

ORIGINAL ARTICLE

Respiratory Muscle Training in Restrictive Thoracic Disease: A Randomized Controlled Trial

Stephan Budweiser, MD, Markus Moertl, MD, Rudolf A. Jörres, PhD, Wolfram Windisch, MD, Frank Heinemann, MD, Michael Pfeifer, MD

ABSTRACT. Budweiser S, Moertl M, Jörres RA, Windisch W, Heinemann F, Pfeifer M. Respiratory muscle training in restrictive thoracic disease: a randomized controlled trial. *Arch Phys Med Rehabil* 2006;87:1559-65.

Objective: To investigate the effects of respiratory muscle training (RMT) in patients with restrictive thoracic disorders and intermittent noninvasive positive-pressure ventilation (NPPV).

Design: Prospective randomized controlled trial.

Setting: Home-based RMT, with assessment in a primary care pulmonary center.

Participants: Thirty patients with restrictive thoracic disorders; 28 patients completed the trial.

Intervention: Three months of RMT by isocapnic hyperpnea or sham training.

Main Outcome Measures: Respiratory muscle strength and endurance, lung function, exercise performance, and health-related quality of life (HRQOL).

Results: After RMT, maximal inspiratory mouth pressure was increased ($27.6\% \pm 36.5\%$, $P=.013$). In patients who could perform cycle ergometer testing ($n=17$), peak oxygen consumption ($2.24 \pm 3.39 \text{ mL} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ vs $-1.71 \pm 2.54 \text{ mL} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$, $P=.014$) and maximal work rate ($9.4 \pm 14.8 \text{ W}$ vs $-5.1 \pm 10.8 \text{ W}$, $P=.043$) increased relative to a control group. Similar differences occurred regarding changes of HRQOL (physical performance, 3.3 ± 11.4 score vs -6.6 ± 9.0 score; $P=.012$) and time of ventilator use ($-0.6 \pm 1.2 \text{ h/d}$ vs $0.4 \pm 0.5 \text{ h/d}$, $P=.010$). Lung volumes, 12-second maximum voluntary ventilation, 6-minute walking distance, and blood gases were unchanged.

Conclusions: In patients with restrictive thoracic disorders and NPPV, RMT improved inspiratory muscle strength. Exercise performance and HRQOL were improved when the 2 groups were compared. RMT was practicable and safe despite severe respiratory impairment. Further evaluation, including different training intensities and modalities, seems warranted.

Key Words: Breathing exercises; Chest; Rehabilitation; Respiratory muscle training; Scoliosis; Ventilation.

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From the Center for Pneumology, Donaustauf Hospital, Donaustauf, Germany (Budweiser, Moertl, Heinemann, Pfeifer); Institute and Outpatient Clinic for Occupational and Environmental Medicine, Ludwig-Maximilians-University, Munich, Germany (Jörres); Department of Pneumology, University of Freiburg, Freiburg, Germany (Windisch); and Department of Internal Medicine II, University of Regensburg, Regensburg, Germany (Pfeifer).

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Reprint requests to Stephan Budweiser, MD, Klinik Donaustauf, Ludwigstraße 68, D-93093 Donaustauf, Germany, e-mail: stephan.budweiser@klinik.uni-regensburg.de.

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IN RESTRICTIVE THORACIC disorders such as kyphoscoliosis, altered respiratory mechanics and decreased chest wall compliance result in impaired respiratory muscle function.^{1,2} As the disease progresses, symptomatic hypercapnic respiratory failure may occur.³ As a therapy of choice, noninvasive positive-pressure ventilation (NPPV) is recommended and is widely used,⁴⁻⁶ although its underlying mechanisms of action are still under debate.⁶⁻⁸ In particular, doubt has been raised as to the existence of chronic respiratory muscle fatigue⁹ and about the hypotheses that NPPV leads to relief of fatigued respiratory muscles or improves respiratory muscle function.^{6,8} Some studies, however, have indeed reported a reduction of maximal inspiratory pressure (P_{imax}) in chronic respiratory failure^{2,10} and an improvement of inspiratory muscle force or respiratory muscle endurance by NPPV.^{11,12}

It is generally accepted, however, that hypercapnic respiratory failure is caused by an imbalance between load and capacity of respiratory muscles.¹³ These considerations suggest that both of 2 contrasting approaches, that is, unloading of respiratory muscles by NPPV and training of muscles by appropriate devices, are therapeutically reasonable in a stable state of the disease.^{13,14}

