ISSN 1413-3555
Rev Bras Fisioter, São Carlos, v. 14, n. 1, p. 16-23, Jan./Feb. 2010
©Revista Brasileira de Fisioterapia

Influence of current smoking on adherence and responses to pulmonary rehabilitation in patients with COPD

Influência do tabagismo atual na aderência e nas respostas à reabilitação pulmonar em pacientes com DPOC

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Abstract

Objective: To investigate the modulating effects of current smoking on adherence and responses to pulmonary rehabilitation (PR) in patients with chronic obstructive pulmonary disease (COPD). **Methods:** In a prospective study, 18 ex-smokers and 23 current smokers (GOLD stages II-III) were enrolled in a 12-week multidisciplinary, supervised PR program. The patients were assessed clinically and as to subjective variables (dyspnea and health-related quality of life) and objective variables (body composition, pulmonary function and 6-min walking distance). The degree of nicotine dependence in current smokers was assessed by the *Fagerström* test. Program completion defined PR "adherence". **Results:** There was a significant association between current smoking and non-adherence to PR with 30.4% vs. 11.1% and odds ratio=2.9 (1.6-4.1; p<0.01). However, the current smokers who completed the program (n=16) had a similar absentee rate to the ex-smokers, as well as similar gains in the subjective (quality of life) and objective (walked distance) items. Additionally, there was a significant reduction in daily cigarette consumption and in the degree of nicotine dependence in current smokers (p<0.05). **Conclusions:** Although current smoking is negatively related to PR adherence, COPD smokers who complete the PR can have similar gains in functionality and quality of life compared to ex-smokers. Moreover, PR may be related to decreased nicotine dependence, even without a formal smoking withdrawal program.

Key words: COPD; rehabilitation; exercise; smoking; physical therapy.

Resumo

Objetivo: Investigar o possível efeito modulador do tabagismo atual na aderência e nos efeitos da reabilitação pulmonar (RP) em pacientes com doença pulmonar obstrutiva crônica (DPOC). **Métodos:** Em um estudo prospectivo, 18 pacientes ex-tabagistas e 23 tabagistas atuais (GOLD estádios II-IV) foram incluídos num programa multidisciplinar de RP com duração de 12 semanas. Os pacientes foram submetidos à avaliação clínica e à de variáveis subjetivas (dispneia e qualidade de vida) e objetivas (composição corporal, função pulmonar e teste da caminhada de 6 minutos). Nos pacientes tabagistas, obteve-se o nível de dependência da nicotina pela escala de *Fagerström*. A interrupção da RP antes do término previsto foi considerada indicativa de não aderência ao programa. **Resultados:** A proporção de pacientes não-aderentes à RP foi maior nos tabagistas do que nos ex-tabagistas (30,4% vs 11,1%, respectivamente; razão de chance=2,9 (1,6-4,1); p<0,01). Entretanto, os tabagistas atuais que completaram o programa (n=16) apresentaram taxa de absenteísmo à RP similar ao observado nos ex-tabagistas, assim como ganhos equivalentes nas respostas subjetivas (qualidade de vida) e objetivas (distância caminhada). Adicionalmente, houve redução significante no número de cigarros consumidos diariamente e no grau de dependência da nicotina nos tabagistas atuais (p<0,05). **Conclusões:** Embora o tabagismo atual reduza a aderência à RP, pacientes tabagistas com DPOC que completam tais programas apresentam ganhos funcionais e na qualidade de vida equivalentes aos observados nos ex-tabagistas. A RP, mesmo sem um programa estruturado de cessação do tabagismo, pode associar-se com redução, ao menos a curto prazo, da dependência da nicotina.

Palavras-chave: DPOC; reabilitação; exercício; tabagismo; fisioterapia.

Received: 15/04/2008 – **Revised:** 18/11/2008 – **Accepted:** 26/05/2009

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Introduction

Pulmonary rehabilitation (PR) has been an important adjunctive treatment for chronic obstructive pulmonary disease (COPD), optimizing the level of independence and exercise tolerance with subsequent improvement in quality of life[1,2]. Although PR has a multidisciplinary character, several randomized controlled trials have shown that structured physical training is crucial for clinical and functional improvement, with prognostic repercussions[3].

