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ORIGINAL ARTICLE

Evaluation of the association of adherence to long-term home oxygen therapy and clinical markers and five-year mortality in patients with Chronic obstructive pulmonary disease

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ABSTRACT

Objective: Assess the relationship between adherence to long-term oxygen therapy (LTOT) with mortality in patients with chronic obstructive pulmonary disease (COPD) and chronic respiratory failure and their clinical features. **Methods:** Longitudinal retrospective analysis of 254 patients with COPD and chronic respiratory failure from 2008 to 2016. At baseline, we evaluated the diagnosis, spirometry values, arterial blood gas analysis, blood count, pulse oximetry, body composition and health questionnaires (dyspnea, quality of life, anxiety and depression). For referred adherence analysis to LTOT we included 199 patients, divided according to prescription of oxygen**:** 12h/day (G1), 15h/day (G2) and 24h/day (G3). The cause of death and dates were studied over the five-year period. **Results:** In five years we identified 124 deaths (62.3%). No significant difference was found in mortality between the adherence groups (p=0.75) nor did we find differences in the clinical parameters evaluated. LTOT prescription was not associated with mortality (p=0.07). In Cox regression analysis, there was no association between mortality and non-adherence to LTOT (HR**:** 0.75; IC95%: 0.21-2.70). The risk of mortality was increased in G3 compared with G1 (HR: 7.16; IC 95%: 1.44-35.38) and in those with a higher depression score (HR: 1.35; IC: 1.14-1.59). **Conclusion:** No association was found between LTOT adherence and mortality in patients with COPD and respiratory failure. There were no clinical differences between the adherence groups.

Keywords: Chronic obstructive pulmonary disease; Oxygen therapy; Cooperation and treatment adherence; Morbidity and mortality indicators.

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a disease characterized by progressive airflow obstruction due to the inhalation of toxic particles or gases, especially smoking, and is not fully reversible.[1] The most serious cases are characterized by chronic respiratory failure, with indication for supplementation of long-term oxygen therapy (LTOT), as it improves quality of life, physical exercise capacity, cardiac output, pulmonary mechanics and reduces hospitalizations due to exacerbations and mortality.[2,3]

LTOT indications include when arterial oxygen pressure (PaO_2) <55 mmHg or pulse oximetry (SpO_2) ≤ 88%. In patients with PaO_2 between 56 and 59 mmHg but with clinical repercussions such as polycythemia (hematocrit ≥ 55%) or cor pulmonale, LTOT is also indicated to decrease the progression of hypoxemia damage.[4]

However, the literature describes markers of worse prognosis that are related to low or high $PaCO_2$, low PaO_2, presence of anemia and greater dyspnea symptoms.[5,6] In addition, a study of 14,000 patients showed that mortality was higher in the group that received an LTOT indication during hospitalization compared to an outpatient indication.[7]

In Brazil, data on survival and its related factors are still scarce. A study carried out in São Paulo showed a 15% survival rate after four years of follow-up, as well as observing a lower survival rate for women compared to men.[8] Another study with 118 patients showed survival of 75.9% in the first year and found an association of lower survival in those with greater severity of hypoxemia and dyspnea.[5]

On the other hand, a characteristic that can influence the prognostic markers of these patients is adherence to LTOT. Studies show that there is wide variation in

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the adherence rate, from 31 to 70%.[9-11] Factors associated with low adherence include age, low education, polypharmacy, few symptoms, active smoking, failure in the doctor-patient relationship and lack of follow-up.[12] Other difficulties are carrying the equipment, social stigma, lack of perceived benefit, fear of side effects, forgetfulness, discomfort, shyness and fear of dependence.[13-16]

In this context, few Brazilian studies have evaluated the influence of adherence to LTOT use on mortality, symptoms and disease evolution. Therefore, the aim of this study was to assess the association between adherence to LTOT use and clinical characteristics, quality of life and mortality after five years of follow-up in patients with very severe COPD.

METHODS

This retrospective longitudinal study evaluated all the medical records of the oxygen therapy outpatient clinic at "Hospital das Clínicas" of the "Faculdade de Medicina de Botucatu" - UNESP between June 2008 and January 2016 (data obtained from the research "Prognostic indicators in patients treated with long-term home oxygen therapy") same service.

