



Impact of adherence to long-term oxygen therapy on patients with COPD and exertional hypoxemia followed for one year

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ABSTRACT

Objective: To determine the impact of adherence to long-term oxygen therapy (LTOT) on quality of life, dyspnea, and exercise capacity in patients with COPD and exertional hypoxemia followed for one year. **Methods:** Patients experiencing severe hypoxemia during a six-minute walk test (6MWT) performed while breathing room air but not at rest were included in the study. At baseline and after one year of follow-up, all patients were assessed for comorbidities, body composition, SpO₂, and dyspnea, as well as for anxiety and depression, having also undergone spirometry, arterial blood gas analysis, and the 6MWT with supplemental oxygen. The Saint George's Respiratory Questionnaire (SGRQ) was used in order to assess quality of life, and the Body mass index, airflow Obstruction, Dyspnea, and Exercise capacity (BODE) index was calculated. The frequency of exacerbations and the mortality rate were noted. Treatment nonadherence was defined as LTOT use for < 12 h per day or no LTOT use during exercise. **Results:** A total of 60 patients with COPD and exertional hypoxemia were included in the study. Of those, 10 died and 11 experienced severe hypoxemia during follow-up, 39 patients therefore being included in the final analysis. Of those, only 18 (46.1%) were adherent to LTOT, showing better SGRQ scores, higher SpO₂ values, and lower PaCO₂ values than did nonadherent patients. In all patients, SaO₂, the six-minute walk distance, and the BODE index worsened after one year. There were no differences between the proportions of adherence to LTOT at 3 and 12 months of follow-up. **Conclusions:** Quality of life appears to be lower in patients with COPD and exertional hypoxemia who do not adhere to LTOT than in those who do. In addition, LTOT appears to have a beneficial effect on COPD symptoms (as assessed by SGRQ scores).

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Keywords: Respiratory insufficiency; Pulmonary disease, chronic obstructive; Patient compliance; Hypoxia; Oxygen inhalation therapy.

INTRODUCTION

Patients with COPD constitute the largest homogeneous group of patients who have arterial hypoxemia,^(1,2) accounting for 67.8-81.6% of all patients on long-term oxygen therapy (LTOT).⁽³⁾ The use of LTOT improves quality of life and respiratory symptoms, as well as reducing the risk of mortality.^(4,5) In some patients, however, hypoxemia occurs only during activities of daily living.⁽⁶⁾ The mechanisms involved in exertional hypoxemia are associated with ventilation/perfusion mismatch, decreased diffusion capacity, and increased pulmonary shunt.⁽⁶⁾ As a result, exercise tolerance and quality of life are reduced in such patients.⁽⁶⁾

The effectiveness of LTOT in patients with exertional hypoxemia has yet to be established. Although one study has shown that the use of LTOT during pulmonary rehabilitation improves the quality of life of patients with exercise-induced hypoxemia,⁽⁷⁾ other studies have shown

that the use of LTOT has no beneficial effect on COPD patients with exertional hypoxemia undergoing physical training.^(6,8,9) In addition, in patients with moderate resting or exercise-induced hypoxemia, LTOT has been shown to have no beneficial effect on the time to death or first hospitalization.⁽¹⁰⁾ There is no consensus regarding the use of LTOT in such patients.^(6,11)

Few studies have examined the impact of adherence to LTOT on clinical outcomes in such patients.⁽¹⁰⁾ Therefore, the objective of the present study was to determine the impact of adherence to LTOT on quality of life, dyspnea, and exercise capacity in patients with COPD and exertional hypoxemia followed for one year.

METHODS

Patients

We evaluated 159 COPD patients referred to the Oxygen Therapy Outpatient Clinic of the São Paulo State University

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Botucatu School of Medicine, in the city of Botucatu, Brazil, in the period between November of 2011 and June of 2012. The inclusion criteria were as follows: having been diagnosed with COPD in accordance with the Global Initiative for Chronic Obstructive Lung Disease criteria⁽¹²⁾ and having exertional hypoxemia.