Patients with chronic obstructive pulmonary disease (COPD) have the most experience with inspiratory muscle training (IMT). Despite some controversy, but based on a meta-analysis¹⁵ and histopathologic findings,¹⁶ it has been concluded that IMT may be justified in patients with COPD and inspiratory muscle weakness to improve respiratory muscle strength, exercise-induced symptoms, and dyspnea.¹⁷ In most investigations, resistive or threshold loading devices were used for IMT.¹⁵

Compared with that, respiratory muscle training (RMT) performed as isocapnic hyperpnea has not been intensively investigated, probably because of complexity of the rebreathing circuit that is used for this purpose.¹⁸⁻²⁰ Earlier work, however, suggested that this training modality could be useful, particularly in patients with respiratory failure or during weaning.^{13,21} Noteworthy enough, in kyphoscoliosis large improvements through RMT have been reported, regarding ventilator dependence, exercise performance, and respiratory muscle performance.^{22,23} These studies, however, were purely observational and did not follow a randomized, controlled design. Thus, the issue of RMT in restrictive thoracic disorders is still not resolved.

Based on these considerations we performed a randomized controlled trial (RCT) to verify our hypotheses that: (1) RMT performed as isocapnic hyperpnea in addition to nocturnal NPPV has beneficial effects on respiratory muscle function; (2) these effects extend to exercise performance and health-related quality of life (HRQOL); and (3) RMT is a safe and feasible treatment for patients with restrictive thoracic disorders and moderate stable chronic hypercapnic respiratory failure.

METHODS

Participants

Between October 2003 and October 2004, consecutive patients with restrictive thoracic disorders and current intermittent nocturnal NPPV who were regularly admitted for a 2-day follow-up visit at the Donaustauf Hospital, University of Regensburg, Germany, were screened for participation in our RCT. Inclusion criteria comprised impaired respiratory muscle function ($P_{\text{imax}} < 70\%$ of predicted), arterial partial pressure of carbon dioxide (P_{aco_2}) less than 50mmHg, and arterial partial pressure of oxygen (P_{ao_2}) greater than 55mmHg while breathing room air at rest, inspiratory vital capacity (IVC) greater than 25% of predicted, forced expiratory volume in 1 second (FEV_1)/IVC greater than 60%, stable drug therapy, no antibiotic treatment, and NPPV for at least 3 months. Exclusion criteria were: dyspnea at rest, current respiratory tract infection, severe concomitant disease, alcohol or drug abuse, and current participation in a rehabilitation program. The study was ended in January 2005.

Patients who agreed to participate gave informed written consent and were randomly assigned to either the RMT or the control group until the scheduled sample, which was derived from a power analysis, was complete (30 patients; 15 in each group). Randomization was done in a double-blind manner. Patients were not told which of the devices was expected to be more effective for RMT, and investigators and technicians performing the tests were given no information about the device individual patients had used. The local ethics committee approved the study protocol.

To recruit 30 patients, 45 patients were screened and 38 met the inclusion criteria. Six patients were excluded because of dyspnea at rest or concomitant disease (myelodysplastic syndrome) and 2 patients refused to participate. Thus, the final study group was comprised of 15 female and 15 male patients. Two patients of the training group discontinued RMT because they lost interest within the first days (fig 1).

Study Protocol

Respiratory parameters, exercise performance, and HRQOL were assessed on 2 consecutive days with a standardized protocol, which was the same before and after the 3-month training period. On the first day, medical histories, anthropometric data, electrocardiograms, and routine laboratory parameters were assessed. Capillary blood gases^a were determined from the hyperemic earlobe. In patients not on long-term oxygen therapy (LTOT), blood gas values were assessed while they were breathing room air, and in patients who were on LTOT, values were assessed while they were breathing their usual oxygen flow. Spirometry and body plethysmography (Master-Screen Body)^b were performed according to American Thoracic Society (ATS) guidelines,²⁴ with European Respiratory Society reference values.²⁵ Furthermore, P_{imax} and expiratory mouth pressure (P_{Emax}) were measured.²⁶ For P_{imax} , peak values were obtained as previously described by Windisch et al²⁷ and the best of 3 reproducible efforts was chosen. Respiratory muscle endurance was determined by a 12-second maximal voluntary ventilation (MVV), with the best of 3 attempts being taken. The 6-minute walking distance (6MWD) was determined using ATS guidelines.²⁸ HRQOL was assessed via the Severe Respiratory Insufficiency (SRI) Questionnaire,²⁹ which has 7 subscales that can be aggregated into 1 summary scale. On the second day, capillary blood gases were determined again. For safety reasons, we would have excluded any patient who showed a rise in P_{aco_2} of more than 20%, but this did not occur. Furthermore, oxygen saturation was measured transcutaneously; there were no values greater than 88% during training in any patient.

