Impact of a Rehabilitation Program on Dyspnea Intensity and Quality in Patients with Chronic Obstructive Pulmonary Disease

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Key Words

Chronic obstructive pulmonary disease • Dyspnea •
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Six-minute walking test

Abstract

Background: It has yet to be determined whether the language of dyspnea responds to pulmonary rehabilitation programs (PRP). **Objective:** We tested the hypothesis that PRP affect both the intensity and quality of exercise-induced dyspnea in patients with chronic obstructive pulmonary disease (COPD). **Methods:** We studied 49 patients equipped with a portable telemetric spirometry device during the 6-min walking test before and 4 weeks after PRP. In a first screening visit, appropriate verbal descriptors of dyspnea were chosen that patients were familiar with during daily living activities. Tidal volume, respiratory frequency, inspiratory capacity, inspiratory reserve volume (IRV) and dyspnea intensity were evaluated by a modified Borg scale every minute during the test. **Results:** Qualitative descriptors of dyspnea were defined by three different sets of cluster descriptors (a–c) at the end of the exercise test, before and after PRP: a – work/effort (W/E); b – inspiratory difficulty (ID) and chest tightness (CT), and c – W/E, ID and/or CT. The three language

subgroups exhibited similar lung function at baseline, and similar rating of dyspnea and ventilatory changes during exercise. The rehabilitation program shifted the Borg-IRV relationship (less Borg at any given IRV) towards the right without modifying the set of descriptors in most patients. **Conclusions:** Rehabilitation programs allowed patients to tolerate a greater amount of restrictive dynamic ventilatory defect by modifying the intensity, but not necessarily the quality of dyspnea.

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Introduction

Our ability to provide the best care possible to patients with dyspnea depends upon our capacity to break down any communication barriers between physicians and patients. The language of dyspnea, i.e. its qualitative aspects, complements physiological measurements, both being essential to a comprehensive understanding of exercise tolerance and dyspnea [1–6]. There is evidence that the quality of dyspnea varies depending on the nature of the dyspnea-generating stimulus or the specific pathophysiological impairment induced by the disease [1–6]. At higher ventilation during exercise, augmented che-

mostimulation, critical restrictive ventilatory mechanics, being associated with dynamic hyperinflation, and increased central respiratory drive decrease the coupling of neural to muscular events in patients with chronic obstructive pulmonary disease (COPD) [7, 8]. The neuromuscular decoupling underpins distinct qualitative sensations such as work/effort (W/E), inspiratory difficulty (ID), air hunger or chest tightness (CT) in these patients [4, 9]. Both pharmacological treatment [8–14] and pulmonary rehabilitation programs (PRP) [15–18] positively affect exercise-induced dyspnea by improving mechanical constraints. However, while the intensity of dyspnea proves responsive to treatment [8–16], whether the language of dyspnea responds to PRP has yet to be defined. We reasoned that if the improvement in mechanical factors underlying neuromuscular decoupling [4, 7, 8, 15, 17] forms the basis, at least in part, for reduced dyspnea perception, a rehabilitation program aiming to improve mechanical constraints [15, 17] might affect both the intensity and quality of dyspnea during submaximal exercise in patients with COPD. The present study was carried out to test this hypothesis. We chose the 6-min walking test (6MWT) because it reflects the capacity to perform day-to-day activities, induces dyspnea and is used to assess the effectiveness of therapies such as pulmonary rehabilitation [19].

Patients and Methods

Patients

Forty-nine COPD patients (5 females) with moderate-severe airway obstruction participated in the study. They were selected from a pulmonary rehabilitation program if they satisfied the following three criteria: (i) long history of smoking and moderate-severe chronic dyspnea score (Medical Research Council >II); (ii) clinically stable condition, with no exacerbation or hospital admission in the preceding 4 weeks, and (iii) free from other significant diseases potentially contributing to dyspnea. Patients were all motivated to participate in the program and did not smoke currently.