At baseline (and while breathing room air), patients experiencing severe arterial hypoxemia during exercise but not at rest were classified as having exertional hypoxemia. To confirm the presence of a $\text{PaO}_2 > 59$ mmHg^(2,13) at rest and on room air, we performed arterial blood gas analysis. All patients performed a six-minute walk test (6MWT) while breathing room air, the presence of exertional hypoxemia being confirmed by an SpO_2 of $< 87\%$ during the test. All patients with exertional hypoxemia received a prescription for oxygen supplementation at a flow rate of 0.5 L/min for at least 12 h per day for one year, to be used when performing activities of daily living (including walking) and during sleep.⁽¹¹⁾ The exclusion criteria were as follows: severe hypoxemia at rest ($\text{PaO}_2 \leq 55$ mmHg), other respiratory diseases, polycythemia, *cor pulmonale*, cancer, and active smoking. Clinically unstable patients (medication changes, disease exacerbations, or hospital admissions in the preceding 6 weeks) and those who presented with severe arterial hypoxemia at rest (a PaO_2 of < 55 mmHg) during the follow-up period were also excluded. Patients were evaluated at baseline and every 4 months in order to determine the frequency of exacerbations and adherence to LTOT. Exacerbations were confirmed by changes in maintenance therapy or the need to prescribe oral corticosteroids, antibiotics, or both. Cause-of-death data were obtained by reviewing patient medical records. The study was approved by the Research Ethics Committee of the Botucatu School of Medicine University Hospital (Protocol no. 4020-2011), and all participating patients gave written informed consent.

Spirometry, arterial blood gas analysis, and pulse oximetry

Pre- and post-bronchodilator spirometry tests were performed with a Koko spirometer (Ferraris Respiratory, Louisville, CO, USA), in accordance with the American Thoracic Society criteria.⁽¹⁴⁾ Disease severity was determined on the basis of criteria established by the Brazilian Thoracic Association and the Global Initiative for Chronic Obstructive Lung Disease.^(2,15) Values of FEV_1 and FVC were expressed as percentages of the predicted values. Radial artery puncture was used in order to collect blood samples for arterial blood gas analysis, PaO_2 , PaCO_2 , and SaO_2 being measured with a blood gas analyzer (Stat Profile 5 Plus; Nova Biomedical, Waltham, MA, USA) and SpO_2 being measured with an Onyx 9500™ pulse oximeter (Nonin Medical, Inc., Plymouth, MN, USA). The aforementioned parameters were assessed with the patients at rest and breathing room air.

Body composition

Body weight and height were measured with participants standing barefoot and wearing light clothing. The body mass index (BMI) was calculated by the formula $\text{weight}/\text{height}^2$ (kg/m^2). Body composition was assessed by bioelectrical impedance analysis (BIA 101A; RJL Systems, Inc., Clinton Township, MI, USA). Resistance was measured on the right side of the body in the supine position. Fat-free mass (FFM, in kg) was calculated by a group-specific regression equation developed by Kyle et al.⁽¹⁶⁾ The FFM index ($\text{FFMI} = \text{FFM}/\text{height}^2$) was also calculated. FFM depletion was defined as an FFMI of < 15 kg/m^2 for women and an FFMI of < 16 kg/m^2 for men.⁽¹⁷⁾

Exercise capacity

The 6MWT was performed in accordance with the American Thoracic Society guidelines.⁽¹⁸⁾ Patients were instructed to walk, attempting to cover as much ground as possible within 6 min. The walk was timed by a research assistant, and standardized verbal encouragement was given. Following a rest period of at least 30 min, each subject performed a second 6MWT in the same manner as the first. Patient SpO_2 was monitored throughout the test. Before and after the test, data were obtained for SpO_2 , heart rate, respiratory rate, and blood pressure. The six-minute walk distance (6MWD) was expressed in meters.

