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Original Article

Effect of Pulmonary Rehabilitation on the Value of the Inspiratory Capacity–to–Total Lung Capacity (IC/TLC) Ratio to Determine Response to Pulmonary Rehabilitation in Patients with Chronic Obstructive Pulmonary Disease

Yelda Varol[1], Hülya Şahin[2], Ülkü Aktürk[3], Berna Kömürcüoğlu[1]

[1]Department of Chest Diseases, Dr. Suat Seren Chest Diseases and Thoracic Surgery Training and Research Hospital, İzmir, Turkey
[2]Pulmonary Rehabilitation Unit, Dr. Suat Seren Chest Diseases and Thoracic Surgery Training and Research Hospital, İzmir, Turkey
[3]Department of Chest Diseases, University of Health Sciences Süreyyapaşa Chest Diseases and Thoracic Surgery Training and Research Hospital, İstanbul, Turkey

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Abstract

OBJECTIVES: In patients with chronic obstructive pulmonary disease (COPD), the inspiratory capacity–to–total lung capacity (IC/TLC) ratio has been found to be correlated with mortality and a reduced exercise capacity. Pulmonary rehabilitation (PR) is known to improve the exercise capacity and respiratory functions of patients with COPD. Our study aims to examine the impact of PR on the IC/TLC ratio in patients with COPD.

MATERIALS AND METHODS: We included a total of 122 patients with COPD who received PR therapy twice a week over a period of 8 weeks in an outpatient clinic.

RESULTS: Patients' mean age was 62.5 (±8.2), and 15 patients (12.3%) were female. Post-PR FEV_1, TLCO, and pO_2 values, and the 6mWD, dyspnea, and quality-of-life (QoL) scores indicated a statistically significant improvement (p<0.05 for all). Patients were grouped as follows: patients with IC/TLC >0.25 as Group 1 and IC/TLC ≤0.25 as Group 2. Both groups exhibited a significantly increased post-PR 6 mWT distance (375–420, 336–400 meters) with no difference between the groups. We observed a significantly increased FEV_1% in both groups after the PR (p=0.007, 0.004). Again, QoL questionnaires and Modified Medical Research Council scores significantly improved for both groups (p<0.001). Although no post-PR IC/TLC improvement was detected in patients with good prognosis, we identified an IC/TLC improvement in the poor prognosis group (Group 2) (p=0.002).

CONCLUSION: COPD patients with IC/TLC ≤0.25 benefit from the PR just as those COPD patients with IC/TLC >0.25.

KEYWORDS: Chronic obstructive pulmonary disease, dyspnea, inspiratory capacity–to–total lung capacity, pulmonary rehabilitation

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INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a treatable and preventable disease that represents an important public health problem [1]. Today, COPD is known to be the fourth leading cause of death worldwide [2]. In the future, by 2020, estimations suggest it to become the third leading cause of death [2]. The inspiratory capacity–to–total lung capacity (IC/TLC) ratio, demonstrated to be in strong association with exercise tolerance and exercise-associated dynamic hyperinflation, has been used as an indicator of static lung hyperinflation in several studies [3, 4]. Moreover, publications showed a powerful association between resting IC and functional exercise limitation in patients with COPD [5]. Casanova et al. [6] evaluating a cohort of 689 subjects (95% male) suggested that an IC/TLC ratio of ≤25% provided the best combined sensitivity and specificity to predict all-cause mortality in COPD patients in comparison with FEV_1 and the BODE index.

The pulmonary rehabilitation (PR) is among the most effective non-pharmacological therapies of patients with COPD [7]. Exercise performance is limited with static pulmonary hyperinflation in COPD patients. Therefore, for an effective PR program, exercise training should be an important component of it [8]. In clinically stable patients with COPD, IC/TLC is a predictor of exercise capacity decline; however, the change of IC/TLC after a PR program is unknown [2]. Therefore, we aimed to study the effect that pulmonary rehabilitation exerts on the value of the IC/TLC ratio in patients with COPD.

MATERIALS AND METHODS

We performed a retrospective cohort study to find out, by comparison, the effectiveness of PR on the value of the IC/TLC ratio in patients with COPD. The study's ethics committee approval was provided by Dr. Suat Seren Chest Diseases and Thoracic Surgery Training and Research Hospital's institutional review board (451:11.05.2016-5301). Subjects included in the present study completed an informed written consent form.