Protocol

This was a single-center, two-period, controlled study in which subjects completed a 6-week non-intervention period before entering a 4-week PRP involving regular exercise training. In an initial screening, subjects were tested for pulmonary function. They were familiarized with testing procedures and scales for rating intensity and quality of dyspnea, and they completed a 6MWT. Three experimental visits were held at 6-week intervals immediately before the control period (baseline), after the control period (before PRP) and after PRP; therefore subjects acted as their own control. All visits were at the same time of the day for each subject. Each patient attended a 4-week outpatient PRP. The program in-

cluded education, breathing retraining and exercise training for 30–60 min daily for 5 days a week. Sessions were closely supervised by a rehabilitation therapist. The study was carried out in accordance with the Declaration of Helsinki (2000) of the World Medical Association. Informed consent was given by the patients. The study was approved by the Ethics Committee of the Institution.

Lung Function

Routine spirometry testing was performed with subjects in a seated position according to European Respiratory Society Guidelines [20]. Functional residual capacity (FRC) was measured by a constant volume whole-body plethysmograph (Autobox D₁ 6200 Sensor Medics; Yorba Linda, Calif., USA) using a breathing frequency <1 Hz [21]. The normal values for lung volumes are those proposed by the European Respiratory Society [20].

Respiratory muscle strength [RMS (% of predicted)] was calculated as reported by Gigliotti et al. [22]: [maximum inspiratory pressure (MIP) (%pred) + maximum expiratory pressure (MEP) (%pred)]/2.

Operating Lung Volumes

Changes in end-expiratory lung volume (EELV) were estimated from measurements of inspiratory capacity (IC) performed at rest, at the end of every minute during exercise and at the end of exercise. Assuming that total lung capacity (TLC) does not change during exercise [4], changes in IC and inspiratory reserve volume (IRV) reflect changes in dynamic EELV ($EELV = TLC - IC$) and end-inspiratory lung volume ($EILV = TLC - IRV$), respectively. This has been found to be a reliable method of tracking acute changes in operating lung volumes [7, 8, 15].

Submaximal Exercise Testing

6MWT was performed according to ATS guidelines [23]. Patients were asked to cover as much ground as possible within 6 min in a 30-m long quiet corridor. Every 60 s they were encouraged by an experienced physiotherapist to continue walking as fast as possible using only standardized phrases.

During exercise tests, the patients equipped with a portable spirometric-telemetric device (K4b² System; Cosmed, Rome, Italy) [24, 25] breathed through a face mask which was carefully adjusted to the patient's face and checked for air leaks. Online determinations of breath-by-breath oxygen uptake ($\dot{V}O_2$), carbon dioxide output ($\dot{V}CO_2$), ventilation ($\dot{V}E$), tidal volume (V_T), respiratory frequency (R_f), heart rate (HR) and EELV and EILV were obtained. The gas analyzers and turbine were calibrated before each test. Due to the light weight (800 g) of the device used to measure gas exchange, patients were able to move freely without discomfort. Quality of the data could be checked online via radio transmission.

Assessment of Dyspnea

The quality of dyspnea was evaluated using a 15-item questionnaire of descriptors of dyspnea [3] to better clarify the respiratory sensation(s) being rated by COPD patients at peak exercise. The questionnaire was filled out retrospectively during the first screening visit. Four cluster descriptors (W/E, ID, CT and air hunger) were chosen that the patients were familiar with during daily living activities including mild-moderate exercise. Many patients were unable to retrospectively select or understand other

descriptors from the proposed questionnaire. This is in line with the limit of the language of dyspnea. It cannot be assumed that all individuals share a common understanding of the same descriptors; differences in language, race, culture and the manner in which concepts or symptoms are held can influence a subject's perception of dyspnea. In practice, during the screening visit patients were capable of understanding the same descriptors, but not others, e.g. concentration, gasping for breath, my breath stops, I am breathing more, I feel that I am smothering or my breath does not go in all the way.