Patients then performed a cardiopulmonary exercise test (Oxycon-Pro Exercise System, Ergoline bicycle ergometer)^b comprising a 1-minute reference period, an initial workload of 5W, and an increase by 1.25W every 15 seconds (ramp protocol), until they were symptom-restricted, that is, until marked dyspnea or peripheral muscle fatigue occurred. Oxygen consumption and carbon dioxide elimination were recorded breath-by-breath and results given as 30-second averages, the final values indicating peak oxygen consumption ($\dot{V}_{O_2\text{peak}}$) at peak exercise performance. Reference values were those described by Hansen et al.³⁰

Respiratory Training Device

Isocapnic hyperpnea is a form of RMT, in which patients maintain a high level of minute ventilation (\dot{V}_E) targeting an improvement in respiratory muscle endurance. The portable RMT appliance^c we used in this study consists of a hand-held unit with tubing, connected with a rebreathing bag and a basic station device.³¹ Subjects must fill and empty the rebreathing bag completely during their breathing maneuver. A sideport in the middle of the connecting piece contains a hole and a valve that ensures inhalation of additional fresh air during inspiration and allows breathing partly out during expiration; thus, hyperventilation is prevented. The basic unit serves as monitor for breathing frequency and depth during training via a light-emitting diode scale and brief sounds. We used a rebreathing bag of about 50% of the IVC. Because the smallest available bag contained 0.5L a clip had to be used with some patients to further reduce volume. Breathing frequency was set to achieve a \dot{V}_E of about 60% of MVV and programmed into the basic station.

On the first study day, patients were familiarized with the device. Rebreathing bag and respiratory frequency were adjusted as described above, as well as to the patient's individual performance and comfort. To avoid premature fatigue and to

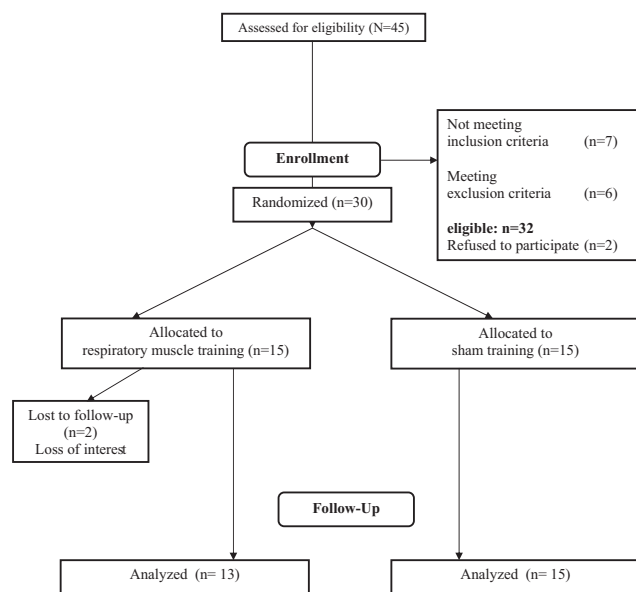


Fig 1. Flowchart for randomization procedure.

sustain motivation, patients were encouraged to only slowly increase their daily training time. The target was to achieve a duration of at least 10 minutes twice a day within the second week, or until discomfort occurred.

The control group performed sham training with an incentive spirometer.^d Patients were instructed to breathe with a low breathing frequency of about 8 to 10 breaths/min (without pacing) after deep exhalation so that no training effect could result. As with the training group, patients were advised to perform this training for at least 10 minutes twice a day, but they were not told that no effects on respiratory muscles were expected.

Patients in both groups were instructed to perform the training procedures for 3 months. They were then readmitted for measurements that were performed during a 2-day hospital stay. Throughout the study, patients documented in a diary the time and duration of respiratory training, with minutes rounded to the nearest value. In addition, they recorded adverse effects. Adherence to the training was further evaluated through telephone interviews. If there was any doubt that training was being adequately done, visits were made to a patient's home to observe performances of the technique.