Address for Correspondence: Yelda Varol, Department of Chest Diseases, Dr. Suat Seren Chest Diseases and Thoracic Surgery Training and Research Hospital, İzmir, Turkey
E-mail: yeldavatansever@hotmail.com

Subject Selection

We recruited stable (for at least 4 weeks, no increase in the use of rescue medication, no worsening of respiratory symptoms, and no unscheduled visits because of COPD worsening) patients with COPD, who were diagnosed based on the Global Initiative for Chronic Obstructive Lung Disease (GOLD) definition. All patients had reduced exercise tolerance and were suffering from dyspnea, and also had limitations in daily living activities. The recruitment criteria included a ratio of FEV_1-to-FVC of 0.7 or less following bronchodilator administration, a smoking history of 10 or more pack/years, and a minimum age of 40 years [9]. The GOLD grading system is used for the patient's COPD severity [10]. At the beginning of the study, respiratory symptoms self-reported by patients, medication usage, smoking history, and coexisting medical conditions were documented. We excluded patients presenting a history of other pulmonary diseases, (coexisting pneumoconiosis, interstitial lung disease, pulmonary tuberculosis, etc.), and any impairment (neurologic, orthopedic, or cardiovascular) that might have prevented the subject from completing the exercise training and also those patients with acute COPD exacerbation. In addition, subjects with poor compliance, those who did not attend the program more than two times, and subjects with poor motivation or transportation difficulties were excluded. We grouped patients as follows: patients with an IC/TLC >0.25 as Group 1 and patients with an IC/TLC ≤0.25 as Group 2 [11].

Measurement of Pulmonary Parameters and Questionnaires

All patients underwent a blood gas analysis and chest X-rays before and after PR, as well as cardiac and respiratory system examinations. We assessed the pulmonary function by measuring the carbon monoxide diffusing capacity (Zan 300, Germany) and body plethysmography (Zan 500, Germany). The IC/TLC is calculated from body plethysmography results. The Modified Medical Research Council (mMRC) dyspnea scale was used to assess dyspnea, and modified BORG scales were used before and after PR [10]. The assessment of the quality-of-life (QoL) was performed using the disease-specific St. George Respiratory Questionnaire and the SF-36 health-related QoL questionnaire [12, 13]. The Hospital Anxiety and Depression Questionnaires were used to assess psychological symptoms [14, 15]. A 6-minute walking test (6 mWT) was used in line with the standards published by the American Thoracic Society [16]. Including the blood gas analysis, all measurements were assessed at admission and at the end of the PR.

Pulmonary Rehabilitation Parameters

In our hospital's PR Unit, patients underwent an 8-week hospital-based outpatient pulmonary rehabilitation program twice a week. PR was totally tailored to conform to a subject's needs. The PR program consisted of supervised exercise training, education, psychological counseling, and nutritional intervention. We chose exercises for each patient based on their disease severity and exercise toleration capacity. Exercises included the following: cycle training (at least 15 minutes), breathing exercises, treadmill (min. 15 minutes), peripheral muscle training, and stretching. In addition, the trainers gave the patients advice on bronchial hygiene techniques, medication, relaxation techniques to reduce dyspnea, energy conservation, and home exercises [17]. Upper and lower extremity stretching and strengthening exercises were performed after respiratory physiotherapy education. The strengthening exercises were initiated with no weight. According to the BORG scale, a half-kilogram weight was added after every four cycles of exercises [7, 8]. The bicycle/arm ergometer and treadmill were used for aerobic exercises. We calculated workloads for cycling and walking speed for treadmill from 6 mWT results [18]. The treadmill walking speed was calculated as 80% of the average 6 mWT speed using the following formula: (6 mWT distance x 10) ÷ 1000 km/hr. The cycling workload was calculated with the following formula: (Watt=03.217 + (30.500 x Sex) + (-1.613 x age) + [(0.002 x distance x weight)] sex; male=1 female=0). Patients were trained at 60%–90% of the maximum heart rate. We used BORG dyspnea scores to regulate exercise duration and loads [10, 17]. Exercise intensity was observed to increase with patients' progress. We used pulse oximetry to supervise patients during the exercise, and supplementation was provided if the SpO_2 dropped below 90% oxygen. Pre-PR and post-PR arterial blood gas analyses were conducted.

Statistical Analysis

For numeric variables, normality distribution was tested using the Kolmogorov–Smirnov test. Continuous variables with normal distribution were presented with means and standard deviations, whereas categorical variables were described by frequencies and percentages. Numeric variables without normal distribution were presented by medians and interquartile ranges. For defining relationship between two categorical variables, the chi-squared test (or Fisher's exact test) was utilized. We compared two independent means using Student's t-test, and two independent medians using the Mann–Whitney U-Test. Two dependent medians were compared using the Wilcoxon test. A p-value <0.05 was considered to indicate a statistically significant difference between parameters examined.

