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# Inspiratory muscle training in pulmonary rehabilitation program in COPD patients

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## Summary

Most pulmonary rehabilitation (PR) programs do not currently incorporate IMT in their PR programs for COPD patients.

The aim of the present study was to assess the influence of adding IMT to the patients already involved in a rehabilitation program.

Thirty-four patients with significant COPD were recruited for the study. All patients participated in a general exercise reconditioning (GER) program for 12 weeks. The patients were then randomized to receive IMT or sham IMT, in addition to GER for the next 6 months.

Following three months of GER training there was a significant increase in the 6-min walk test (6MWT) (from mean  $\pm$  SEM 254  $\pm$  38 to 322  $\pm$  42 m,  $p < 0.01$ ), and small but non-significant decreases in the perception of dyspnea (POD), and in the St. George Respiratory Questionnaire score (SGRQ). Following the addition of IMT to the GER program there was a significant increase in the  $P_{I_{max}}$  in the GER+IMT group (from 66  $\pm$  4.7 to 78  $\pm$  4.5 cm H<sub>2</sub>O,  $p < 0.01$ ). This was accompanied by a significant improvement in the POD and a further significant improvement in the SGRQ score.

IMT provides additional benefits to patients undergoing PR program and is worthwhile even in patients who have already undergone a GER program.

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## Introduction

A recent guideline by the American Thoracic Society defined pulmonary rehabilitation (PR) as “a multidisciplinary program of care for patients with chronic respiratory impairment that is individually tailored and designed to optimize physical and social performance and autonomy”.<sup>1</sup>

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PR is a therapy that, without affecting lung function, impacts positively upon some of the other sensory and metabolic consequences of the disease.

For example, PR decreases the perception of dyspnea (POD),<sup>2,3</sup> enhances exercise capacity,<sup>4,5</sup> reduces healthcare resource utilization,<sup>6,7</sup> and improves health status.<sup>8</sup> Reduction of lactic acidosis, reduction in minute ventilation and heart rate for a given work rate and enhanced activity of mitochondrial enzymes and improved capillary density in the trained muscles, are among the underlying physiological changes that contribute to these improvements.<sup>9</sup>

Although not universally accepted many studies have shown that patients with significant COPD have inspiratory muscle weakness that may contribute to dyspnea and to exercise intolerance.<sup>10,11</sup> Inspiratory muscle dysfunction appears to be the result of geometric changes of the thorax and diaphragm, due to hyperinflation, as well as systemic factors and potential structural changes within the muscles.<sup>12,13</sup>

Recent evidence suggests that there is a fundamental deficit of diaphragm fibre contractile force in patients with COPD.<sup>14</sup> Thus, there would appear to be a sound theoretical rationale for inspiratory muscle training, in order to reverse the functional deficit that is present in these patients.

In 1997, the joint ACCP/AACVPR committee<sup>15</sup> concluded that there was sufficient evidence to recommend IMT as part of a program of PR. They concluded that in studies where the stimulus or load placed on the inspiratory muscles during training was sufficient to augment inspiratory muscle strength, there was an associated increase in exercise capacity and decrease in dyspnea. Similarly, the findings of the meta-analysis of IMT in patients with COPD performed by Lotters and associates<sup>16</sup> suggest that IMT reduces exertional dyspnea in patients with COPD. In addition, when dyspnea is attenuated, an associated effect of IMT is improved functional exercise capacity. In studies that used appropriate selection criteria and where post-IMT changes in exercise tolerance were assessed, most have found a significant improvement.<sup>17–21</sup> In the most recent meta-analysis, that was also conducted in order to determine the effect of IMT in adults with COPD, it was concluded that controlled IMT significantly improves inspiratory muscle strength and endurance, decreases dyspnea and improves some outcomes of exercise capacity.<sup>22</sup>

Despite the ample evidence that IMT generates improvements in inspiratory muscle function that yield functional benefits for patients with COPD, IMT does not appear to be incorporated routinely into PR programs for COPD patients.<sup>23</sup>

The present study was designed in order to evaluate the effect of adding IMT to the training of COPD patients already involved in a long term PR program. We assessed lung function, inspiratory muscle strength, POD, exercise performance, and quality of life, in patients with significant COPD.