Adherence

Adherence to treatment was assessed by asking questions regarding the oxygen flow rate and the number of hours of LTOT use per day. The information thus obtained was confirmed by comparing it to the prescription data on patient medical records. Treatment nonadherence was defined as LTOT use for < 12 h per day or no LTOT use during exercise. To improve the use of LTOT, adherence education was provided at each medical visit. In addition, nurse home visits were provided in order to reinforce the importance of and assess adherence to LTOT.

Quality of life, the Baseline Dyspnea Index, the Hospital Anxiety and Depression Scale, the Charlson comorbidity index, and the Body mass index, airflow Obstruction, Dyspnea, and Exercise capacity index

The Brazilian Portuguese version of the Saint George's Respiratory Questionnaire (SGRQ)⁽¹⁹⁾ was used in order to evaluate quality of life. Dyspnea was assessed by the Brazilian Portuguese version of the modified Medical Research Council scale, as well as by the Baseline Dyspnea Index (BDI).^(20,21) The Hospital Anxiety and Depression Scale was used in order to evaluate anxiety and depression.⁽²²⁾ Comorbidities were quantified by the Charlson comorbidity index.⁽²³⁾ The **B**ody mass index, **a**irflow **O**bstruction, **D**yspnea, and **E**xercise capacity (BODE) index was calculated by using the model of Celli et al.⁽²⁴⁾ All questionnaires

were administered at baseline and after a one-year follow-up period.

Statistical analysis

For a power of 80% and a type I error of 0.05, the required sample size to detect a mean difference in quality of life ($4.0 \pm 4.5\%$) or dyspnea (1.0 ± 2.0) at the end of the follow-up period was calculated to be 34. Data were expressed as mean \pm standard deviation or median (interquartile range). The Student's t-test or the Mann-Whitney test was used in order to compare two independent groups according to their distribution. A paired t-test or the Wilcoxon test was used in order to compare repeated measures. The chi-square test was used in order to compare proportions. Multiple linear regression analysis was used in order to evaluate factors associated with the 6MWD and dyspnea after one year. A value of $p < 0.05$ was defined as statistically significant. All analyses were performed with the Stata statistical software package, version 10.0 (StataCorp LP, College Station, TX, USA).

RESULTS

A flow chart of inclusion and exclusion of patients is presented in Figure 1. A total of 60 patients with COPD and exertional hypoxemia were included in the study. Of those, 10 died during the study period. The causes of death were pulmonary complications of COPD, in 6 patients, and cardiovascular disease, in 4. In addition, 11 patients experienced severe hypoxemia during follow-up and were excluded from the analysis, 39

patients therefore being included in the final analysis. The BODE index and the BMI were lower in the patients who died than in those who survived ($2.0 [1.0-3.0]$ vs. $1.0 [0.0-2.0]$, $p = 0.005$ and $17.8 [16.4-27.6]$ vs. $23.7 [19.5-30.0]$, $p = 0.028$, respectively), as was adherence to LTOT.

The characteristics of the 39 patients at baseline and after one year of follow-up are presented in Table 1. All 39 were using long-acting beta-adrenoceptor agonists, which were used in combination with long-acting anticholinergics in 15 and in combination with inhaled corticosteroids in 15. In all patients, the 6MWD and the BODE index worsened after one year, whereas SGRQ symptoms domain scores showed significant improvement. The proportion of patients with a lower FFMI at baseline was 12.8%. Adherence to LTOT was low during the study period (46.1%). Nonadherent patients reported using oxygen supplementation for 8.0 ± 1.2 h per day. In comparison with adherent patients, nonadherent patients showed significantly lower resting SpO_2 (91.1 ± 2.5 vs. 93.3 ± 2.3 ; $p = 0.011$), higher $PaCO_2$ ($39.5 [35.8-47.3]$ vs. $35.7 [34.2-39.4]$; $p = 0.044$), and worse scores for the SGRQ domains of symptoms (41.5 ± 19.6 vs. 27.6 ± 18.7 ; $p = 0.039$), activity ($72.9 [66.2-79.7]$ vs. $60.4 [45.9-70.3]$; $p = 0.014$), and impacts (39.5 ± 15.1 vs. 27.8 ± 18.3 ; $p = 0.047$), as well as significantly worse total SGRQ scores (49.9 ± 11.9 vs. 36.4 ± 17.7 ; $p = 0.012$), after one year (Table 2).