RESULTS

The majority of included patients were male (87.7%). Patients had a mean age of 62.5 years (±8.2) and a mean FEV_1% predicted of 40.5% (±27.5%). Patient characteristics are presented in Table 1. Apart from the body mass index and COPD stages classification, all baseline variables were well balanced between the two groups (Table 2). The median IC/TLC ratio (IQR) was 0.29 (0.19) for all participants and did not significantly changed after PR (p=0.291). For all participants after PR, there was an increase in FEV_1% predicted, TLCO, and pO_2 levels, and an improvement in QoL and dyspnea scores (p<0.05 for all). Patients with IC/TLC >0.25 were classified as Group 1 and IC/TLC ≤0.25 as Group 2. The differences after PR for both groups are shown in Table 3. The 6mWD improved in both groups after PR (375–420, 336–400 meters, respectively), but the difference in between groups was not significant. In both groups, the pO_2 levels significantly increased after PR (p<0.001), but the difference between groups were not significant (p>0.05). Also, after PR there was a significant increase in the FEV_1% predicted level in both groups (p=0.007, 0.004). Both QoL scores and mMRC scores improved significantly after PR in the two groups (p<0.001).

Table 1. Baseline demographic and clinical features of patients

Age (Mean, SD)	62.5	8.2
Sex (n, %)		
Female	15	12.3
Male	107	87.7
BMI kg/m^2 (median, IQR)	26	8
Comorbidity (n, %)		
Absent	55	45.1
Present	67	54.9
Biomass exposure (n, %)	6	4.9
Smoking history (n, %)	116	95.1
Smoking pack x years (median, IQR)	60	40
FEV_1 (%) mean ± SD	40.5	27.5
IC/TLC median IQR	0.29	0.19
Stage (n, %)		
I	4	3.3
II	35	28.7
III	53	43.4
IV	30	24.6

SD: standart deviation; BMI: body mass index; FEV_1: Forced expiratory volume in 1. second; IC: inspiratory capacity; TLC: total lung capacity; IQR: Interquartile range

Table 2. Comparison of demographic differences between the two groups

	IC/TLC>0.25	IC/TLC≤0.25	p
Age (Mean, SD)	61.9±7.2	63.1±9.3	0.406
Sex (n, %)			
Female	9 (12.5)	6 (12.2)	0.967
Male	63 (87.5)	43 (87.8)	
BMI (median, IQR)	27 (7)	25 (8)	0.015
Comorbidity (n, %)			
Absent	31 (43.1)	23 (46.9)	0.673
Present	41 (56.9)	26 (53.1)	
Biomass exposure (n, %)			
Smoking	68 (94.4)	47 (95.9)	>0.999
Others	4 (5.6)	2 (4.1)	
Smoking (median, IQR)	50 (43.75)	60 (30)	0.330
Stage (n, %)			
I	4 (5.6)	0 (0)	0.003
II	26 (36.1)	8 (16.3)	
III	31 (43.1)	22 (44.9)	

SD: standart deviation; BMI: body mass index; IQR: interquartile range

In Group 1 (IC/TLC >0.25), there was a statistically significant decrease in this ratio after PR (p=0.001). In Group 2 (IC/TLC <0.25), there was a statistically but not clinically significant improvement in the IC/TLC score after PR (p=0.002), whereas this improvement was not observed in Group 1. When we compare the difference in IC/TLC (ΔIC/TLC) before and after PR, there was a statistical significance between the two groups (p<0.001).

DISCUSSION

The IC/TLC ratio is an important predictor of mortality in emphysematous patients with COPD. Moreover, IC/TLC ≤25% is associated with a higher risk of death [6]. In our study, we showed that in patients with COPD with IC/TLC <0.25; a significant improvement in the FEV_1, QoL parameters, and exercise capacity was observed, and also there was a statistically significant but not clinically insignificant improvement in IC/TLC after PR.

