of life, which are important parameters (30, 31). Without subjective benefits, patients will hardly be willing to engage in daily training of their respiratory muscles. We therefore included the SF-12 Health Survey and Mahler's dyspnea indices in our study. The SF-12 Health Survey is a 12-item questionnaire that closely mirrors the scores of the SF-36 short-form Health Survey (32), and which had proved to reflect health status in patients with chronic lung disease (33). The significant impact of RMT on the physical component of the SF-12 health questionnaire is an important finding, because the effect of hyperpnea training on quality of life has not yet been tested. It is already known that pulmonary rehabilitation with and without additional inspiratory muscle training can improve quality of life in patients with COPD (34–36); however, the effect of RMT without additional intervention is unknown.



**Figure 5.** Change in Transition Dyspnea Index (TDI) score. RMT = respiratory muscle endurance training group; C = control group.



**Figure 6.** Change in treadmill endurance (TM). RMT = respiratory muscle endurance training group; C = control group.

The TDI of 4.7 in our RMT group represents a distinct improvement in dyspnea. Lisboa and coworkers (6) reported comparable results after TL training at 30% of  $P_{I_{max}}$ . Their subjects achieved significant increases in  $P_{I_{max}}$  (+23 cm H<sub>2</sub>O; +34%) and 6-min walking distance (+114 m; +38%), and these improvements were associated with a TDI of 3.8. In the study by Harver and coworkers (7), subjects with COPD increased their  $P_{I_{max}}$  by 11 cm H<sub>2</sub>O (+13%) after targeted inspiratory muscle training, which was associated with a TDI of 3.5. Lisboa and coworkers (6) reported that their subjects, who trained with an inspiratory threshold load of 10% of their  $P_{I_{max}}$ , were able to increase their  $P_{I_{max}}$  by 12 cm H<sub>2</sub>O (+19%), and this improvement was associated with a TDI of 1.7. Direct comparison of these studies done with different training modes is not possible. The optimal training mode in subjects with COPD remains to be investigated.

The breathing exercises in our control group probably affected  $P_{I_{max}}$  (+12 cm H<sub>2</sub>O; +18%) and dyspnea (TDI = 2.9). Although we originally designed our study to have a control group undergoing sham training, subjects assigned to the control group experienced an improvement in their inspiratory muscle performance. In some subjects who were eager to undergo training, this training effect was generated by the subjects' intention to continuously increase their training  $V_T$  above the preset volume. Additionally, subjects who started inspiration at a level well above their FRC generated some load on their inspiratory muscles at the end of inspiration. We assume that the improvement in these subjects' dyspnea resulted from their increased inspiratory muscle performance, as reflected by the increase in their  $P_{I_{max}}$  and inspiratory muscle endurance. Although it can be argued that these changes were a placebo effect or based purely on motivation, the fact that  $P_{I_{max}}$  and TL, but not  $P_{E_{max}}$  or respiratory muscle endurance (involving unaffected expiratory muscles) improved suggests that a mild training effect occurred. The increase in  $P_{I_{max}}$  in the control group may have been at least partly responsible for the lack of difference in the training-induced change in  $P_{I_{max}}$  between the two groups.

The training-induced increase in  $P_{E_{max}}$  was significantly greater in the RMT than in the control group. This was probably caused by the load on the expiratory muscles induced by the hyperpnea training. Suzuki and coworkers (37) reported that expiratory muscle training in healthy subjects could improve expiratory muscle strength and decrease  $\dot{V}_E$  and the sensation of respiratory effort during exercise. It is conceivable that the increase in expiratory muscle strength in our RMT group contributed to the decrease in their dyspnea. Further studies are needed to clarify this issue.

RMT with normocapnic hyperpnea requires personal effort and good motivation. Of the 49 persons screened for our study, 10 refused to participate, mainly because of lack of motivation. This shows that not every patient is a good candidate for this kind of treatment. Furthermore, it remains to be clarified whether the addition of RMT to a pulmonary rehabilitation program is worthwhile, and which patients in particular will benefit from it. Results of published trials are equivocal

(38–40). Currently, it is recommended that ventilatory muscle training be considered within a pulmonary rehabilitation program only for selected patients with decreased ventilatory muscle strength (41).

In summary, the results of the present study show that respiratory muscle endurance training with normocapnic hyperpnea improves respiratory muscle and exercise performance, health-related quality of life, and dyspnea. The new portable training device used in the study makes home-based endurance training with normocapnic hyperpnea feasible, and allows its widespread application.

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