The scores for the SGRQ domain of symptoms improved significantly after one year of follow-up in the nonadherent group (47.3 ± 18.7 vs. 41.5 ± 19.6 ;

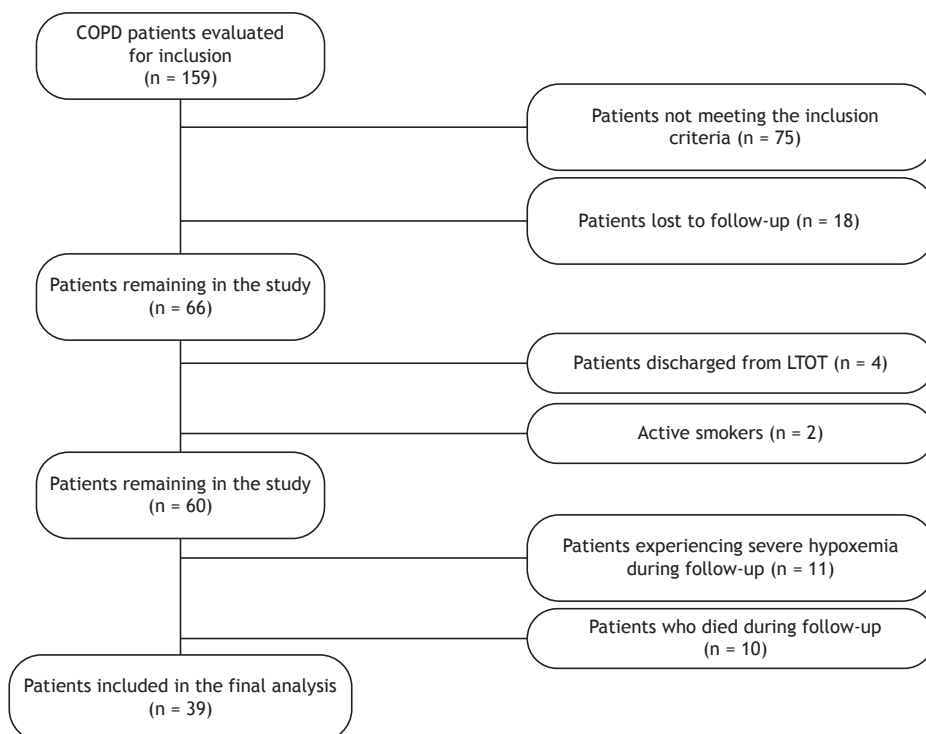


Figure 1. Flow chart of inclusion and exclusion of patients. LTOT: long-term oxygen therapy.

Table 1. General characteristics of patients with COPD and exercise-induced hypoxemia at baseline and after one year of follow-up (N = 39).^a