NPPV and Oxygen Therapy

Intermittent nocturnal NPPV was maintained using a pressure-cycled assist-controlled mode and ventilation parameters were not changed. Table 1 shows the ventilator settings in both groups. Patients were advised to use their home ventilator as usual during the night, or as necessary to maintain their comfort. The average duration of NPPV per day was calculated from the counter readings of the ventilator between the first day of training and readmission to the hospital. These data were available for 23 of the 28 patients (10 in the RMT, 13 in the control group) who completed the study. Previously installed

LTOT was continued without change (5 patients in the control group, 3 patients in the training group), however, oxygen was not administered during the training sessions. Characteristics of patients did not apparently differ between groups with and without LTOT.

Statistical Analysis

Data were collected in Microsoft Access^e and analyzed with the SPSS software package.^f Results are presented as mean and standard deviation (SD). We used the nonparametric Wilcoxon test to evaluate changes within groups. Similarly, we used the nonparametric Mann-Whitney *U* test to compare absolute training-related changes relative to baseline between the 2 groups. Correlation analysis was done by computing the Spearman rank correlation coefficient (*ρ*). *P* values less than .05 were considered statistically significant. Our sample size was derived from expected changes in P_{imax} because this measure seemed to be least affected by the patients' physical handicaps. We estimated that an improvement by at least 20% could be detected with a power of 80% on the 5% level (1-sided) using a sample size of 15, provided the variability of measurements was not larger than 30%. This was achieved by requiring a high degree of patient cooperation and repeated measurements of P_{imax} on both visits.

RESULTS

There were no significant differences in the baseline characteristics of the 28 patients who completed the trial (RMT, *n*=13; control, *n*=15) (see table 1). In the majority of patients (86%), lung restriction was due to kyphoscoliosis (idiopathic in 16 patients, congenital in 3 patients, postpoliomyelitis in 2 [1 in each group], post rachitis in 3 patients). Two subjects had a fibrothorax (1 in each group) and 2 patients (in the control group) had post-tuberculosis syndrome. The daily (total) duration of training was 14±8 minutes (103±27d) in the RMT and 20±8 minutes (97±16d) in the control group. These values did not differ statistically (*P*=.080, *P*=.801, respectively). Patients in the RMT group who documented a training duration of more than 15min/d (*n*=6) showed higher IVC than patients with a shorter duration (1.54±0.45L vs 1.06±0.31L, *P*=.051). There was no similar difference in the control group when a corresponding cutoff value of 20 minutes was taken. Three patients in the RMT group complained of pain (eg, sore muscles) after training sessions.

Respiratory Muscle and Lung Function

In the RMT group but not in the control group, inspiratory mouth pressure increased significantly (0.86±1.14kPa or 27.6%±36.5%, *P*=.013) (table 2); changes in both groups differed from each other (*P*=.046). In patients with a training duration of more than 15min/d (*n*=6), improvements of P_{imax} in the training group were even more pronounced (1.14±1.35kPa, *P*=.046) compared with the control group (.00±.80kPa). There were no significant differences from zero or from each other regarding P_{Emax} or 12-second MVV within the training and control groups. There were no significant changes in total lung capacity, IVC, or blood gases at rest in the 2 groups (see table 2).

Exercise Capacity

Because of spine and skeleton deformations in some patients, only 7 patients in the training group and 10 patients in the control group could perform the cycle ergometer tests. Baseline characteristics of these patients did not differ from the characteristics of patients who could not participate in that test.

Table 1: Baseline Characteristics

Parameter	RMT Group	Control Group	<i>P</i>
N	13	15	NA
Sex (male/female)	8/5	6/9	.339
Age (y)	64.9±11.2	64.1±11.9	.786
BMI (kg/m ²)	27.4±5.0	30.1±6.7	.294
IVC (% predicted)	50.0±14.7	49.0±14.7	.866
TLC (% predicted)	67.8±14.0	60.5±10.7	.130
P _{imax} (kPa)	4.1±1.43	3.6±1.5	.440
P _{Emax} (kPa)	6.0±3.0	6.0±2.6	.964
12-s MVV (L)	33.5±12.1	29.8±10.2	.462
PaO ₂ (mmHg) [†]	65.3±6.6	66.2±11.1	.683
Paco ₂ (mmHg) [†]	42.7±3.4	40.8±7.3	.693
Maximal work rate (W)*	38.7±18.1	38.7±17.3	.887
ṀE (L)*	29.3±4.5	28.4±6.6	.813
Vo _{2peak} /kg (mL·kg ⁻¹ ·min ⁻¹)*	15.2±3.2	15.7±2.9	.962
6MWD (m)	337±93	328±61	.717
SRI summary score	72.5±12.0	71.6±14.2	.981
IPAP (cmH ₂ O)	19.8±4.4	18.9±3.5	.521
EPAP (cmH ₂ O)	4.0±2.9	2.6±2.0	.157
Frequency (L/min)	19.0±4.4	19.4±4.1	.831

NOTE. Values are mean ± standard deviation (SD).