Patients diagnosed with COPD and clinical stability (absence of exacerbation three months before the initial evaluation), who agreed with the research conditions, were included. The COPD diagnosis was realized according to the guidelines of the Global Initiative for Chronic Obstructive Lung Disease (GOLD).[4] Exclusion criteria were: other respiratory diseases, cancer and diagnosis for myocardial infarction four months before the start of the study.

As a routine of the service, in the first consultation, all patients are evaluated regarding demographic characteristics, medical diagnoses, indication and titration of oxygen and time of daily use. The flow is prescribed according to the oxygen titration at rest. In patients without severe hypoxemia at rest, but with effort desaturation, we indicated the use of oxygen therapy during efforts and at night 12h/day (Group G1/intermittent). Patients with severe hypoxemia, but who tolerate some period without oxygen supplementation, were prescribed 15 hours/day (Group G2). Patients with the worst clinical condition were prescribed 24 hours/day (Group G3).

After six months, patients were assessed for quality of life, anxiety and depression and dyspnea scores. Complete blood count, blood gas analysis and anthropometric evaluation were also collected. In addition, adherence to LTOT supplementation treatment is assessed. All patients were evaluated every six months for the maintenance of the LTOT indication, as well as their titration.

Pulse oximetry was obtained by a portable oximeter. Arterial gases were collected with the patient breathing room air. Spirometry was performed using a computerized system according to criteria established by the American Thoracic Society.[17] The forced expiratory volume in the first second (FEV_1), the forced vital capacity (FVC) and the FEV_1/FVC ratio were determined before and after the administration of inhaled salbutamol.

Clinical evaluation, height and weight were evaluated and measured by a stadiometer. The body mass index (BMI) was calculated applying the relationship between weight in kilograms (kg) and height in meters squared (m^2).

Quality of life was assessed by the Saint's George Respiratory Questionnaire (SGRQ), considering the total score, which corresponds to the sum of three domains: symptoms, impact and activity.[18] Dyspnea intensity was assessed by the Baseline Dyspnea Index (BDI) and also by the Modified Medical Research Council (MMRC) dyspnea index, which rank dyspnea in relation to the performance of day-to-day activities.[19,20] The hospital anxiety and depression scale (HADS) was used, consisting of seven items aimed at assessing anxiety (HADS-A) and seven for depression (HADS-D).[21]

Anemia was considered when women had hemoglobin <12 g/dL or hematocrit <35% and for men when hemoglobin <13 g/dL or hematocrit <40%.[22] We considered polycythemia when hematocrit> 55%.

Adherence to treatment was assessed during a medical consultation every six months throughout the follow-up. To consider adherence to the study protocol, data were considered after six months of using LTOT . Patients who adopted flow and number of hours according to medical prescription were considered adherent to the treatment. Adequate assessment of cause and date of death were assessed by medical records, family documents and the obituary system. This study was approved by the Research Ethics Committee of "Faculdade de Medicina de Botucatu" (60430116.2.0000.5411).

The comparative statistical analysis between continuous variables with normal distribution was expressed as mean values and standard deviation using the Student's t test. Mann-Whitney analysis was used to compare non-parametric continuous variables. For multiple group comparisons, ANOVA test followed by Tukey test was used. The proportions test was performed using the X^2 test. To assess adherence and survival time, a Kaplan Meier curve was used, followed by Log Rank Test analysis and a Cox proportional hazard multiple regression model was constructed to assess the clinical characteristics associated with follow-up time and mortality. The level of significance was 5%.

RESULTS

425 patient records were evaluated, 66 of whom were excluded with interstitial lung disease and 79 with pulmonary arterial hypertension.

From the 280 patients included, 26 missed follow-up. Table 1 shows the characteristics of the remaining 254 patients, of whom 124 (48.8%) died during the five-year follow-up. Both groups showed similar age, sex and active smoking status. Patients who died

Table 1. Patient characteristics, separated by life status at the end of the study.