## Patients and methods

### Subjects

Thirty-four consecutive patients, 26 men and eight women were recruited. They had spirometric evidence of significant

chronic air-flow limitation ( $FEV_1 < 50\%$  predicted,  $FEV_1/FVC < 70\%$  predicted) and were diagnosed as having COPD according to American Thoracic Society criteria.<sup>24</sup> All patients were new to a PR program, and none took any additional regular exercise or nutritional supplements. All were on regular long-acting bronchodilators, and inhaled corticosteroid therapy. Patients were observed during a four-week run-in period, when their regular treatment was maintained, to verify stability in their clinical and functional status.

Patients with cardiac disease, poor compliance, or requirement of supplemental oxygen, were excluded from the study.

### Study design

The study had a double-blind, randomized controlled design. The PR program was divided into the two phases: pre- and post-randomization. In the pre-randomization phase all patients participated in a general exercise reconditioning (GER) program that included lower extremity endurance exercise (walking or cycling), upper extremity exercise and strength training with free weights. This phase included 36 sessions of 1½ h duration (three times a week for 12 weeks).

After the first 12 weeks, the patients were randomized into two groups, for the second phase of the study (post-randomization), using a random numbers table. Half of the group was assigned to receive GER plus IMT (training group) using a pressure threshold device (POWERbreathe®, Gaiam Ltd., Southam, UK) and a protocol similar to that described previously.<sup>20,25</sup> The other half of the group undertook GER plus IMT at a load known not to yield improvements in inspiratory muscle function (sham training control group).<sup>20,25</sup> During this phase, GER took place for 1 h three times a week, for six months. Patients were not aware which group they had been allocated to.

Several practice tests were performed by all patients prior to baseline data collection in order to minimize possible learning effects. All data were collected by the same investigator, who was blinded to the training group.

The training was performed in a community-based rehabilitation center under the supervision of a respiratory therapist.

The study protocol was approved by the institutional ethics committee and informed consent was obtained from all the patients.

### Outcome measures

All assessments were performed before and three, six, and nine months after starting the PR intervention.

**Spirometry:** The forced vital capacity (FVC) and the forced expiratory volume in one second ( $FEV_1$ ) were measured three times on a computerized spirometer (Compact, Vitalograph, Buckingham, England) and the best trial is reported.

**Six-minute walk test (6MWT):** The distance the patient was able to walk in 6 min was determined in a measured corridor as described for the 12-min walk test by McGavin

and coworkers.<sup>26</sup> The patients were instructed to walk at their fastest pace and cover the longest possible distance over 6 min under the supervision of a physiotherapist. The test was performed twice and the best result is reported.

**Inspiratory muscle strength:** Inspiratory muscle strength was assessed by measuring the maximal inspiratory mouth pressure ( $PI_{max}$ ) at residual volume (RV), as previously described by Black and Hyatt.<sup>27</sup> Mouth pressures were measured with a vacuumed 1002 mouthpiece (Ventura, CA), that has a small air leak to prevent pressure generation by glottis closure, connected to a pressure transducer (1050 BP transducer, Biopac System) and recorded on a strip chart recorder. Some training sessions were performed before the measurements, until reproducibility was obtained. The value obtained from the best of at least three efforts was used.

**Dyspnea:** The POD was measured while the subject breathed through a device similar to that described by Nickerson and Keens,<sup>28</sup> and using a protocol described previously.<sup>25</sup> The subjects breathed against progressive resistance, at 1 min intervals, in order to achieve mouth pressure of 0 (no resistance), 5, 10, 20 and 30 cm H<sub>2</sub>O. After breathing for 1 min at each inspiratory load, the subjects rated the sensation of difficulty in breathing (dyspnea) using a modified Borg CR-10 scale.<sup>29</sup> This is a linear scale of numbers ranking the magnitude of difficulty in breathing, ranging from 0 (none) to 10 (maximal).