Abbreviations: BMI, body mass index; EPAP, expiratory positive air pressure; IPAP, inspiratory positive air pressure; NA, not applicable; TLC, total lung capacity.

*Cardiopulmonary exercise test (*n*=17).

[†]With usual oxygen flow in patients with LTOT and with breathing of room air in patients without LTOT.

Table 2: Changes in Outcome Measures After 3 Months Compared With Baseline

Parameter	RMT Group	<i>P</i> *	Control Group	<i>P</i> *	<i>P</i> [†]
IVC (% predicted)	-1.4±4.5	.279	-0.9±5.5	.609	.717
TLC (% predicted)	-1.7±8.7	.650	3.5±6.3	.053	.098
P _{imax} (kPa)	0.86±1.14	.013	0.00±0.80	.820	.046
P _{emax} (kPa)	0.76±2.71	.382	-0.59±1.88	.256	.185
12-s MVV (L)	2.0±6.4	.158	5.7±9.5	.060	.769
P _{aO₂} (mmHg) [‡]	-7.3±15.1	.213	-4.1±9.3	.182	.631
P _{aCO₂} (mmHg) [‡]	0.8±6.1	.753	0.8±3.8	.502	.494
Maximal work rate (W)	9.4±14.8	.176	-5.1±10.8	.213	.043
\dot{V}_E (L)	4.0±6.3	.104	-1.4±5.1	.406	.055
V _{O₂peak} /kg (mL·kg ⁻¹ ·min ⁻¹)	2.24±3.39	.128	-1.71±2.54	.066	.014
6MWD (m)	-4.6±55.1	.969	13.0±57.8	.581	.756
Time of NPPV (h/d)	-0.6±1.2	.203	0.4±0.5	.028	.010

NOTE. Values are mean ± SD.

*With regard to changes relative to baseline.

[†]With regard to the comparison of changes between the 2 groups.

[‡]With usual oxygen flow in patients with LTOT and with breathing of room air in patients without LTOT.

Changes of V_{O₂peak} and maximal workload differed between groups (*P*=.014, *P*=.043, respectively) (see table 2), although changes within groups were not significant. Regarding maximal ventilation, changes within groups did not differ significantly from zero or from each other. Similarly, there were no significant changes in 6MWD or differences between these changes, neither in the whole group (see table 2) or the subgroup of patients participating in the ergometer test (data not shown).

Health-Related Quality of Life

Changes in SRI scores after 3 months are shown in table 3. There were no significant changes of scores or differences between these changes except for the SRI physical functioning score, whose changes differed between groups (*P*=.012) mainly because of a decrease in the control group. Furthermore, the SRI summary score and social functioning score tended to decrease in the control group, whereas it remained about the same in the RMT group.

Table 3: Training-Related Changes in HRQOL (SRI Questionnaire)

Parameter	RMT Group	<i>P</i> *	Control Group	<i>P</i> *	<i>P</i> [†]
SRI-SS	0.4±5.6	.875	-3.7±7.0	.061	.093
SRI-RC	1.8±8.7	.433	-4.8±9.1	.080	.139
SRI-PF	3.3±8.4	.201	-6.6±9.0	.021	.012
SRI-AS	3.3±11.4	.473	-1.7±9.8	.624	.943
SRI-SR	-1.7±9.0	.482	-1.1±8.1	.383	.516
SRI-AX	-0.8±9.5	.717	-3.0±15.3	.226	.867
SRI-WB	-3.2±7.6	.202	-2.2±12.4	.477	.183
SRI-SF	0.5±11.8	.878	-6.7±13.0	.051	.486

NOTE. Values are mean ± SD.

Abbreviations: AS, attendant symptoms and sleep; AX, anxiety; PF, physical functioning; RC, respiratory complaints; SF, social functioning; SR, social relationships; SS, summary score; WB, psychological well-being.