	Survivors	Deaths	p
N= Number	130	124	
Gender (Female/Male)	74/56	59/65	0.17
Average follow-up time (days)	1377.4 ± 1051.8	1168.2 ± 989.8	0.10
Active smoking (%)	18 (13.8)	22 (17.7)	0.49
Age (years)	67.12 ± 9.94	68.4 ± 10.07	0.32
FEV_1 (L)	0.93 ± 0.31	0.98 ± 0.44	0.26
FEV_1 (%)	39.6 ± 13.1	42.7 ± 16.7	0.10
FVC (L)	1.89 ± 5.6	2.03 ± 0.74	0.08
FVC (%)	61.8 ± 16.6	68.7 ± 22.2	0.05
FEV_1/FVC	0.50 ± 0.09	0.48 ± 0.11	0.31
$PaCO_2$ (mmHg)	42.8 ± 6.8	42.4 ± 8.9	0.7
PaO_2 (mmHg)	56.2 ± 8.9	53.4 ± 9.9	0.02
SGRQ (%) Symptoms	49.35 ± 22.1	56.3 ± 21.9	0.031
Activity	64.22 ± 22.31	65.9 ± 23.7	0.59
Impact	37.8 ± 17.6	37.96 ± 20.2	0.95
Total	46.8 ± 18.9	51.7 ± 15.7	0.07
Anxiety	4.7 ± 4.1	6.11 ± 4.96	0.05
Depression	3.56 ± 4.02	5.6 ± 5.3	0.07
BDI	5.75 ± 2.7	4.38 ± 3.1	0.56
BMI (kg/m^2)	26.2 ± 6.4	24.08 ± 6.5	0.13
Ht (%)	45.8 ± 7.4	44.73 ± 6.9	0.32

FEV_1: forced expiratory volume in the first second; FVC: forced vital capacity; BMI: Body Mass Index; PaO_2: partial pressure of oxygen in arterial gas; $PaCO_2$: partial pressure of carbon dioxide in arterial gas; SGRQ: Saint George's Hospital Questionnaire on Respiratory Illness; Anxiety and Depression: values of the Hospital Anxiety and Depression Scale; BDI: Baseline Dyspnea Index; BMI: Body Mass Index; Ht: hematocrit. "Student t" test, level of significance: 5% ($p<0.05$).

had a worse baseline PaO_2 compared to survivors (53.4 ± 9.9 vs 56.2 ± 8.9mmHg, p=0.02). When we evaluated the SGRQ quality of life questionnaire, we observed a statistically significant difference in the score of the symptom domain, that is, those who died had greater impairment from symptoms compared to survivors (56.3 ± 21.9 vs 49.35 ± 22, 1%, p=0.03). The same statistical difference between the groups was not observed when assessed by the BDI dyspnea index (p=0.56). We also observed no difference between the groups for severity of spirometry, the mean values of hematocrit, BMI or the scores of anxiety and depression.

The average follow-up time was 2.8 years (1.14 - 4.8 years). Respiratory failure was the main cause of death (46.8%), followed by cardiovascular disease (12.1%), neoplasia (8.8%), and other causes (8%). The cause of death was not identified in 22.6%.

To assess adherence and mortality, those who did not have information about the prescription and those who were not using LTOT due to active smoking were excluded. Thus, 199 patients were separated between adherent and non-adherent in each LTOT prescription group (Table 2). The G1 group showed 27.16% non-adherent individuals, G2 26.66% and G3 25.86%, with no statistically significant difference between the adherent and non-adherent groups according to the type of LTOT prescription (p=0. 61). We did not identify any statistically significant difference when comparing the mortality rate in relation to the type of LTOT prescription (G1: 36.36%, G2: 56.14%, G3: 44.68%, p=0.07) (Table 2). When comparing the groups, we identified that the patients in the G3 group experienced greater impairment from airway obstruction, gas exchange and quality of life and more intense dyspnea (Table 2).

We did not identify statistically significant differences in age, BMI, PaO_2, $PaCO_2$, FEV_1, hematocrit, hemoglobin, quality of life, dyspnea index or patients' anxiety and depression in relation to adherence to LTOT (Table 3).

Regarding mortality after five years, among adherents, we observed 79 (54.86%) live patients and 65 (45.13%) deaths. Among non-adherents, 26 remaining alive (50.98%) and 25 (49.01%) deaths (p=0.75).