Pulmonary rehabilitation is an evidence-based non-pharmacological treatment in managing patients with COPD. PR has been shown to mitigate symptoms of dyspnea, improve exercise capacity, and increase health-related QoL [19]. Respiratory function tests present differing results following the PR. No significant change in FEV_1, FVC, and FEV_1/FVC values was observed in most of them [20, 21]. However, the findings seem to be controversial. In a study by Cecily et al. [22], 100 patients with COPD showed significant improvement in FEV_1 and FVC, as well as the value of peak expiratory flow rate. Shebl et al. [23] showed that after a supervised 2-month home-based exercise program, FEV_1 increased exclusively in severe COPD, while the FVC and FEV_1/FVC ratios were increased in the medium and severe COPD. However, such increases were insignificant. In a study comparing the differences of improvement by gender, FEV_1 and FVC increased in both genders; however, a greater improvement was obtained in men after a PR program [24]. In another study assessing 225 patients based on the severity of COPD after a PR program, FEV_1 increased significantly in Stages 3 and 4, the vital capacity rose significantly to 2, 3 and 4, TLC was reduced significantly in Stage 3 only, and residual volumes were significantly lower in Stages 3 and 4 [25]. In our study, we found a significant increase in the FEV_1% predicted level in both groups. We believe that after breathing exercises and techniques, patients with COPD were able to achieve better pulmonary functions test results.

Our knowledge about the process concerning COPD has been increasing continuously. Despite the initial studies' promotion of FEV_1 to be one of the best predictors of COPD-associated mortality, more recent publications have shown that other factors prove more accurate predictors of mortality than FEV_1 [4-6]. It is capable of showing that the IC/TLC ratio was in correlation with the risk of death in patients with an emphysematous phenotype of COPD, using an IC/TLC ratio of ≤25%, which is a representation of static lung hyperinflation. For those patients with an IC/TLC ≤25%, French et al. [11] showed that patients with an IC/TLC ratio ≤25% had a median survival of 4.3 years versus 11.9 years. In our study, patients with a good prognosis showed a decrease in the IC/TLC ratio after PR; reversely, the bad prognosis group had an increase in this ratio after PR. It has not been well defined whether these alterations have a clinically significant importance. More data are needed to confirm these results. However, we believe that this is the one of the few studies showing that patients with COPD with a high risk of mortality benefit from a pulmonary rehabilitation program.

Cebollero et al. [26] studied 35 men presenting moderate-to-severe COPD, and the patients were categorized into those with IC/TLC ≤25% (n=16) and >25% (n=19). The authors concluded that IC/TLC≤25% was associated with lower maximal strength and peak power output of the lower extremities. IC/TLC≤25% may have an important clinical relevance as an index to determine the peripheral muscle dysfunction. In a study by Ramon et al. [27], it was demonstrated by a bivariate analysis that patients with lower levels of IC/TLC presented a greater 6MWD decline (−27.4 ± 42.5, −24.9 ± 36.5, and −13.4 ± 39.9 meters/year in the first, second, and third tertile of IC/TLC, respectively; P-for-trend=0.018). We believe that

Table 3. Comparison of the two groups before and after pulmonary rehabilitation (pulmonary function tests, blood gas analysis, exercise capacity, and quality-of-life parameters)