*With regard to changes relative to baseline.

[†]With regard to the comparison of changes between the 2 groups.

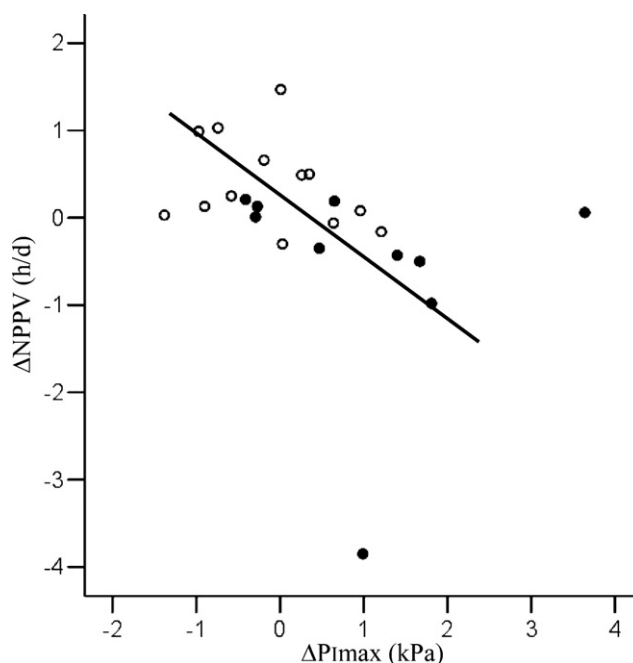


Fig 2. Relation between the changes in P_{imax} (ΔP_{imax}) after 3 months and the changes in daily duration of NPPV (ΔNPPV) at home in the RMT group (●) and control group (○). There was a significant correlation between both measures when taken over both groups (ρ = -.61, *P* = .002). The line indicates the relationship derived from orthogonal linear regression.

Noninvasive Positive Pressure Ventilation

The duration of ventilator use at home during the 3 months decreased in the training group and increased significantly in the control group; these changes differed from each other (*P* = .010) (see table 2). There were no significant relationships between the daily duration of NPPV at home and P_{imax} within each of the 2 groups; however, when patients of both groups were evaluated, there was a correlation between the change in P_{imax} and the change in daily NPPV duration (ρ = .61, *P* = .002) (fig 2). Correspondingly, when both groups are included, changes in the daily duration of NPPV within 3 months were different between patients who showed an increase in P_{imax} compared with those showing a decrease (-0.3 ± 1.2 h/d vs 0.4 ± 0.4 h/d, *P* = .033).

DISCUSSION

The data from this study indicate that in patients with restrictive thoracic disorders who were treated with NPPV, inspiratory muscle strength as assessed by P_{imax} increased after 3 months of RMT compared with results in patients who performed a sham procedure. Improvements in exercise performance or HRQOL, however, were very small and significant only when compared with the slight deteriorations observed in the control group. Overall, RMT appears to be a safe and feasible treatment option in patients with restrictive thoracic disorders and moderate stable chronic hypercapnic respiratory during nocturnal domiciliary NPPV.

Despite controversial views,³² the American College of Chest Physicians and the American Association of Cardiovascular and Pulmonary Rehabilitation³³ have stated that RMT may be justified, particularly in patients with COPD and respiratory muscle weakness.¹⁷ This has also been supported by a

meta-analysis.¹⁵ In contrast, there is less knowledge about the efficacy of RMT for patients with restrictive thoracic disorders and, consequently, fewer recommendations for its use. Improved respiratory muscle endurance may be of special value in patients with respiratory failure in order to overcome respiratory muscle fatigue or to facilitate the process of weaning.^{8,34} Isocapnic hyperpnea as a training modality has been demonstrated to be effective in COPD, cystic fibrosis, and in healthy subjects.^{18-20,31,35,36} Therefore, we evaluated this approach in an RCT. We considered this effort worthwhile despite the fact that the number of eligible subjects was limited, even in a large specialized center. We also restricted the spectrum of patients further by excluding patients with very pronounced impairments for safety reasons and because of the possibility that RMT in chronic, stable respiratory failure could be harmful.

This study found an increase in inspiratory muscle strength of about 20%, assessed noninvasively by measurement of P_{imax}. This result is in line with a previous case report²² of 2 patients with kyphoscoliosis who performed ventilatory muscle training.