Regarding survival according to LTOT adherence, we found that there was no statistically significant difference between groups (Log Rank Test: p=0.80) (Figure 1).

We also did not identify any difference in mortality according to the type of LTOT prescription (Log Rank Test: p=0.22) (Figure 2).

When Cox multiple regression was analyzed, we identified that patients with a 24-hour LTOT indication had a higher risk of mortality over time when compared to those with a 12-hour indication (HR: 7.16; 95% CI: 1, 45-35.4). The variation in the depression score also presented a risk of mortality (HR: 1.35; 95% CI: 1.14-1.59) (Table 4).

Table 2. Relation between LTOT prescription and adherence, mortality and clinical characteristics.

Status	G1 (12h)	G2 (>15h)	G3 (24h)	p
Adherent (%)	59 (72.83)	44 (73.33)	43 (74.13)	0.61
Non-adherent (%)	22 (27.16)	16 (26.66)	15 (25.86)	
Alive (%)	49 (63.63)	25 (43.85)	26 (55.31)	0.07
Deaths (%)	28 (36.36)	32 (56.14)	21 (44.68)	
Age (y)	69.6 ± 9.2	67.4 ± 10.2	66.1 ± 11.9	0.25
PaO_2 (mmHg)	62.8 ± 5.7a	52.5 ± 7.4b	45.6 ± 6.9c	<0.001
$PaCO_2$ (mmHg)	40.0 ± 5.5a	42.4 ± 9.0a	45.8 ± 9.2b	<0.001
SpO_2	91.7 ± 3.7a	85.8 ± 6.7b	79.4 ± 8.3c	<0.01
FVC (L)	2.02 ± 0.69a	2.01 ± 0.58a	1.69 ± 0.50b	0.002
FVC (%)	65.7 ± 20.1	66.4 ± 18.7	60.6 ± 19.9	0.175
FEV_1 (L)	0.96 ± 0.39a	0.98 ± 0.37a	0.82 ± 0.27b	0.021
FEV_1 (%)	40.9 ± 15.6	41.0 ± 14.5	37.9 ± 14.0	0.382
FEV_1/FVC	0.47 ± 0.09	0.48 ± 0.10	0.49 ± 0.11	0.425
HT (%)	43.6 ± 7.1a	44.6 ± 5.9ab	46.9 ± 5.9b	0.027
HB (g/dL)	14.3 ± 1.9	14.7 ± 1.9	15.2 ± 1.9	0.049
Symptoms	46.5 ± 18.0	54.0 ± 22.9	60.4 ± 21.5	0.054
Activity	63.3 ± 20.5	67.0 ± 26.2	74.9 ± 16.2	0.122
Impact	34.6 ± 17.6a	38.8 ± 19.9ab	48.5 ± 16.8b	0.034
Total	45.7 ± 15.2a	49.4 ± 20.0ab	58.5 ± 16.1b	0.038
MMRC	1.88 ± 0.87a	2.29 ± 1.16ab	2.61 ± 1.03b	0.029
BDI	6.27 ± 2.2a	4.84 ± 2.54a	3.96 ± 2.71b	<0.001
Anxiety	4.95 ± 4.32	6.41 ± 4.94	4.85 ± 3.94	0.171
Depression	3.83 ± 4.63	5.43 ± 4.76	4.47 ± 4.72	0.152

G1: patients with a 12-hour oxygen prescription per day; G2: patients with a 15-hour oxygen prescription per day; G3: patients with a 24-hour oxygen prescription; PaO_2: partial pressure of oxygen in arterial gas; $PaCO_2$: partial pressure of carbon dioxide in arterial gas; SpO_2: pulse oximetry; FEV_1: forced expiratory volume in the first second; FVC: forced vital capacity; HT: hematocrit; HB: hemoglobin; MMRC: Modified Medical Research Council dyspnea index; BDI: Baseline Dyspnea Index. X^2 test to compare proportions. Significance level: 5% (p=0.05). For the comparison of the means between the groups, the ANOVA test was used, followed by the Tukey test for the pair comparisons. Different letters (a, b, c) mean statistically significant differences between the groups, with p<0.05.

Table 3. Adherence in relation to clinical characteristics.