Characteristic	Baseline	One year later	p
Men, %	41.1		
Age, years ^b	69.0 (62.0-77)		
BMI, kg/m ^{2b}	23.7 (19.5-30.0)	26.5 (21.7-30.8)	0.674
FFM, kg ^b	45.6 (41.1-51.6)	44.3 (38.5-51.8)	0.544
FFMI, kg ^b	18.0 (16.8-20.0)	18.0 (16.3-19.8)	0.642
Charlson comorbidity index	3.2 ± 1.1	3.2 ± 1.1	1.000
BODE index ^b	1.0 (0.0-2.0)	1.5 (0.0-2.0)	0.031
SpO ₂ , %	92.1 ± 2.5	92.3 ± 2.6	0.885
PaO ₂ , mmHg	67.0 ± 5.4	63.6 ± 7.9	0.128
PaCO ₂ , mmHg	38.1 ± 6.0	38.6 ± 8.5	0.633
FVC, L	2.23 ± 0.78	2.11 ± 0.73	0.177
FEV ₁ , L	1.13 ± 0.49	1.07 ± 0.40	0.056
FEV ₁ /FVC, L ^b	0.50 (0.41-0.58)	0.53 (0.41-0.58)	0.754
SGRQ symptoms domain score, %	53.0 ± 19.8	34.5 ± 20.4	< 0.001
SGRQ activity domain score, %	63.6 ± 20.5	65.2 ± 19.4	0.695
SGRQ impacts domain score, %	34.6 ± 18.7	33.5 ± 17.7	0.707
Total SGRQ score, %	46.7 ± 16.5	43.3 ± 16.5	0.232
Anxiety, HADS	4.3 ± 4.4	2.8 ± 2.1	0.065
Depression, HADS	3.3 ± 3.7	4.3 ± 3.8	0.170
mMRC scale ^b	2.0 (1.0-2.5)	2.0 (1.0-2.5)	0.612
BDI	5.5 ± 2.7	5.2 ± 2.7	0.601
6MWD, m ^b	336.0 (264.0-390.0)	306.0 (210.0-355.0)	< 0.001

BMI: body mass index; FFM: fat-free mass; FFMI: fat-free mass index; BODE: Body mass index, airflow Obstruction, Dyspnea, and Exercise capacity; SGRQ: Saint George's Respiratory Questionnaire; HADS: Hospital Anxiety and Depression Scale; mMRC: modified Medical Research Council; BDI: Baseline Dyspnea Index; and 6MWD: six-minute walk distance. ^aValues expressed as mean ± SD, except where otherwise indicated. ^bValues expressed as median (interquartile range). p < 0.05 (Student's t-test or Mann-Whitney test).

p = 0.005) and in the adherent group (36.8 ± 16.8 vs. 27.6 ± 18.7; p = 0.001). With regard to the scores for the remaining SGRQ domains and total SGRQ scores, there were no significant differences (Figure 2).

Of the 39 patients in the sample, 16 (41%) were diagnosed with COPD exacerbation, and 26% required hospitalization, the need for hospitalization being unrelated to adherence to LTOT (p = 1.00). The multiple linear regression model showed a negative association between the BDI and SGRQ symptoms domain scores after one year (p = 0.04; Table 3).

DISCUSSION

The objective of the present study was to determine the impact of adherence to LTOT on quality of life, dyspnea, and exercise capacity in patients with COPD and exertional hypoxemia followed for one year. The main finding of our study is that quality of life is worse in patients who do not adhere to LTOT than in those who do. Adherence to LTOT contributes to improving quality of life by improving symptoms. In comparison with the COPD patients who did not adhere to LTOT in the present study, those who did had better quality of life after one year of follow-up. Nevertheless, respiratory symptoms were found to have improved in the group of nonadherent patients, despite the fact that they did not use LTOT for as long as recommended. The mean duration of LTOT use in our study was quite

similar to that in a trial conducted by the Long-Term Oxygen Treatment Trial Research Group (i.e., 10.4 h/day). That trial included 148 patients receiving LTOT during exercise and sleep.⁽¹⁰⁾