Unfortunately, the capacity of health services to offer such programs for all patients with indication of PR is known to be lower than the real demand[1,2,4]. One of the common eligibility criteria for a PR program is the exclusion of current smokers[1,3], based on the assumptions that such patients would be less adherent to PR[5,6] and that the potential gains would be lower than those observed in non-smokers because of the harmful effects of smoking on pulmonary function[7] and the skeletal muscle[8]. Additionally, it is known that smokers are less likely to initiate and maintain regular physical activity[9,10]. However, the available evidence to substantiate the concept that PR should not be offered to current smokers is scarce, as admitted recently[2]. In fact, some randomized studies accepted smokers in their program[11,12], and the influence of current smoking on the main clinical and functional outcomes of PR in COPD remains controversial.

Therefore, the main purpose of this study was to assess adherence to the PR and its subjective effects (dyspnea and health-related quality of life) and objective effects (body composition, pulmonary function and exercise capacity) on current smokers and ex-smokers with COPD. The main hypothesis of the study was that current smoking did not influence negatively on adherence and on the gains provided by the PR in this population.

Methods

Sample

We assessed a consecutive convenience sample of 41 patients of both sexes with a diagnosis of COPD (GOLD stages II-IV) [13] referred by the institution's outpatient clinic and private pulmonology care services. All patients had obstructive respiratory disease, typically of moderate to severe intensity (FEV_1/FVC <0.7 and FEV_1 <60% of predicted). The patients were divided into: group I (n=18), consisting of ex-smokers for at least 6 months and group II (n=23), consisting of current smokers. The inclusion criteria were chronic dyspnea in activities of daily living (dyspnea score >I according to the modified Medical Research Council [MRC] dyspnea scale)[4] and clinical stability, as indicated by the absence of changes in the therapeutic regimen or exacerbation of any severity in the previous 12 weeks. Exclusion criteria were: presence of motor or neurological disorder, indication and/or use of long-term home oxygen therapy, pulmonary rehabilitation in the previous year, chronic use of oral steroids, concomitant diagnosis of malignant disease, chronic heart failure, liver disease or nephropathy. This study was approved by the Ethics Committee of Faculdade de Medicina do ABC, protocol No. 132/2006, and all patients signed an informed consent form.

Protocol

Before and after PR, the participants underwent a clinical and anthropometric assessment, measurement of chronic dyspnea scores (modified MRC dyspnea scale)[4] and health-related quality of life (St. George's respiratory questionnaire - SGRQ)[14], assessment of the degree of nicotine dependence (Fagerstrom test)[15], spirometry, measurement of maximal respiratory pressures and the six-minute walking distance (6MWD). All questionnaires were administered by the same examiner who remained blind to the participants' smoking history.

Measurements

Adherence to PR

Adherence to the PR was defined as the participant's ability to complete the proposed program, with at least 80% attendance of sessions[16-18]. If the participant withdrew from the PR before the end of the proposed period, he/she was asked to state the reasons for withdrawal.

Dyspnea scale in daily living

The degree of dyspnea in daily activities was measured by the modified MRC dyspnea scale[4]. In this instrument, "0" represents dyspnea during intense exercise and "4", dyspnea at rest. A previously validated Portuguese version of the quality of life SGRQ[14] was used to assess the participant's symptoms and their influence on daily activities. The SGRQ addresses issues related to three components: Symptoms, Activity and Impacts. In this instrument, the quality of life is inversely related to the score: reductions equal to or greater than 4 points after intervention indicate a significant improvement in quality of life[19].

Scale of nicotine dependence

The Fagerstrom scale was used in the active smokers to verify the degree of nicotine dependence[15]. This scale has six questions about smoking habits and rates the degree of dependency as mild (0-4), moderate (5-7) or severe (8-10).

Anthropometric measurements

Body mass (kg) and height (m) were obtained with an anthropometric Filizola® scale (Filizola, São Paulo, Brazil). These data were used to calculate the body mass index (BMI = weight/height^2, kg/m^2). Body fat was also assessed by measuring the skinfolds of the right side of the body with a Sanny® skinfold caliper (American Medical do Brasil, São Bernardo do Campo, Brazil). The same evaluator measured the following skinfolds three times: triceps, suprailiac, chest, abdominal and crural. The mean value of the measures was considered for analysis. Based on this data, the mean density[20] and percentage of fat and lean body mass[20] were calculated.