**Health-related quality of life:** Health-related quality of life was measured by the St. George's Respiratory Questionnaire.<sup>30</sup>

### Data analysis

The results are expressed as mean  $\pm$  SEM. Comparisons of lung function, inspiratory muscle strength, the 6MWT, and POD, within and between the two groups were carried out using the two-way ANOVA with repeated measures.

## Results

### First phase

Three patients dropped out of the first phase of the study. The remaining 31 patients were randomized for the second phase of the study. Their characteristics are summarized in Table 1. There were no significant differences between the two groups in age, height, weight, mean baseline ABG, FEV<sub>1</sub> and FVC,  $PI_{max}$ , the 6MWT, and health-related quality of life, at the beginning of the study.

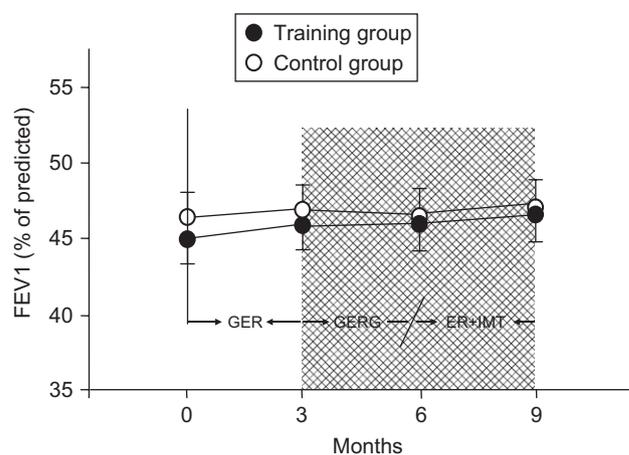
The attendance rate in the first phase of the study was 68%  $\pm$  7% in the training group (GER+IMT) and 70%  $\pm$  8% in the control group (GER+sham IMT).

Following the first three months of GER-only training there was no statistically significant change in the FEV<sub>1</sub>, FVC or  $PI_{max}$  in either group (Figs. 1 and 2). However, there was a significant increase in the 6MWT (from mean  $\pm$  SEM 254  $\pm$  38 to 322  $\pm$  42 m, 26%,  $p < 0.01$ ), and a small but non-significant decrease in the POD (from 22.8  $\pm$  0.6 to 20.6  $\pm$  0.5 total Borg score), and the St. George Respiratory Questionnaire (SGRQ) score (from 60.1  $\pm$  2.1 to 56.3  $\pm$  2.5 total SGRQ score) (Fig. 3–5).

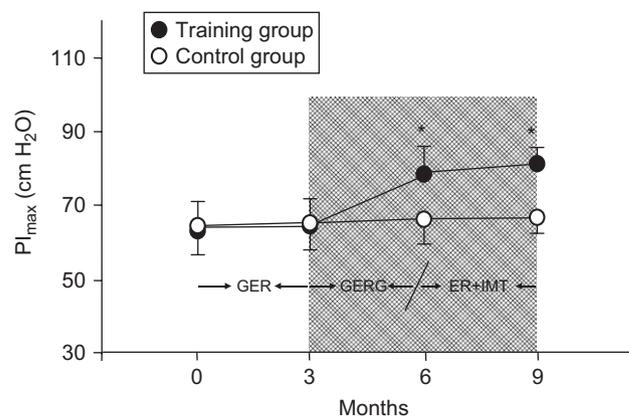
**Table 1** Characteristics of patients with COPD<sup>a</sup>.

	IMT (n = 16)	Control (n = 15)
Age (yr)	65.2 $\pm$ 3.4	66.1 $\pm$ 3.2
Sex (M/F)	11/5	12/3
Weight (kg)	78.1 $\pm$ 3.6	79.7 $\pm$ 3.4
Height (m)	1.68 $\pm$ 3.2	1.70 $\pm$ 3.4
FVC (L)	2.41 $\pm$ 1.2	2.43 $\pm$ 1.0
% Predicted	66 $\pm$ 4.6	68 $\pm$ 4.4
FEV <sub>1</sub> (L)	1.28 $\pm$ 0.4	1.29 $\pm$ 0.4
% Predicted	45 $\pm$ 2.4	46 $\pm$ 2.7
6MWT (m)	244 $\pm$ 31	253 $\pm$ 39
$PI_{max}$ (cm H <sub>2</sub> O)	66 $\pm$ 4.7	67 $\pm$ 4.6
Current smokers	3	2
Ex-smokers	13	13