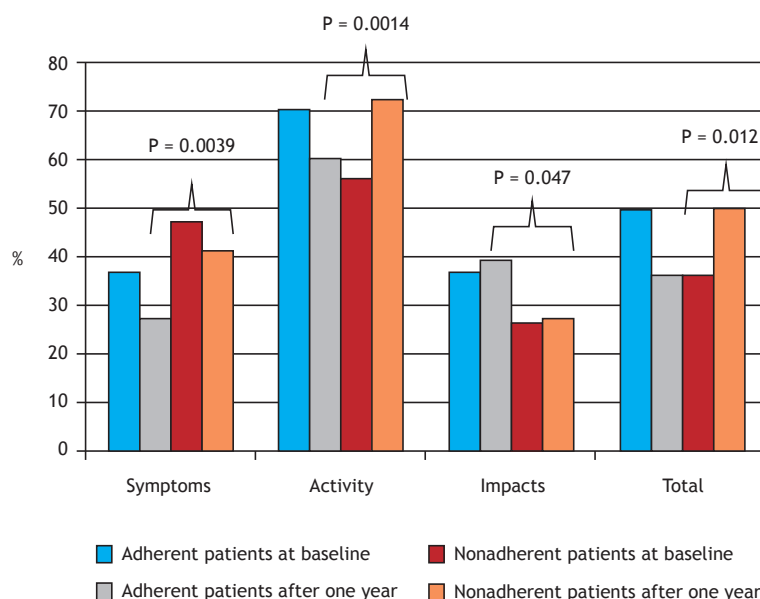
In a study analyzing 191 patients with severe hypoxemia, only 52.4% adhered to LTOT as prescribed,⁽²⁵⁾ a finding that is consistent with those of the present study. The authors of the aforementioned study reported 51 adverse events attributed to the use of oxygen supplementation, 23 patients having reported tripping on the device.⁽²⁵⁾ Adverse events can contribute to poor adherence to treatment.⁽¹⁰⁾ In a qualitative study of 27 COPD patients receiving LTOT,⁽²⁶⁾ most (59.2%) reported nonadherence to LTOT, which was reported to be difficult to use during physical activity and was associated with social stigma and fear of side effects.

Previous studies^(4,5,27,28) have shown the beneficial effects of LTOT on mortality, quality of life, and respiratory symptoms in COPD patients with severe hypoxemia. The use of LTOT might also be beneficial for patients with exertional hypoxemia, improving their symptoms, dyspnea, functional capacity, and disease progression. Analysis of data from the National Emphysema Treatment Trial, a longitudinal study conducted in the United States, showed that 33.8% of 1,215 patients with emphysema were using LTOT despite having no severe hypoxemia.⁽⁶⁾ In comparison

Table 2. Comparison between adherent and nonadherent patients with COPD and exertional hypoxemia.^a

Variable	Patients who adhered to LTOT (n = 18)	Patients who did not adhere to LTOT (n = 21)	p
Men, %	33.4	28.3	
Age, years	69.1 ± 10.0	71.5 ± 8.7	0.433
BMI, kg/m ²	23.2 ± 8.4	25.5 ± 6.0	0.684
FFM, kg	45.8 ± 9.3	45.0 ± 8.7	0.787
FFMI, kg	17.5 ± 2.1	18.1 ± 2.6	0.459
Borg scale ^b	0.0 (0.0-1.7)	0.0 (0.0-0.0)	0.420
BODE index	1.1 ± 0.9	1.4 ± 1.1	0.081
SpO ₂ , %	93.3 ± 2.3	91.1 ± 2.5	0.011
PaO ₂ , mmHg	64.4 ± 6.9	62.7 ± 9.1	0.536
PaCO ₂ , mmHg ^b	35.7 (34.2-39.4)	39.5 (35.8-47.3)	0.044
SaO ₂ , % ^b	93.3 (90.6-94.3)	91.2 (90.6-94.1)	0.509
FVC, L ^b	1.8 (1.4-2.6)	2.1 (1.5-2.4)	0.609
FEV ₁ , L ^b	0.9 (0.7-1.0)	1.0 (0.8-1.3)	0.083
FEV ₁ /FVC, L	0.4 ± 0.1	0.5 ± 0.1	0.072
SGRQ symptoms domain score, %	27.6 ± 18.7	41.5 ± 19.6	0.039
SGRQ activity domain score, % ^b	60.4 (45.9-70.3)	72.9 (66.2-79.7)	0.014
SGRQ impacts domain score, %	39.5 ± 15.1	27.8 ± 18.3	0.047
Total SGRQ score, %	36.4 ± 17.7	49.9 ± 11.9	0.012
Anxiety, HADS	3.1 ± 2.6	2.4 ± 1.7	0.373
Depression, HADS ^b	3.5 (1.0-5.0)	3.0 (0.0-7.0)	0.981
mMRC scale	1.9 ± 0.7	1.6 ± 1.2	0.384
BDI ^b	5.0 (4.0-5.0)	6.0 (3.0-8.0)	0.392
6MWD, m	309.6 ± 90.3	266.5 ± 97.1	0.190