Effort-dependent parameters such as P_{imax} are affected by learning and motivation; therefore they might not be best suited for assessing changes in inspiratory muscle strength after RMT.³² It should be noted, however, that our study followed a double-blind design and most of the patients were familiar with P_{imax} measurement before they entered the study. Nevertheless, the fact that isocapnic hyperpnea improved P_{imax}, although its primary aim was to improve respiratory muscle endurance, deserves an explanation. Patients with severe restrictive thoracic disorders are characterized by a remarkable stiffness of the thoracic cage that is associated with decreased chest wall compliance. Thus, we consider it likely that the mechanical resistance of breathing is always intrinsically high in these patients. Therefore, in considering the total wall chest system, all types of training necessarily involve resistive training. In addition, despite its being low, the internal resistance of the device used might have implied some degree of resistive training in view of the severely impaired lung function. These considerations may also explain why the targeted and recommended training time^{33,37,38} was not reached by most of the patients.

Respiratory muscle endurance as assessed by 12-second MVV did not indicate training-related changes. Previous authors³⁹⁻⁴¹ used this test to evaluate the effects of IMT in patients with neuromuscular disease and described highly reproducible improvements after training; thus, we also used this measure. It can be argued, however, that the 12-second MVV is a complex maneuver that is highly dependent on learning, motivation, and cooperation.³⁹ Indeed, we observed a significant improvement in 12-second MVV after 3 months when both groups were considered together ($P=.024$; data not shown). We consider, however, the tendency toward augmented \dot{V}_E during cycle exercise in the RMT group to be indicative of improved respiratory muscle endurance. Taking into account the relatively short duration of daily training, it was not likely to result in a considerable improvement in respiratory muscle endurance. Retrospectively it might be argued that more reliable tests would have been the maximal sustained ventilatory capacity¹⁹ or the time over which a targeted submaximal ventilation can be sustained.³¹

Exercise performance is not only determined by respiratory muscle strength, but also by vital capacity, peripheral muscular mass, and cardiovascular conditioning.² This might explain why the gain in maximum work load and \dot{V}_{O_2} peak was small and only significant in comparison to the control group. Accordingly, in a meta-analysis of studies of patients with COPD

performing an IMT, no significant improvements were reported for exercise performance despite the beneficial effects on respiratory muscle function.¹⁵ In our study, no changes were found in 6MWD, probably because in kyphoscoliosis, walking is highly limited by deformations of the skeleton and lower extremities, as previously mentioned.⁴² Based on the dominant role of deformation, it was also not expected that the 3-month training altered chest wall compliance and, thereby, static lung volumes. Indeed, none of the lung function parameters showed significant changes.

A previous study²⁹ reported improvements in HRQOL and daily life activities after IMT in 5 of 7 patients with kyphoscoliosis postpoliomyelitis. We used the SRI Questionnaire, which is specifically designed for patients with home mechanical ventilation. There was no overall improvement in HRQOL, but there was an advantage in the RMT group after 3 months in the physical functioning domain. Interestingly, the difference seemed to be again attributable to a trend toward decreased HRQOL in the control group. Particularly, the longer training times in the control group may have been regarded as cumbersome and boring, thus resulting in a negative impact on HRQOL. In this respect, dyspnea scales may reflect effects of RMT better than HRQOL; indeed, most studies investigating RMT in COPD reported beneficial effects on dyspnea.¹⁵ Although the use of the training device was considered bothersome by some patients, the training appeared at least to be capable of compensating the loss in HRQOL that was observed in the control group. This implies that the perceived benefit of RMT relative to the time spent training was greater in the RMT group than in the control group. We conclude that the increase in P_{imax} does not necessarily imply a benefit in everyday life. The concomitant gain in maximum tolerable workload and \dot{V}_{O_2} peak, however, indicated a shift toward higher maximum exercise capacity, although these changes were statistically significant only relative to the control group, which showed an impairment.