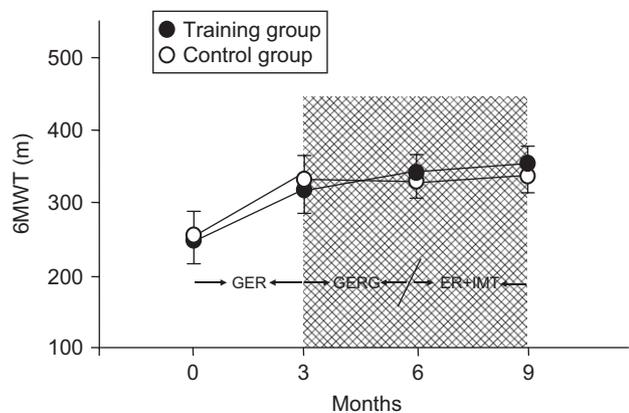
<sup>a</sup>Values are expressed as mean  $\pm$  SEM.



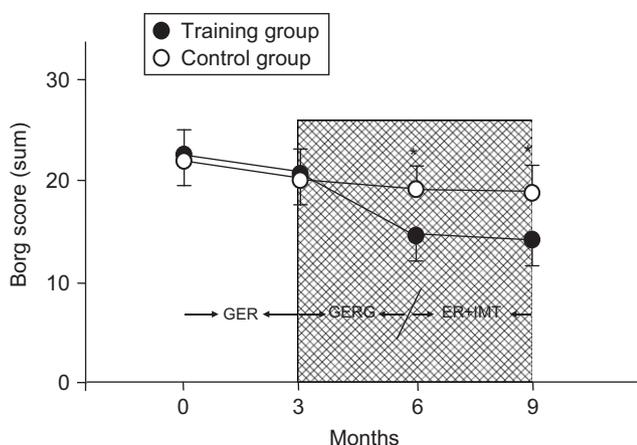
**Figure 1** FEV<sub>1</sub> (% of predicted) of the patients involved in the PR program before and following the GER period and before during and following the GER+IMT period.



**Figure 2** Inspiratory muscle strength, as assessed by the  $PI_{max}$  (maximal mouth inspiratory pressure), before and following the GER period and before during and following the GER+IMT period, in the study group and in the control group. Already at the three month period after the addition of IMT there was a statistically significant difference between the groups.



**Figure 3** The mean  $\pm$  SEM distance walked in 6 min, before and following the GER period and before during and following the GER+IMT period, in the study group and in the control group.



**Figure 4** The mean  $\pm$  SEM perception of dyspnea (Borg score), before and following the GER period and before during and following the GER+IMT period, in the study group and in the control group. Already at the three month period after the addition of IMT there was a statistically significant difference between the groups.

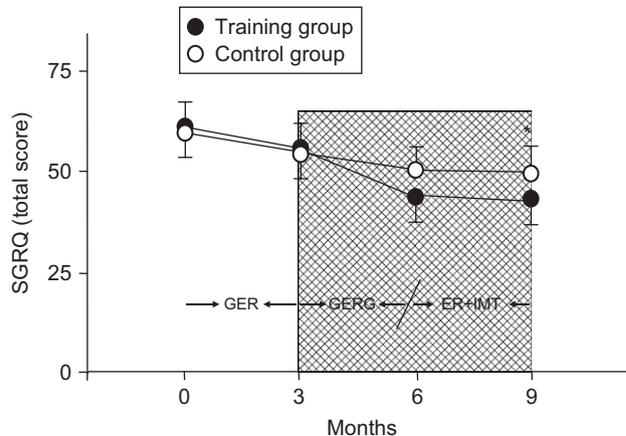
**Second phase**

During the second phase of the study four more patients dropped out of the study (two from the study group and two from the control group).