Pulmonary function tests

Spirometry pre- and post-bronchodilator (400 μg of salbutamol via inhalation dosimeter) was performed in the Koko system® (Koko spirometry, Louisville, CO, USA), by the same technician, using a calibrated pneumotachograph. The criteria for acceptability and reproducibility were those defined by the Brazilian Society of Pulmonology and Phthisiology[21]. The forced vital capacity (FVC, L), forced expiratory volume in one second of FVC (FEV_1, L) and the relationship between them were obtained; in the slow maneuvers, the inspiratory capacity (IC, L) was obtained. The values obtained were compared to those predicted for the adult Brazilian population[22]. In this study, only the optimal functional values are shown, i.e. after the bronchodilator.

Measurements of maximal inspiratory pressure (MIP, cmH_2O) from residual volume and maximal expiratory pressure (MEP, cmH_2O) from the total lung capacity were also carried out. The test was performed with the patient seated, using a Newmed® manovacuometer (Newmed, São Paulo, Brazil), with measurement of -150/+150 cmH_2O. At least three measures were taken by the same observer, recording the highest value obtained as long as it was not the last to be recorded.

Six-minute walking distance

The 6MWD measures the distance walked in six minutes (m) in a 30-meter corridor with standardized encouragement. The technical aspects were those recommended by the American Thoracic Society[23]. During the test, oxyhemoglobin saturation by pulse oximetry (SpO2%) and heart rate (HR bpm) were measured (Moriya®, model 1005; Moriya, São Paulo, Brazil). Lower limb fatigue and dyspnea were assessed at the end of the test using the Borg categorical scale[23].

Interventions

The PR program was carried out in three months, with a frequency of three times per week, lasting 60 minutes each, with a total of 36 sessions. In addition to physical training (see below), monthly educational lectures were delivered to address aspects of the disease, activities of daily living, energy conservation, body awareness and nutrition education. The harmful effects of smoking and its role in the maintenance of symptoms were discussed, but there was no standardized smoking withdrawal program or administration of adjuvant drug treatment.

The two groups were submitted jointly to the same physical training program, based on the recommendations of the American Thoracic Society[1]. The program consisted of: (i) warm-up followed by 20 minutes of aerobic conditioning on Movement® stationary bicycles (Movement Bike vertical BM2800, with electromagnetic resistance, Manaus, Brazil), with modulated intensity according to individual tolerance (Borg scores for dyspnea from 4 to 5)[23]; (ii) stretching of the muscles to be exercised during the session; (iii) upper and lower limb resistance training at 50% of the maximum load reached in a previous incremental test and an additional 0.5 kg according to participant tolerance; and (iv) cool-off including stretching of the muscles exercised during the session. The training was constantly monitored, and supplemental oxygen was used when a significant decrease in SpO_2 (<90%) was observed.

Statistical analysis

The minimum sample size (N = 15) for each group was calculated assuming a gain of 54m in walking distance as a primary outcome[24], risk α of 5% and statistical power of 80%. Adherence to PR was not used to calculate the sample size because it is a dichotomous categorical variable (withdrawal or not). The data collected were analyzed in a specific program for statistical analysis (Statistical Package for Social Sciences™ - SPSS, version 13.0).

An initial descriptive analysis was performed to assess the distribution of variables and the presence of inconsistencies in the database (outliers). The variables were expressed as mean and standard deviation or median (variation) according to the symmetrical or asymmetrical nature of the distributions (Kolmogorov-Smirnov). Unpaired Student t-tests or Mann-Whitney tests were performed to compare the groups at baseline assessment. The χ^2 test and Fisher's exact test, when necessary, were used to investigate the association between variables. Odds ratio for adherence to PR, with its respective confidence interval of 95% (CI 95%), was calculated from a contingency table. The sign test was used to analyze individual changes in the occurrence of dichotomous variables. Two-way repeated measures ANOVA was used to compare the groups in the pre- and post-PR assessment and any intergroup differences in the magnitude of improvement with PR. The probability of type I error was set at 5% for all tests ($p < 0.05$).

Results

Adherence to PR in current smokers and ex-smokers

Eighteen ex-smokers and 23 current smokers were assessed. There was a statistically significant relationship between current smoking and withdrawal from PR ($p < 0.05$). Two (11.1%) of the 18 ex-smokers withdrew from the PR program before its completion, whereas 7 (30.4%) of the 23 current smokers did not complete the program (odds ratio = 2.9 (1.6-4.1); $p < 0.01$; Table 1). The reasons given for withdrawal from the program were similar in both groups: "lack of motivation," "the requirement of frequent attendance" and "transportation problems". However, three patients in the current smoker group reported that the contributing factors to withdrawal were the references to the harmful effects of smoking and to the need to quit to control the disease. All patients who completed the program attended at least 80% of sessions, regardless of smoking history. Additionally, there was no significant difference in physiological and subjective baseline variables between the current smokers who completed and those who did not complete the PR ($p > 0.05$; data not included).