	Adherent N=146	Non-adherent N=53	p
Age (years)	67.6 ± 10.6	67.4 ± 9.3	0.90
BMI (kg/m²)	24.7 ± 6.3	26.7 ± 6.6	0.05
PaO_2 (mmHg)	55.2 ± 9.6	53.3 ± 9.3	0.21
$PaCO_2$ (mmHg)	42.2 ± 7.8	43.8 ± 8.5	0.22
FEV_1 (L)	0.94 ± 0.36	1.01 ± 0.44	0.26
FEV_1 (%)	40.7 ± 14.4	42.6 ± 18.3	0.34
FVC (L)	1.92 ± 0.62	2.02 ± 0.74	0.36
FVC (%)	64.7 ± 18.8	2.02 ± 0.74	0.34
FEV_1/FVC	0.49 ± 0.11	0.49 ± 0.09	0.69
Hematocrit (%)	44.9 ± 6.8	46.0 ± 8.7	0.42
Hemoglobin (g/dL)	14.8 ± 2.2	14.8 ± 2.1	0.92
Total SGRQ (%)	48.0 ± 18.7	45.9 ± 16.1	0.53
Dyspnea - MMRC (0-4)	2.20 ± 1.2	2.0 ± 1.0	0.26
HADS-anxiety (0-21)	5.35 ± 4.4	5.21 ± 4.8	0.86
HADS-depression (0-21)	4.48 ± 4.8	3.34 ± 4.0	0.41

N= number of patients; BMI: Body Mass Index; PaO_2: partial pressure of oxygen; $PaCO_2$: partial pressure of carbon dioxide; FEV_1: forced expiratory volume in the first second; FVC: forced vital capacity; SGRQ: Saint George's Hospital Questionnaire on Respiratory Illness; MMRC: Modified Medical Research Council dyspnea index; HADS: Hospital Anxiety and Depression Scale. Student's "t" test, significance level: 5% (p<0.05).

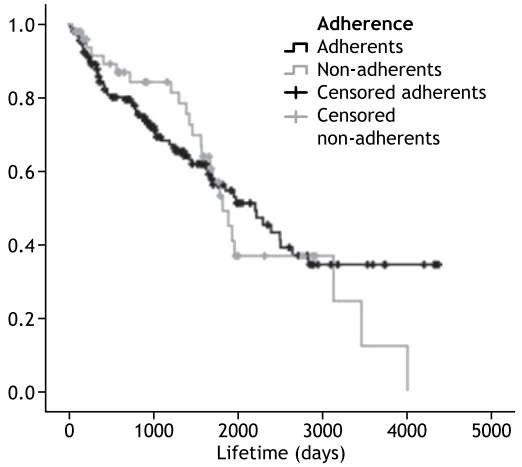

Figure 1. Kaplan Meier curve of survival time according LTOT adherence.

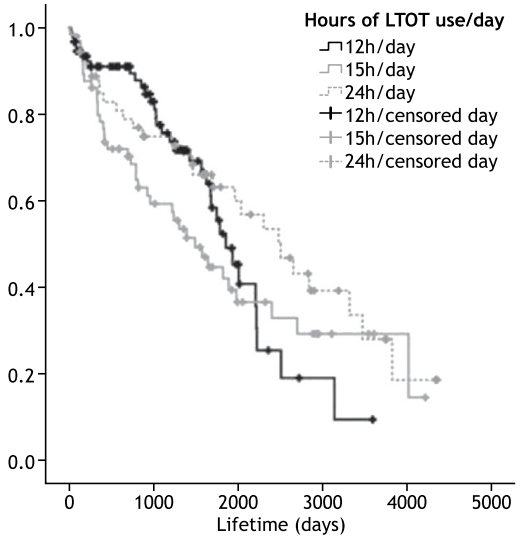

Figure 2. Kaplan Meier curve in survival time according to the type of LTOT prescription.

DISCUSSION

The findings of the present study show that adherence to LTOT was not associated with mortality, nor did we identify clinical differences between groups. Prescribing hours of LTOT use has also not been shown to be associated with LTOT adherence.