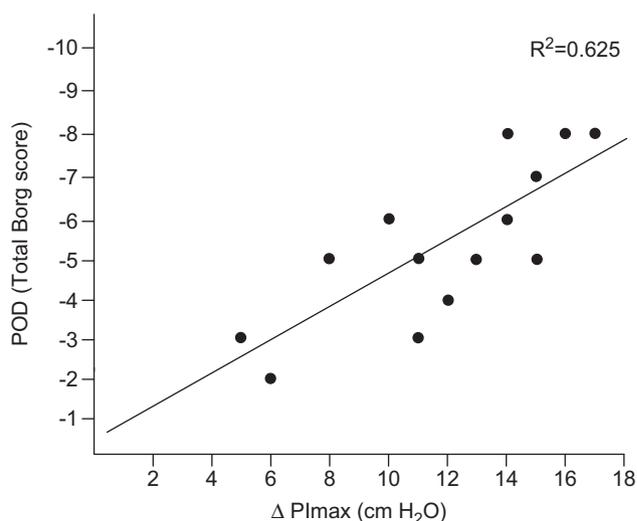
Following the addition of IMT to the GER program the FEV<sub>1</sub> and the 6MWT remained unchanged, with no difference between the groups (Fig. 1 and 3).

There was a significant difference in the PI<sub>max</sub> between the training group and control groups after three months of training and this difference was maintained after a further three months of training (Fig. 2). The difference arose via an increase in PI<sub>max</sub> in the training group that did not occur in the control group.

There was a significant decrease in the POD in the training group (from 20.2 $\pm$ 0.4 to 14.9 $\pm$ 0.3 total Borg score,  $p$ <0.001), but not in the control group (Fig. 4). The



**Figure 5** Changes in health-related quality-of-life scores determined by the St. George Respiratory Questionnaire, before and following the GER period and before during and following the GER+IMT period, in the study group and in the control group. At the six month period after the addition of IMT there was a statistically significant difference between the groups.



**Figure 6** The correlation between the increase in the inspiratory muscle strength and the decrease in the perception of dyspnea, in the GER+IMT group.

difference between the two groups was statistically significant.

There was a close correlation between the individual increase in the PI<sub>max</sub> and the decrease in the POD ( $p$ <0.005) in the GER+IMT group (Fig. 6).

There was a continuous decrease in the SGRQ score in both groups. However, the decrease in the score was greater in the training group and the difference between the groups became significant at the end of the sixth month of training ( $p$ <0.05) (see also Fig. 5).

**Discussion**

The results of this study are in concordance with previous studies demonstrating that in patients with significant COPD,

GER yields improvements in exercise tolerance and quality of life. Further, the data suggest that the addition of IMT to GER results in an increase in the inspiratory muscle strength that is accompanied by a decrease in the POD, and in an improved quality of life. There was no additional improvement in exercise performance, as was expressed by the 6MWT, when IMT was added to GER. There were no changes in lung function during any phase of the intervention.

In patients with COPD, exercise capacity, health-related quality of life, and participation in activities of daily living are often impaired out of proportion to lung function impairment.<sup>31</sup> Comprehensive PR programs are designed to tackle the systemic consequences of COPD. Since the first controlled trials on PR in the mid-1970s, PR has been shown to result in clinically significant improvements in quality of life, dyspnea during daily activities and exercise capacity.<sup>32</sup> According to the World Health Organization's Global Initiative for Chronic Obstructive Lung Disease (GOLD) consensus document on the management of COPD,<sup>33</sup> PR should be considered in all patients with an FEV<sub>1</sub> below 80% of the predicted value. In our study, following the first three months of PR without IMT, there was a small but non-significant decrease in the POD and the SGRQ score. We believe that with a larger group of patients or longer duration of rehabilitation we could have shown also statistical significance in these two parameters.