	IC/TLC>0.25			IC/TLC≤0.25	
	Before Median (IQR)	**After Median (IQR)**	**p**	**Before Median (IQR)**	**After Median (IQR)**
FEV_1	47 (27.8)	49 (26.5)	0.007	33 (14.5)	35 (16.5)
FEV_1/FVC	61 (19.5)	62 (21)	0.552	51 (21)	51 (23.5)
IC	70.5 (34.5)	67.5 (38)	0.061	41 (22.5)	46 (32.5)
TLC	92 (32)	95.5 (33)	0.832	103 (26.5)	114 (33.5)
IC/TLC	0.37 (0.19)	0.31 (0.17)	0.001	0.19 (0.1)	0.22 (0.16)
TLCO	42 (27)	43.5 (28)	0.026	34 (27)	34 (21)
	IC/TLC>0.25			**IC/TLC≤0.25**	
	Before Median (IQR)	**After Median (IQR)**	**p**	**Before Median (IQR)**	**After Median (IQR)**
pO_2	74 (16)	79.5 (15.8)	<0.001	67 (11.4)	73.7 (13)
pCO_2	40.4 (7.2)	40 (7.8)	0,022	40.3 (9)	41 (7.7)
Saturation	95 (2)	96 (2.5)	<0.001	93.6 (4.6)	95 (3)
pH	7.4 (0.04)	7.4 (0.04)	0.923	7.4 (0.04)	7.4 (0.04)
	IC/TLC>0.25			**IC/TLC≤0.25**	
	Before Median (IQR)	**After Median (IQR)**	**p**	**Before Median (IQR)**	**After Median (IQR)**
Distance	375 (140)	420 (117.5)	<0.001	336 (130)	400 (130)
BORG difference	1.5 (1)	1 (0.5)	<0.001	2 (2)	2 (1.8)
Saturation difference	2 (2.8)	1 (3.8)	0.436	2 (5)	3 (5.5)
	IC/TLC>0.25			**IC/TLC≤0.25**	
	Before Median (IQR)	**After Median (IQR)**	**p**	**Before Median (IQR)**	**After Median (IQR)**
SGRQ symptoms	48.4 (31)	39.2 (27.6)	0.001	67.4 (36)	50.7 (27.9)
SGRQ activity	60.5 (31.7)	48.05 (30.5)	<0.001	72.3 (32.9)	60.4 (38.3)
SGRQ impact	42.3 (31.4)	27.8 (26.6)	<0.001	50.7 (31.7)	35.6 (34.3)
SGRQ total	52.7 (32.5)	37.4 (25.7)	<0.001	61.3 (31)	46.5 (33.6)
Physical functioning	57.5 (40)	70 (35)	0.002	45 (45)	60 (35)
Social functioning	75 (37.5)	87.5 (31.3)	0.001	50 (50)	75 (50)
Role limitations due to physical health	25 (75)	75 (75)	<0.001	0 (25)	25 (100)
Role limitations due to emotional problems	33.3 (100)	66.7 (66.7)	0.024	5 (66.7)	66.7 (100)
General health	45 (36.3)	62 (35)	<0.001	30 (36.3)	40 (47)
Emotional well-being	70 (24)	76 (22)	0.033	60 (36)	68 (36)
Pain	67 (45.3)	84 (34)	0.001	42 (52)	74 (48)
Energy/fatigue after	55 (35)	70 (27.5)	0.002	40 (35)	60 (30)
HADA	7 (6)	5 (5.5)	<0.001	8 (8)	7 (5)
HADD	5 (6)	4 (6)	0.005	7 (5)	7 (6)

HADD: hospital depression scale; HADA: hospital anxiety scale; SGRQ: Saint George respiratory questionnaire; BORG: pre and post execise test; pH: acidity; pCO_2: partial pressure of carbon dioxide; pO_2: partial pressure of oxygen; TLCO: CO difusion capacity; IC: inspiratory capacity; TLC: total lung capacity; FEV_1: forced expiratory volume in 1. second; FVC: forced vital capacity IQR: interquartile range with the new studies investigating the IC/TLC ratio, this index will not only be a prognostic marker, but also a severity index and a follow-up marker.

In our daily practice, PR is known to be a standard method effective in increasing the exercise capacity, reducing perceived dyspnea, and improving the QoL in patients with COPD [17-19]. As part of the present study, all COPD patients who completed the PR program showed reduced perceived dyspnea, an increased exercise capacity, and improved QoL. Our PR program has multi-component interventions included in supervised physical exercise training: theoretical training, psychological counseling, and nutritional intervention. We believe that the improvement in COPD patients after PR may be due to multi-component interventions. Coventry et al. [28] showed that, after receiving training and psycho-social support in the PR program, patients with COPD reported lower levels of anxiety and depression. Yet this study found that anxiety scores decreased significantly in both groups, but the depression scores only significantly decreased in Group 1.

Our results must be considered in the context of the limitations of our study. First of all, our pulmonary function test laboratory is not a research but a clinical laboratory. The IC/TLC ratio is calculated from body plethysmography results; therefore, like any clinical test, the body plethysmography results must be interpreted carefully. Second, COPD is a heterogeneous disease, and prediction of mortality depends on various factors. Only a pulmonary function test ratio may not reflect the whole disease process.

The IC/TLC ratio is a significant predictor of mortality in patients with COPD. As a conclusion, our study showed that COPD patients with IC/TLC ≤25% had a significant improvement in FEV_1, QoL parameters, and functional exercise capacity. Also there was a statistically but not clinically significant improvement in the IC/TLC ratio after the PR program. We believe that to benefit most from a PR program, further studies should be performed to provide an opportunity to COPD patients, those with IC/TLC ≤25% in particular.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Dr. Suat Seren Chest Diseases and Thoracic Surgery Training and Research Hospital (451:11.05.2016-5301).

Informed Consent: Written informed consent was obtained from the patients who participated in this study.

Peer-review: Externally peer-reviewed.

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Conflict of Interest: The authors have no conflicts of interest to declare.

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