On the study days, subjects were requested to rate their breathing discomfort each minute of exercise, matching their subjective magnitude to a number on the Borg scale [26]. At the end of exercise after the Borg rating, patients were asked to select one or more descriptors that best described the quality of their dyspnea. Because the test would need to be simplified by reducing the number of verbal descriptors to be useful during exercise, if more than three descriptors were chosen, the subject was asked to select the three that best described the quality of their dyspnea (fig. 1).

Data Analysis

Results were expressed as means $\pm$ SD unless otherwise reported. The level of significance was set at $p < 0.05$. The t test was used to test differences in paired and unpaired samples. ANOVA was used for differences among subgroups. Responses to exercise were compared at peak exercise and at equivalent IRV values. Pearson's correlation was performed using the difference in dyspnea intensity as a dependent variable and concurrent differences in measurements of lung hyperinflation indices (IC and IRV and VT) as independent variables. All statistical procedures were carried out using the Statgraphics Plus 5.1 statistical package (Manugistics, Rockville, Md., USA). Selection frequencies of dyspnea descriptor phrases and clusters with 6MWT were compared before and after the rehabilitation program using Fisher's exact test.

Results

Before Rehabilitation

Anthropometric and functional data of the study group (tables 1, 2) did not change after a 6-week non-intervention period (nonsignificant).

Patients exhibited a moderate-severe level of airway obstruction and a mild level of hyperinflation. Diffusing capacity of the lung for carbon monoxide (DLCO) was $<80\%$ of the predicted value in 28 subjects. RMS was within normal limits in most subjects. During 6MWT, both Rf and VT contributed to the increase in VE. Figure 2 shows the time course of changes in IC, IRV and Borg rating: IC decreased less than IRV (1.1 ± 0.52 vs. 1.6 ± 0.5 liters, respectively; $p < 0.0001$), with both exhibiting the greatest decrease at min 1 of exercise, at a time when dyspnea showed the lowest increase. The increase in dyspnea from min 1 to 6 was associated with a decrease in IRV ($0.57 \pm$

Fig. 1. Selection frequency of cluster descriptors for exertional breathlessness in patients with COPD before and after PRP.

Table 1. Anthropometric and functional data in the study group

	Baseline	Before PRP	After PRP
Age, years	68.9 $\pm$ 8.0		
Body mass index	26.0 $\pm$ 4.6		
Smoking, pack-years	54.6 $\pm$ 27.3		
VC, liters	3.6 $\pm$ 0.8	3.7 $\pm$ 0.8	3.8 $\pm$ 0.7
VC, %pred	104.1 $\pm$ 20.5	104.8 $\pm$ 20.8	108.9 $\pm$ 19.7
FEV ₁ , liters	1.4 $\pm$ 0.4	1.4 $\pm$ 0.4	1.4 $\pm$ 0.4
FEV ₁ , %pred	52.2 $\pm$ 14.8	52.7 $\pm$ 15.7	54.5 $\pm$ 16.3
FEV ₁ /VC, %	38.0 $\pm$ 9.8	38.2 $\pm$ 10.7	37.8 $\pm$ 10.1
FRC, liters	4.8 $\pm$ 1.2	4.8 $\pm$ 1.2	4.8 $\pm$ 1.3
FRC, %pred	142.8 $\pm$ 36.4	142.0 $\pm$ 36.9	140.4 $\pm$ 36.5
TLC, liters	7.5 $\pm$ 1.4	7.5 $\pm$ 1.4	7.48 $\pm$ 1.4
TLC, %pred	120.6 $\pm$ 20.5	120.4 $\pm$ 20.6	120.6 $\pm$ 19.5
DLCO, %pred		65.6 $\pm$ 21.0	
RMS, %pred	73.6 $\pm$ 18.2	75.8 $\pm$ 17.5	84.8 $\pm$ 19.6*

* $p < 0.00001$ vs. before PRP.