General characteristics of the sample

The main demographic, anthropometric and respiratory function characteristics of the ex-smokers (group I, n = 16) and current smokers (group II, n = 16) who completed the PR are presented in Table 1. The distribution of severity, according to the GOLD criteria[13], was similar between groups I and II: 2/3, 8/6 and 6/7 for stages II, III and IV, respectively. However, group II showed significantly lower inspiratory capacity values, an index of lung hyperinflation (Table 1)[25].

Although not statistically significant, there was a tendency for lower BMI and lean body mass values in group II. In fact, the rate of underweight participants and those with reduced BMI[26] was higher in this group compared to group I (9/16 vs. 4/16). The quality of life scores at baseline were significantly lower in group II than in group I ($p < 0.05$). It was also observed that 81% of participants in group II had moderate nicotine dependence and 19%, severe dependence according to the Fagerstrom test[15].

Table 1. Baseline values and objective and subjective responses to pulmonary rehabilitation (PR) in ex-smokers (Group I) and current smokers (Group II) with COPD.

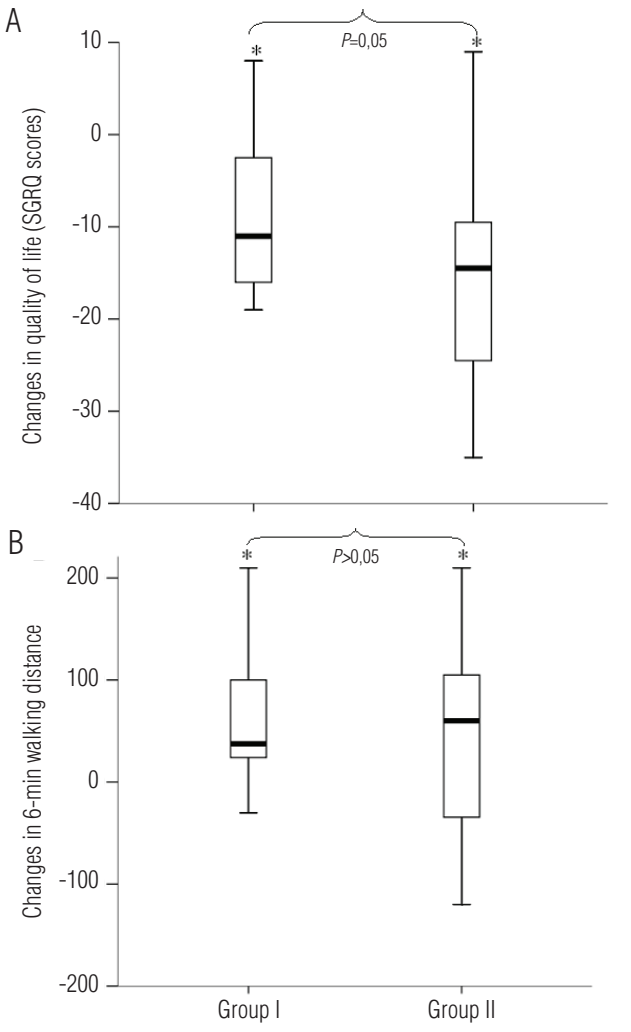
	Group I (N= 18)		Group II (N= 23)	
Variables Demographics	Pre-PR	Post-PR	Pre-PR	Post-PR
Gender, male/female	9/9	-	13/10	-
Age (yrs)	64.1±8.7	-	63.1±8.3	-
Anthropometric				
BMI (kg/m^2)	25.8±6.7	27.8±7.3	22.5±6.89	22.6 ± 67
% Lean mass	69.9±8.5	73.8±9.2 †	73.0±11.5	74.9 ± 9.30
Lung function				
FVC (%)	66.2±22.8	76.3±25.3	64.3±18.6	67.6 ± 15.8
FEV^1 (%)	42.8±15.7	48.0±19.3	45.4±18.1	45.9 ± 17.3
FEV^1/FVC	0.46±0.09	0.48±0.11	0.50±0.10	0.50±0.13
IC (%)	81.4±14.5	80.9±13.7	65.4±12.5*	80.1 ± 11.0 †
MIP (cmH$_2$O)	65.0±22.2	77.1±24.3	57.1±24.0	60.3 ± 24.4
MEP (cmH$_2$O)	78.7±26.9	75.0±28.9	71.5±37.2	72.8 ± 26.9
Exercise tolerance				
Distance walked (m)	415±147	495±78 †	427±131	503 ± 113 †
Leg effort score	3 (0-7)	1.5 (0-5) †	2 (0-5)	3 (0-5)
Dyspnea score	4 (0-7)	2.5 (0-5) †	3 (0-5)	2.5 (0-4)
Subjective responses				
MRC score	2 (1-4)	2 (1-4)	2 (1-3)	1 (1-3) †
SGRQ	33.5 (21-58)	28.5 (8-45) †	39 (20-62)*	23.5 (5-53) †‡
Non-adherence to PR (%)	11.1% (2)	30.4% (7)		