One question of interest is why most of the changes in exercise performance or HRQOL were only significant when the training group was compared with the sham group, which showed a deterioration of most of the outcome measures after 3 months. We can only speculate about this unexpected finding, which occurred despite strict randomization of the consecutive patients included. It is not likely that the sham training per se had a negative effect on the physical outcome measures. Both groups showed similar characteristics on entry, thus the only explanation besides a real impairment was a potential lack of cooperation in the re-evaluation after 3 months. The increase in the time of ventilator use (see below), however, seems to indicate that the patients indeed experienced a deterioration even within only 3 months despite the fact that in patients with restrictive thoracic disorders hypercapnic respiratory failure usually remains stable once NPPV is initiated.⁷

The RMT appeared to be safe since there were no adverse effects on blood gases, in particular no increase in P_{aCO_2} , although all patients were receiving NPPV therapy because of chronic hypercapnic respiratory failure. One patient with prior poliomyelitis experienced pain (eg, sore muscles) after training sessions, which might indicate a muscle overuse in this group of patients. Indeed, the role of training in patients with prior poliomyelitis is controversial.⁴³ The 2 patients in our study, however, very clearly suffered from chest wall deformity and scoliosis, thereby suggesting predominately mechanical disadvantage. Furthermore, muscle training in patients with prior poliomyelitis is feasible and without negative effects.⁴⁴ In addition, beneficial effects of IMT on respiratory endurance have been reported in patients who used part-time assisted

ventilation.²³ As in our study, all patients in that study were under NPPV, thus a safety back-up assuring muscle rest was provided.

We consider it a noteworthy finding that patients in the RMT group reduced the duration of daily ventilator use compared with the control group, despite the additional load represented by the training. The difference was largely due to an increased time of use by the control group, whereas the variation in the magnitude of changes was larger in the training group. This might well indicate an effect of RMT on daily life, at least in a subgroup of patients, irrespective of the fact that the SRI Questionnaire showed only few changes. Possibly the patients' behavior over time was a more sensitive measure than the Questionnaire, which represented a single-point assessment subject to interpretation and daily conditions. The observed reduction in ventilator use confirms the findings of earlier, nonrandomized, noncontrolled trials in patients with restrictive thoracic disorders and home ventilation.^{22,23} It is also reassuring that the changes in P_{imax} were associated (see fig 2) with changes in the duration of the ventilator use, when both groups were analyzed; this might suggest a true improvement of respiratory muscle performance by RMT. Taken together, the results indicate that RMT is effective in these diseases and that nocturnal NPPV is not a contraindication for RMT, as might be argued from the overload of muscles that led to the initiation of NPPV.

Study Limitations

Our study was subject to several limitations, although it followed a randomized controlled design. First, the domiciliary RMT was not directly or daily supervised and training duration could only be estimated from the diaries. In future studies, recording devices attached to the breathing device could be helpful in supervising training. Furthermore, some interpretations of our findings could only be tentative, as the number of patients studied was small, particularly when compared with samples sizes that are commonly used for such analyses. This was particularly true when those effects that turned out to be statistically significant only when comparing groups are considered, due to changes occurring in the control group. In addition, the small number of subjects did not allow us to correct for multiple comparisons of experimental conditions and variables. We therefore provided numeric *P* values in order to allow the reader to judge on the individual results. This did not seem fully inappropriate, inasmuch as the results appeared consistent and conceivable.

CONCLUSIONS

The data of this randomized, controlled, double-blind trial provided some evidence that in severe restrictive thoracic disorders, RMT performed as isocapnic hyperpnea over 3 months can improve respiratory muscle function. It is probable that in patients with restrictive thoracic disorders and severe pulmonary impairment, even RMT that is primarily targeted on endurance necessarily includes a significant component of resistive training. This improvement, however, was not directly translated in other measures of general physical capacity such as cycle exercise performance, or 6MWD, or HRQOL. Nevertheless, RMT was safe and feasible in patients with restrictive thoracic disorders and its benefits appeared even as a reduction of home ventilator use compared with controls. Future large-scale, multicenter studies should evaluate whether RMT in addition to NPPV in restrictive thoracic disorders is a promising therapeutic approach, with positive long-term outcome and an impact on disease progress. Such studies should include different training intensities and modalities.

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Suppliers

- a. Rapidlab; Bayer Inc, East Walpole, MA 01021-1597.
- b. Jaeger Inc, Leibnizstrasse 7, 97204 Würzburg-Hoechberg, Germany.
- c. Spirotiger; IDIAG AG, Chriesbaumstrasse 6, 8604 Volketswil, Switzerland.
- d. Coach II; Tyco Healthcare Inc, Gewerbepark 1, 93333 Neustadt a. D., Germany.
- e. Microsoft Corp, One Microsoft Way, Redmond, WA 98052.
- f. Version 11.0; SPSS Inc, 233 S Wacker Dr, 11th Fl, Chicago, IL 60606.