0.34 liters) exceeding that in IC (0.3 ± 0.2 liters; $p < 0.0001$). IC was still 2.05 ± 0.06 liters during the 4-min recovery period, indicating a loss of ~ 650 ml after exercise.

Based on the percent frequency response (fig. 1) of the three clusters describing dyspnea, three language groups were defined based on sets of cluster descriptors: Group A: 13 patients (27%) selected W/E; group B: 12 patients

Fig. 2. Changes in lung volumes and dyspnea perception during 6MWT and over 4 min during recovery before PRP. Data are presented as means $\pm$ SEM.

Table 2. Cardiorespiratory variables at rest and during 6MWT in the study group

	Baseline	Before PRP	After PRP	p value (before vs. after PRP)
Rest				
Rf, s ⁻¹	21.4 $\pm$ 4.7	21.4 $\pm$ 4.9	20.1 $\pm$ 4.3	<0.0003
VT, liters	0.8 $\pm$ 0.2	0.8 $\pm$ 0.2	0.8 $\pm$ 0.2	NS
VE, l·min ⁻¹	17.0 $\pm$ 3.2	16.7 $\pm$ 3.5	15.8 $\pm$ 3.0	<0.02
VO ₂ , ml·min ⁻¹	385.3 $\pm$ 79.8	386.2 $\pm$ 80.5	370.8 $\pm$ 75.5	NS
VO ₂ , % of max.	20.5 $\pm$ 4.4	20.5 $\pm$ 4.5	19.7 $\pm$ 4.2	NS
VCO ₂ , ml·min ⁻¹	331.6 $\pm$ 74.3	332.2 $\pm$ 75.0	315.7 $\pm$ 63.6	NS
IC, liters	2.7 $\pm$ 0.6	2.7 $\pm$ 0.6	2.7 $\pm$ 0.5	NS
IC, % of TLC	36.0 $\pm$ 7.2	36.3 $\pm$ 7.4	37.2 $\pm$ 7.1	NS
IRV, liters	1.8 $\pm$ 0.6	1.8 $\pm$ 0.6	1.9 $\pm$ 0.4	NS
HR, b.p.m.	85.8 $\pm$ 10.7	86.2 $\pm$ 10.9	85.5 $\pm$ 14.1	NS
HR, % max.	57.0 $\pm$ 7.7	57.2 $\pm$ 7.9	56.8 $\pm$ 10.2	NS
Borg, AU	0.2 $\pm$ 0.4	0.2 $\pm$ 0.6	0.1 $\pm$ 0.2	NS
Exercise				
Rf peak, s ⁻¹	30.9 $\pm$ 5.1	31.2 $\pm$ 5.2	30.4 $\pm$ 4.8	<0.05
VT peak, liters	1.35 $\pm$ 0.3	1.36 $\pm$ 0.3	1.44 $\pm$ 0.3	<0.01
VE peak, l·min ⁻¹	41.4 $\pm$ 9.8	41.8 $\pm$ 9.6	43.1 $\pm$ 9.8	NS
VO ₂ peak, ml·min ⁻¹	1,302.6 $\pm$ 336.3	1,303.1 $\pm$ 336.4	1,383.3 $\pm$ 331.0	<0.004
VO ₂ peak, % of max.	68.7 $\pm$ 13.6	68.8 $\pm$ 13.6	73.3 $\pm$ 17.2	<0.004
VCO ₂ peak, ml·min ⁻¹	1,114.0 $\pm$ 356.8	1,134.1 $\pm$ 326.6	1,200.1 $\pm$ 309.2	<0.03
IC peak, liters	1.6 $\pm$ 0.3	1.6 $\pm$ 0.4	1.8 $\pm$ 0.4	<0.00001
IC peak, % of TLC	22.2 $\pm$ 6.6	22.1 $\pm$ 6.6	24.2 $\pm$ 6.3	<0.00002
IRV peak, liters	0.3 $\pm$ 0.2	0.2 $\pm$ 0.2	0.3 $\pm$ 0.3	<0.004
HR peak, b.p.m.	114.5 $\pm$ 15.4	114.8 $\pm$ 16.5	117.0 $\pm$ 17.0	NS
HR, % of max.	76.0 $\pm$ 11.8	76.2 $\pm$ 12.0	77.7 $\pm$ 12.4	NS
Borg peak, AU	6.8 $\pm$ 2.4	6.7 $\pm$ 2.4	4.7 $\pm$ 2.2	<0.00001
6MWT distance, m	472.9 $\pm$ 86.0	474.0 $\pm$ 84.4	522.3 $\pm$ 71.7	<0.00001