Definition of abbreviations: BMI = body mass index; FVC = forced vital capacity; FEV_1 = forced expiratory volume in one second; IC = inspiratory capacity; MIP= maximal inspiratory pressure; MEP= maximal expiratory pressure; MRC = Medical Research Council; SGRQ = St. George's Respiratory Questionnaire.

* $p<0.05$= pre-PR between-group differences; † $p<0.05$= post-PR within-group differences; ‡ $p<0.05$= between-group differences in changes induced by PR (repeated measures ANOVA).

Subjective effects of PR on current smokers and ex-smokers

According to Table 1, although both groups showed significantly improved SGRQ scores[19], this improvement was more pronounced in group II (Figure 1A). In fact, there was a decrease of more than four points in 15/16 (93.7%) group II participants and in 12/16 (75%) group I participants (p <0.05). In accordance with these findings, only group II showed a significant reduction in the MRC dyspnea scores[4].



* p<0.05= post-PR within-group differences; † p<0.05= between-group differences in changes induced by PR (repeated measures ANOVA).

Figure 1. Effects of pulmonary rehabilitation on quality of life (St. George's Respiratory Questionnaire, panel A) and exercise tolerance (6-min walking distance, panel B) in ex-smokers (Group I) and current smokers (Group II) with stable COPD. The box plots give the range, the central interquartile and the median. Note that both groups presented significant improvements after PR. However, the improvement in quality of life was greater in Group I (lower scores) compared to Group II.

The PR was associated with a significant reduction in the nicotine dependence scores in group II, and post-PR, 50% had mild dependence and 50%, moderate (p <0.05). Additionally, 3/16 (18.7%) participants quit smoking. In accordance with these data, there was a significant decrease in the number of cigarettes per day (20±8 pre-PR vs. 7±6 post-PR; p <0.001).

Objective effects of PR on current smokers and ex-smokers

There was no significant change in BMI and lean mass in both groups, however, there was a significant reduction in the percentage of lean mass in group I (p <0.05; Table 1). As expected, the PR had no significant influence on the main spirometry variables in both groups. Interestingly, only group I showed significant improvement in MIP, while IC increased in group II (p <0.05; Table 1). With regard to functional exercise capacity (6MWD), the PR was associated with similar gains in both groups (Figure 1B, Table 1). Thus, individual analysis showed that a clinically significant gain (change in walking distance greater than 54 m)[24] was found in 7/16 (43.7%) participants in group I and 9/16 (56.2%) in group II (p> 0.05). However, there was a significant reduction in symptoms of "leg effort" and "dyspnea" at the end of the test only in group I (Table 1).

Discussion

This study assessed the modulating effect of current smoking on adherence and the possible subjective and objective gains related to PR in participants with stable COPD. The results of this study indicate that, although current smoking was negatively related to adherence to PR, the clinical and physiological gains were generally similar in ex-smokers and current smokers (Table 1, Figure 1). In addition, the PR was associated with a significant reduction in nicotine dependence in current smokers. These results indicate that although a higher rate of withdrawal from PR can be anticipated in smokers with COPD, there seems to be no a priori clinical or physiological grounds to exclude such patients from PR programs.