BMI: body mass index; FFM: fat-free mass; FFMI: fat-free mass index; BODE: Body mass index, airflow Obstruction, Dyspnea, and Exercise capacity; SGRQ: Saint George's Respiratory Questionnaire; HADS: Hospital Anxiety and Depression Scale; mMRC: modified Medical Research Council; BDI: Baseline Dyspnea Index; and 6MWD: six-minute walk distance. ^aValues expressed as mean ± SD, except where otherwise indicated. ^bValues expressed as median (interquartile range). p < 0.05 (Student's t-test or Mann-Whitney test).


Figure 2. Saint George's Respiratory Questionnaire (SGRQ) domain scores for adherent and nonadherent patients at baseline and after one year of follow-up. p < 0.05 (paired t-test or Wilcoxon test).

with the patients who were not using LTOT, those who were had worse dyspnea, lower quality of life, and

lower functional capacity, exercise-induced desaturation being more common in those using LTOT.⁽⁶⁾

Table 3. Multiple linear regression analysis of factors associated with the Saint George's Respiratory Questionnaire symptoms domain after one year of follow-up.

Dependent variable	Variable	Coefficient	(95% CI)	p
Symptoms after one year ($R^2 = 0.23$)	Baseline SpO ₂ , mmHg	0.01	-2.62 to 2.65	0.99
	BDI	-2.85	-5.59 to -0.107	0.04
	Adherence after one year, yes	-0.86	-18.40 to 16.77	0.91

BDI: Baseline Dyspnea Index.

According to international guidelines, LTOT should not be used in patients with exertional hypoxemia.^(6-8,11,19,29,30) In a recently published study,⁽¹⁰⁾ patients with moderate resting or exercise-induced hypoxemia were followed for six years and no differences were found between those using LTOT and those not using it regarding quality of life, lung function, or the 6MWD. In addition, the BODE index was lower in the patients using LTOT than in those not using it ($p = 0.007$).⁽¹⁰⁾ However, the fact that the study included a heterogeneous sample of patients might have affected the results.

In the present study, quality of life (as assessed by SGRQ symptoms domain scores) was found to have improved after one year (53.0 ± 19.8 vs. 34.5 ± 20.4 ; $p < 0.001$). Eaton et al.⁽⁷⁾ divided 41 COPD patients with exertional hypoxemia into two groups on the basis of LTOT use during physical exercise performed three times a week for 4 months. The group of patients using LTOT showed significant improvement in quality of life.⁽⁷⁾ Garrod et al.⁽⁸⁾ reported that patients participating in an 8-week exercise training program and receiving supplemental oxygen showed significant improvement in the 6MWD (169 ± 112 m vs. 269 ± 124 m; $p = 0.001$) and in Chronic Respiratory Disease Questionnaire scores (24.0 vs. 17.4 ; $p < 0.001$) when compared with those who participated in the program but did not receive supplemental oxygen.⁽⁸⁾ The finding of a higher mean 6MWD is consistent with those of Morakami et al.,⁽³¹⁾ who compared COPD patients in Brazil and Austria and found that mean walking time and movement intensity were greater in the former than in the latter.

Wadell et al.⁽⁹⁾ found that the use of LTOT did not improve quality of life or dyspnea in COPD patients with exercise-induced hypoxemia. The authors evaluated 20 patients with COPD and exercise-induced hypoxemia. The participants were randomized to undergo exercise training while breathing room air or receiving supplemental oxygen for 30 min three times per week for 8 weeks.⁽⁹⁾ Unlike our study, in which LTOT use was found to improve dyspnea, the study by Wadell et al. included no other periods of LTOT use during the day.⁽⁹⁾

Although our results showed no significant changes in dyspnea scores, multiple linear regression analysis showed that a higher BDI translated to worse SGRQ symptoms domain scores after one year of follow-up. This result is consistent with those obtained by Ferrari et al.,⁽³²⁾ who followed 90 COPD patients for three years and found that dyspnea perception was positively associated with impaired quality of life at the end of the follow-up period.