Fig. 3. Operational lung volumes during 6MWT in the three dyspnea language groups. Data are presented as means $\pm$ SEM. Shaded areas = TLC. **a** Group A. **b** Group B. **c** Group C.

(24%) reported *ID* and *CT*, and group C: 24 patients (49%) selected *W/E*, *ID* and/or *CT* cluster descriptors. Data did not significantly differ during the period with no intervention.

The three language study groups exhibited similar demographic characteristics and baseline function at rest: FEV_1 was 57.6 ± 16.8 , 57 ± 8.9 and 47.9 ± 16.7 %pred;

FRC was 137.2 ± 29.9 , 141.5 ± 35.6 and 144.9 ± 41.8 %pred; DLCO was 69 ± 18.8 , 67.7 ± 21.5 and 62.7 ± 22.3 %pred; RMS was 80.7 ± 11.1 , 78.1 ± 23.3 and 72.1 ± 16.8 %pred for groups A, B, C, respectively. Similar changes in Borg score and ventilatory variables during 6MWT were also found in the three language groups (table 3).

Correspondingly, in the three groups EELV increased during the 1st min of exercise and then tended to level off; EILV progressively increased and leveled off at an absolute value of ~ 0.250 liters (below TLC; fig. 3). The vertical distance between EELV and EILV in figure 3 is V_T which plateaus after the 2nd min of exercise. In the patients as a whole, or in the language groups, changes (Δ) in the Borg scale from rest to peak exercise did not significantly correlate with either ΔIC (or ΔV_T). In contrast, in the patients as a whole, and similarly in the language groups, a negative relationship was found between dyspnea and IRV (fig. 4); as shown in the figure, dyspnea steeply increased when IRV was < 500 ml below TLC. The average correlation coefficient of the data set of patients was: $r = -0.78 \pm 0.13$.

Effect of the Rehabilitation

Compared with before rehabilitation, functional parameters, e.g. VC and FEV_1 but not RMS, did not significantly increase (table 1). As shown in table 2, R_f and VE mildly decreased at rest, while V_T , VO_2 , VCO_2 , IC and IRV increased, and R_f and the Borg score decreased at peak exercise. Again, changes in the Borg scale from rest to peak exercise did not correlate with concurrent changes in IC or V_T .

The rehabilitation program shifted the relationship of the Borg score with IRV towards the right (mean $r = -0.72 \pm 0.27$) during 6MWT, indicating a greater IRV decrease for a given Borg score (fig. 5). The slope of this relationship changed from -3.75 ± 2.35 before to -2.46 ± 1.55 AU/l ($p < 0.0000$) after rehabilitation. Conversely, for similar increases in ventilation the calculated Borg score at similar decrease in IRV and at iso-IRV was significantly less after PRP (table 4).