PR is currently considered a standard procedure for optimizing the clinical treatment of COPD patients with dyspnea and limitations in daily activities[1,2,4,13,27]. Although PR is considered useful for most patients in the moderate to advanced stages of the disease, the availability of such programs is limited, which stimulated the investigation of the most common limiting factors, especially current smoking. In this context, it should be recognized that smokers with

lung or heart disease known to be associated with smoking and who continue to smoke have lower adherence to drug treatment than those who quit[28,29].

Interestingly, such evidence has been extrapolated to non-pharmacological interventions, such as PR, without a clear experimental basis. In fact, previous studies considered the inclusion of smokers[11,12,30,31]. The negative and nihilistic psychological profile of many of these patients[29] and its possible influence on adherence to the program and relapse of ex-smokers have been cited as possible deterrents to their inclusion in PR. Young et al.[32], for example, reported that current smoking was associated with non-adherence to the PR. Our results are consistent with these findings because the risk of withdrawal was nearly three times that observed in current smokers compared to ex-smokers, i.e. a hazard ratio of 2.9. Thus, the inclusion of current smokers could be questionable, especially in countries with low availability of PR services, at least from the operational and cost minimization point of view.

A finding of great practical importance in the present study was the positive effect of PR on quitting smoking and the degree of nicotine dependence in group II. Obviously, although it is not possible to measure the relative importance of the different components of PR in this outcome, the anti-smoking educational activity, the information about the disease, the closer contact with the health team and reinforcing example of ex-smokers may have been influential. Additionally, increased physical activity and better body care may also have contributed. These results are particularly noteworthy, considering that there was no systematic anti-smoking intervention in this study.

PR programs have also had a significant effect on subjective improvement in patients with COPD[33]. Current smoking may, at least in theory, offset the positive impact of these post-PR gains[33]. Surprisingly, however, our data indicate the opposite, i.e. the current smokers not only improved in these aspects but they also exceeded the non-smokers (Table 1, Figure 1A). Although the tendency for greater dyspnea, poorer quality of life and higher baseline lung hyperinflation may have influenced these results (Table 1), our data combined with the improved nicotine dependence indicate that PR should not be discarded a priori for smokers with COPD, at least from a clinical point of view.

Another important aspect regarding the non-inclusion of smokers in PR is related to the lower potential for objective gains. Thus, the pro-inflammatory and systemic hyperoxidative effects related to current smoking, the suppression of myogenic activity, the lower tolerance to heavy work loads and the accelerated loss of lung function could reduce functional gains in PR, as extensively reviewed by the American Thoracic Society and the European Respiratory Society[34]. In the present study, this hypothesis was not confirmed, and functional gains (6MWD) were similar in both groups. Additionally, there was a significant increase in IC in group II (Table 1). Nevertheless, this result should be viewed with extreme caution because there is no evidence that PR alone can reduce lung hyperinflation in COPD. Furthermore, the lower baseline IC values in group II may have induced the phenomenon of regression to the mean, i.e. the probability of increasing the scores in a re-assessment is inversely proportional to the pre-intervention values.

The present study has some important limitations. Although the sample size was suitable to demonstrate functional improvement with the 6MWD, the number of participants assessed may have been insufficient to detect all possible factors related to non-adherence to PR. In this sense, the absence of psychosocial measures may also have been relevant. However, it should be noted that the number of assessed patients was higher than previously used in similar studies on adherence to PR[17,18]. Another important limitation is the non-inclusion of more complex measures of lung function, such as static lung volumes and diffusing capacity, thus not allowing a better phenotypic characterization of the participants[35]. Moreover, our results should not be extrapolated to patients with milder degrees of nicotine dependence or, in contrast, to more severe patients undergoing long-term oxygen therapy. Finally, there was no longitudinal follow-up of this sample, and the positive effects of long-term PR on reducing dependence and quitting smoking are not known.

In conclusion, although current smoking in COPD patients reduces adherence to PR, smokers who complete the program have shown improvement in quality of life and functional exercise capacity equivalent to that of ex-smokers. Even without a structured program for quitting smoking interruption, PR may be associated with short-term reduction in nicotine dependence. Therefore, the decision to accept smokers with COPD into a PR program should be made in light of the local conditions at each center, considering adverse economic factors and favorable clinical elements.

Acknowledgments

Thanks to all the staff of the Center of Pulmonology and Pulmonary Rehabilitation of Faculdade de Medicina do ABC and especially to the patients who took part in this research with effort and dedication.

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