Reduced functional capacity is a marker of severity and mortality in patients with COPD and exercise-induced hypoxemia.⁽³³⁾ In the present study, the 6MWD decreased significantly after one year of follow-up. Takigawa et al.⁽³⁴⁾ reported that COPD patients with a $\geq 6\%$ decrease in SpO₂ during the 6MWT were at an increased risk of death. Casanova et al.⁽³⁵⁾ reported that COPD patients with a $\geq 4\%$ decrease in SpO₂ or an SpO₂ of $< 90\%$ during the 6MWT had a relative risk of death of 2.63 when compared with those without those changes.

Exacerbations can potentiate chronic inflammation and, consequently, have a detrimental effect on symptoms, quality of life, and exercise capacity, as well as accelerating the functional deterioration of COPD patients.⁽³⁵⁻³⁷⁾ With regard to the frequency of exacerbations in our sample of COPD patients, nearly 50% experienced at least one exacerbation during follow-up. Of those, 26 required hospitalization, the need for which was unrelated to adherence to LTOT. In another study conducted at our institution,⁽³²⁾ 90 COPD patients were followed over a three-year period. Of those, 75% experienced at least one exacerbation, which was classified as severe in 26.6%.⁽³²⁾ In a recent study, no significant differences were found between patients with COPD and moderate hypoxemia using LTOT and patients with COPD and moderate hypoxemia not using LTOT in terms of disease exacerbation and hospitalization.⁽¹⁰⁾ In a study conducted by Marino et al.,⁽³⁸⁾ 47 COPD patients were followed for 6 months, and 27.6% experienced at least one exacerbation during the study period. In the present study, the mortality rate was 15%. In a study involving 78 COPD patients receiving LTOT for one year, the mortality rate was 15.4%.⁽³⁹⁾

Nutritional depletion is a risk factor for clinical worsening in COPD patients receiving LTOT.⁽³⁷⁾ In the present study, there were no significant changes in the prevalence of nutritional depletion during follow-up. However, the BMI was found to be lower in the patients who experienced worsening hypoxemia or died than in those with transient hypoxemia. In a study evaluating 128 COPD patients using LTOT and followed for three years, the number of deaths was higher among those with a BMI of < 25 kg/m² and a higher number of comorbidities.⁽³⁹⁾

Our study has some limitations. First, given that patient adherence to LTOT was self-reported, it is impossible to determine actual adherence. Nevertheless, in a recent study conducted by the Long-Term Oxygen Treatment Trial Research Group,⁽¹⁰⁾ adherence to LTOT was also self-reported, and adherence education was

provided at each medical visit in order to improve LTOT use, as was done in the present study. Unfortunately, there is currently no other method for accurately determining patient adherence to LTOT. Second, there was no true control group (i.e., a group of patients receiving no supplemental oxygen). Second, by including a group without oxygen (true control group) will probably add more significant alterations on several parameters of disease progression and quality of life. If there had been one, we might have observed significant changes in several disease progression and quality of life parameters. However, although the changes observed in the group of patients who did

not adhere to LTOT were not as marked as they might have been in a true control group, quality of life was found to have improved in the group of patients who adhered to LTOT. Therefore, our findings are relevant.

In conclusion, quality of life appears to be lower in patients with COPD and exercise-induced hypoxemia who do not adhere to LTOT than in those who do. In addition, LTOT appears to have a beneficial effect on COPD symptoms (as assessed by SGRQ scores) in patients with COPD and exercise-induced hypoxemia. Further studies investigating LTOT use during exercise are needed in order to provide a better understanding of patient clinical response to LTOT.

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