In the patients as a whole, the frequency of the responses in the cluster descriptors of dyspnea after 6 MWT did not significantly differ from before rehabilitation (fig. 1). Also, only in 16 of the 49 patients the sets of clusters did change. Among these 16 'modifiers', 8 patients with IC increase ≥ 200 ml (200–660 ml) did change their cluster set from B or C into A group. Conversely, the remaining 8 patients with minimal increase (≤ 100 ml) or decrease (≤ 100 ml) in IC modified their cluster set either

Table 3. Cardiorespiratory variables at rest and during 6MWT in the three language study groups

	Dyspnea descriptors		
	A	B	C
Rest			
Rf, min ⁻¹	21.4 ± 3.9	21.5 ± 5.2	21.4 ± 5.3
VT, liters	0.8 ± 0.2	0.9 ± 0.2	0.8 ± 0.2
VE, l·min ⁻¹	15.3 ± 2.6	18.0 ± 3.8	16.9 ± 3.6
VO ₂ , ml·min ⁻¹	377.8 ± 99.9	393.8 ± 57.6	387.0 ± 81.7
VCO ₂ , ml·min ⁻¹	330.3 ± 106.4	338.1 ± 51.8	330.2 ± 67.2
IC, liters	2.6 ± 0.7	2.8 ± 0.5	2.7 ± 0.6
IRV, liters	1.8 ± 0.6	1.9 ± 0.6	1.8 ± 0.6
HR, b.p.m.	86.6 ± 5.8	84.5 ± 15.1	86.8 ± 10.9
VO ₂ /HR, ml·beat ⁻¹	4.4 ± 1.3	4.9 ± 1.3	4.5 ± 0.8
Borg, AU	0.2 ± 0.3	0.1 ± 0.2	0.3 ± 0.8
Exercise			
Rf peak, s ⁻¹	30.9 ± 4.0	32.7 ± 6.1	30.5 ± 5.4
VT peak, liters	1.4 ± 0.4	1.4 ± 0.2	1.3 ± 0.3
VE peak, l·min ⁻¹	42.5 ± 10.8	45.7 ± 8.8	39.4 ± 9.0
VO ₂ peak, ml·min ⁻¹	1,393.0 ± 418.0	1,384.2 ± 271.9	1,213.9 ± 305.5
VCO ₂ peak, ml·min ⁻¹	1,268.6 ± 438.9	1,179.3 ± 206.3	1,038.6 ± 284.6
IC peak, liters	1.6 ± 0.5	1.7 ± 0.2	1.5 ± 0.3
IC, % of control	63.9 ± 16.7	61.6 ± 12.3	59.1 ± 12.5
VT/IC peak	0.9 ± 0.1	0.9 ± 0.1	0.9 ± 0.1
IRV peak, liters	0.2 ± 0.2	0.26 ± 0.1	0.2 ± 0.2
HR peak, b.p.m.	121.7 ± 9.6	111.7 ± 15.1	111.3 ± 17.2
VO ₂ /HR peak, ml·beat ⁻¹	11.6 ± 3.6	12.7 ± 3.6	11.1 ± 3.0
Borg peak, AU	7.0 ± 2.5	6.1 ± 2.4	6.8 ± 2.5
6MWT distance, m	504.2 ± 71.9	472.3 ± 115.1	458.5 ± 71.0

selecting or including *ID* cluster. Both patients who modified their cluster set (*modifiers*) and those who did not (*non-modifiers*) exhibited similar changes in IC [0.2 ± 0.2 ($p < 0.000$) vs. $+0.16 \pm 0.2$ liters ($p < 0.002$)], walking distance [44 ± 45 ($p < 0.000$) vs. 58 ± 61 m ($p < 0.001$)] and BORG score [-2.1 ± 1.45 ($p < 0.00000$) vs. 1.7 ± 1.2 AU ($p < 0.0000$)] at peak exercise.

Discussion

The novel findings of this study are as follows: (i) patients with COPD could select different sets of cluster descriptors of dyspnea during 6MWT; (ii) the rehabilitation program reduced the intensity of dyspnea by shifting the relationship of Borg with IRV towards the right, but did not consistently modify the quality (the language) of dyspnea.