In patients with advanced COPD, dyspnea is reported as a limiting factor during exercise, and as a common complaint during daily activities.<sup>10,11</sup> Inspiratory muscle weakness would be expected to increase the intensity of dyspnea for a given minute ventilation, since greater motor outflow is required for a given level of pressure generation by the muscles.<sup>11</sup>

Inspiratory muscle training has been extensively investigated in patients with COPD. The findings of Lotters and associates' recent meta-analysis of IMT in patients with COPD<sup>16</sup> suggest that IMT reduces exertional dyspnea in these patients. These authors concluded that "inspiratory muscle training is an important addition to a PR program directed at COPD patients". They also concluded that "IMT significantly increased inspiratory muscle strength and clinically significant decrease in dyspnea sensation at rest and during exercise was observed". In the most recent systematic review on this subject<sup>22</sup> it is stated that "IMT was associated with significant improvements in some outcomes of inspiratory muscle strength (P<sub>I,max</sub>) and endurance (inspiratory threshold loading), exercise capacity (Borg scale for respiratory effort (modified Borg scale), work rate maximum (Watts), and dyspnea (Transition Dyspnea Index)". The addition of IMT to PR was also recommended by the joint ACCP/AACVPR committee.<sup>15</sup>

Some controversy remains regarding the mechanism for the enhanced inspiratory muscle force output (strength) following IMT, with some authors arguing that the inspiratory muscles of patients with COPD are already well adapted to chronic loading and do not express any adaptation in response to training. However, significant changes in the proportions and sizes of external intercostal muscle fibers have been observed following IMT,<sup>34</sup> and these changes were accompanied by an increase in both the strength and endurance properties of the inspiratory muscles.

Somewhat surprisingly, the rationale of adding IMT to PR is still questioned, and there has been some debate about whether IMT should be part of rehabilitation programs for

COPD patients. This may be because of two fundamental misconceptions. Firstly, that the diaphragm of patients with severe COPD is already well trained. However, the endurance adaptations that have been observed are also associated with a loss of type 2 muscle fibers, which likely contributes to the loss of inspiratory muscle strength that is also observed.<sup>35</sup> Loss of inspiratory muscle strength has negative sensory implications for exertional dyspnea,<sup>36</sup> since the muscles are required to act at a mechanical disadvantage due to hyperinflation. Thus, the inspiratory muscles of patients with COPD are not well trained, they are merely adapted to the requirement for an increased pressure generation during resting breathing. A second misconception is that GER is capable of providing a training stimulus that will yield improvements in inspiratory muscle strength, and that additional, specific, IMT is therefore redundant. Our data do not support this contention.

The absence of an additive influence of GER and IMT upon 6MWT is somewhat surprising in light of the reduction in POD elicited by IMT in our study, as well as observations on healthy young adults that have reported amelioration of dyspnea assessed during exercise after IMT.<sup>37,38</sup> An explanation for this observation may reside within the magnitude and time course of the changes in 6MWT performance that we observed. The improvement in 6MWT in response to GER was substantial, some 26% (68 m), and was achieved almost entirely over the first three months of the nine month intervention. It is possible that the 26% improvement that we observed represented full extent of the adaptive potential of these patients. The finding that a further six months of GER failed to elicit any additional improvements in 6MWT performance would tend to support this notion. Thus, IMT may not have led to any additional improvements in 6MWT because the patients had already achieved their full potential in response to GER alone.

Quality of life and dyspnea are unarguably the most important outcomes from a patient perspective. Since both of these variables showed significantly greater improvements following the addition of IMT to GER, we argue that this alone justifies the inclusion of IMT in PR programs. In addition, a recent randomized controlled trial from our laboratory<sup>39</sup> also demonstrated that patients who had undergone a 12 month program of IMT (without GER) showed a reduction in the use of healthcare resources. This was primarily as a result of a decrease in the time spent in hospital after admission for an exacerbation. The underlying mechanism for this appeared to be that the patients undergoing IMT felt more confident about coping with their dyspnea, and were therefore released from hospital earlier. These data lend further support to the inclusion of IMT in PR.

Our findings support the addition of IMT to GER as part of a program of PR. Although the addition of IMT did not yield further improvements in 6MWT, it did result in significantly greater improvements in quality of life and POD than GER alone.

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