When requested to qualitatively assess their dyspnea on the basis of the language of dyspnea [4–8], patients

Table 4. Significant effect of rehabilitation on Borg scores at similar VE and IRV during 6MWT

VE, l · min ⁻¹	IRV, liters	Borg, AU	p value
16.7 ± 3.5 (15.8 ± 3.0)	1.84 (1.89)	0.2 (0.1)	<0.05
34.6 ± 9.1 (34.8 ± 8.8)	0.55 (0.60)	2.7 (1.6)	<0.0000001
41.1 ± 9.5 (43.1 ± 9.8)	0.33 (0.33)	5.5 (4.6)	<0.0003

Data after rehabilitation are shown in parentheses. IRV and Borg values are the same as in figure 5.

with COPD describe the symptom as an increased respiratory W/E along with ID, air hunger and CT during cycling exercise [4, 9]. These distinct sensations are associated with dynamic hyperinflation and its negative mechanical effects: the threshold load and uncoupling of the normal association between inspiratory effort and ventilatory output [4, 7, 8, 15, 17]. To the extent that

Fig. 4. Relationship between Borg rating of dyspnea intensity and IRV during 6MWT before PRP. Data are presented as means $\pm$ SEM. **a** Subset A. **b** Subset B. **c** Subset C. **d** Total patients.

Fig. 5. Relationship between Borg rating of dyspnea intensity and IRV during 6MWT before (◆) and after (◇) PRP. The dyspnea/IRV curve shifted towards the right after rehabilitation. Data are presented as means $\pm$ SEM.

TLC does not change appreciably during exercise [4, 27, 28], the change in IC accurately reflects changes in dynamic hyperinflation. IC is determined by the degree of hyperinflation, inspiratory muscle strength and the extent of mechanical loading on these muscles. In turn, dynamic hyperinflation provides a mechanistic link between dyspnea and expiratory flow limitation which is the result of the permanent destructive change in COPD [4, 8].

The IC decrease we found was much more than that reported previously at the end of 6MWT [29]. Two factors may account for the differences in dynamic hyperinflation in the two studies. The first is the different severity of the disease; our patients were less obstructed (e.g. FEV₁ %pred) and with a greater IC/TLC ratio at baseline. Conceivably, a low decrease in dynamic IC can occur in patients with a very high resting EELV who are unable to hyperinflate as they have no room to do so [29]. Second, unlike our study, a certain time lag between the end of exercise and the determination of IC took place in

the study of Marin et al. [29]. In this regard, our IC measurements over the first 4 min during recovery are in line with the data of Vogiatzis et al. [30]. They recently found a significant increase in EELV during exercise, amounting to 750 ± 90 ml at peak exercise in a subgroup of patients with COPD. EELV was still 254 ± 130 ml higher 3 min into the recovery period than at quiet breathing, indicating a loss of EELV of ~ 500 ml 3 min after exercise. These data suggest that the level of dynamic hyperinflation was underestimated in the study by Marin et al. [30].

The results of the present study carried out during a submaximal exercise test which mimics some of a patient's daily activities are in line with those of O'Donnell et al. [8] during constant cycle exercise. Dynamic hyperinflation early in exercise allowed expiratory flow-limited patients to increase ventilation while minimizing respiratory discomfort, an advantage negated later, when VT expanded to reach a critically low IRV < 0.5 liters. After reaching this minimal IRV, dyspnea rose to an intolerable level and reflected the disparity between inspiratory effort and the concurrent fixed VT response after the 1st min of exercise (fig. 3). In many patients, the expiratory time available during exercise was insufficient to allow EELV to decrease to its relaxation volume. As a consequence, VT increased only marginally, reaching a plateau. At this point, a further increase in ventilation was mostly achieved by increasing Rf.

Based on the distinctive qualitative sensations of dyspnea on exercise (different sets of clusters), patients were grouped as follows: group A selected W/E, group B selected ID and CT, and group C selected W/E, ID and/or CT cluster descriptors. It is worth noting that the three language subgroups exhibited similar levels of dynamic hyperinflation (IC and IRV), cardiovascular responses (HR and VO_2/HR) and dyspnea intensity (Borg score; table 3). This is not unexpected considering the mix of descriptors in the 73.5% of the patients. O'Donnell et al. [4] found that the frequency responses of respiratory effort ($\sim 90\%$), ID and unrewarded inspiration ($\sim 70\%$), and shallow breathing ($\sim 40\%$) during cycling exercise were higher in 12 COPD patients than in healthy subjects. Hence, it is reasonable to assume a high rate of association of qualitatively distinct exertional sensations in those patients. In turn, our data suggest that patients with COPD can exhibit different frequencies of responses and cluster sets of dyspnea during maximal and submaximal exercise testing. We also found the following: (i) the language used during exercise was the same the patients were familiar with during daily living activities,

and (ii) in line with the data of Elliot et al. [2] there was low variation in the reproducibility of the descriptors chosen, indicating that it was easier for patients to give the same answer when they were sure of the meaning of descriptors and believed that it applied to their sensation.

The distinctively qualitative sensations of dyspnea we found in patients imply that they were receiving afferent information from a number of mechanosensors throughout the ventilatory muscles, chest wall, lung and airways whose afferent inputs project to the central cortex and convey the sense of thoracic motion and volume displacement for a given electrical activation of the muscle [31–33]. This information was likely indicating to patients that the mechanical response of the ventilatory system was inappropriate for the effort expended [31]. In turn, the data suggest individual patient's ability to discriminate, as a healthy subject does, between sensation related to volume displacement and effort [31].

Effects of the Rehabilitation Program

PRP increased IC, VT, and IRV at peak exercise. The improved mechanical defect was consistently associated with quantitatively decreased sensation of dyspnea (Borg ratings). In particular, the PRP shifted the relationship of the Borg scale to IRV to the right, indicating that a greater decrease in it was needed to a given increase in the Borg score, i.e. patients were able to tolerate a greater amount of reduction in IRV during exercise before experiencing intolerable dyspnea (fig. 5). The improved dyspnea at similar ventilation and IRV after rehabilitation (table 4) might reflect non-physiologic factors such as tolerance or desensitization to dyspnea [15, 34, 35].

At peak exercise, patients selected the cluster descriptors with a frequency not different from that before rehabilitation (fig. 1). In contrast, a qualitatively unchanged sensation of dyspnea was found in the majority of patients we called *non-modifiers*. In the 16 patients we called *modifiers*, 8 patients with the greatest increase in IC (≥ 200 ml) changed their cluster descriptors from group B or C into A, i.e. they lost ID. The remaining 8 subjects selected or included ID in their cluster set with PRP, data in keeping with the results of a pharmacological study where the main descriptors selected to represent the quality of exertional dyspnea were similar after placebo and salmeterol [9].

With the exception of group A, many patients selected more than one cluster descriptor; this did not allow us to define the potential impact of PRP on underpinning mechanical constraints. However, the 8 *modifiers*

who lost *ID* exhibited a noticeable increase in *IC* (from 200 to 650 ml), reflecting the decrease in dynamic hyperinflation, i.e. underpinning *ID* [7]. Conversely, the unchanged or decreased *IC*, associated with an increase in *Rf*, explains the selection of *ID* in the remaining *modifiers*. Also, the finding of unchanged frequency response in *W/E* with PRP (fig. 1) suggests that the level of central motor command was not substantially affected by the program.

Finally, although the reasons for changing cluster descriptors are likely to be complex, the role of the psychological or behavioral state [35] and/or the affective com-

ponent (that part of the sensation which evokes distress and motivated behavior) cannot be disregarded [34].

In summary, the present results indicate that a standard rehabilitation program (1) allows dynamically hyperinflated COPD patients to tolerate a greater amount of restrictive dynamic ventilatory defect, and (2) modifies the intensity but not necessarily the quality of dyspnea during submaximal exercise in these patients. Nonetheless, the possibility that a larger rehabilitation period may impact on the quality of dyspnea cannot be disregarded.

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