The adherence found in the present study was higher than that described in the scientific literature, which ranges from 31 to 70%.[9-11] This may be associated with our service offering multidisciplinary treatment for care of LTOT dependents, in addition to medical assistance, individualized guidance by social service professionals, nutritionist, physiotherapist and nurse and home visits. In fact, a recent study shows that the role of nurses in the management of LTOT is essential for the follow-up of these patients, showing the importance of multiprofessional care for patients who have multi-comorbidities in respiratory diseases.[23]

However, the method used to assess adherence to treatment is subjective because it does not directly assess how great the patient's adherence is. In a review article by Bourbeau and Bartlett[12] the interview was the most used means in studies to assess adherence in COPD patients, due to the ease of application. Other forms of assessment exist, such as electronic devices capable of measuring oxygen therapy, providing more reliable data, but they are expensive and subject to technical malfunction.[24]

We can speculate whether the modification of the pharmacological treatment of COPD over the past few years has not also changed survival of patients with hypoxemia, as adherence to oxygen therapy did not improve survival and also did not show better clinical characteristics in this sample. In this regard, we asked whether changes in survival in patients with hypoxemia and who are adherent to the LTOT treatment, can really benefit from the large studies of the 1980s of the last century. It is possible that adherence to drug treatments involving inhalation devices has a greater impact on survival even in those with hypoxemia.

Table 4. Analysis of regression of survival time and adherence and LTOT prescriptions by Cox regression model.

	p	HR	IC 95%
Age years)	0.19	1.03	0.98-1.09
BMI (kg/m²)	0.08	0.90	0.80-1.01
PaO2 (mmHg)	0.05	0.90	0.82-1.00
FEV_1 (L)	0.64	0.99	0.95-1.02
12h/day (reference)	--	--	--
15h/day	0.13	5.92	0.57-60.7
24h/day	0.01	7.16	1.44-35.4
Non-adherence	0.66	0.75	0.21-2.70
Total SGRQ	0.44	1.02	0.96-1.08
Hematocrit (%)	0.63	0.98	0.91-1.05
BDI	0.22	1.24	0.87-1.77
Depression	<0.001	1.34	1.14-1.59
Anxiety	0.09	0.85	0.71-1.02

BMI: Body Mass Index; PaO2: partial pressure of oxygen; FEV_1: forced expiratory volume in the first second; 12-24h/day: time in hours of oxygen therapy per day; SGRQ: Saint George's Hospital Questionnaire on Respiratory Illness; BDI: Baseline Dyspnea Index; Depression and Anxiety: scores on the Hospital Anxiety and Depression Scale; HR: Hazard Ratio; 95% CI: 95% confidence interval. Statistically significant difference of p values <0.05.

This assumption still needs to be confirmed by other clinical studies.

Although adherence is not related to the mortality rate, which was still high and in agreement with previous studies on the topic,[6,8,25] these very serious patients, who already have failure of the compensatory mechanisms responsible for adequate oxygenation, are at increased risk of mortality. In addition, the symptoms in these very severe patients show greater impact than those of lesser severity. The present study identified that the quality of life of patients who died, suffered greater impact due to symptoms, compared to those who survived, pointing to this parameter as a possible marker of worse prognosis. A Brazilian study with 118 patients showed that more intense dyspnea was related to mortality.[5] Another study with 142 patients with respiratory failure also showed that hypoxemia and dyspnea were determinants for the highest risk of mortality.[6] This finding points to the importance of a detailed assessment of the intensity of dyspnea and the impact of the disease on the patient's quality of life.

The presence of anxiety and depression can be associated with adherence or mortality,[26] but that was not observed in the present study. In addition, anxiety can influence the intensity of the sensation of dyspnea. A Turkish study evaluated 54 patients with COPD grade IV and use of LTOT, finding that 63% suffered major depression. Depression was proportionally more frequent in patients who did not adhere correctly to LTOT (90.6%) compared to adherents (22.7%). This suggests that depression can affect adherence to treatment and the prognosis of the disease.[26]

The other clinical parameters evaluated in the study were also not associated with adherence to LTOT. Similarly, a study by Hernandez et al.[11] demonstrated that there was no relationship between poor adherence and disease severity (blood gas analysis, spirometry or Charlson's comorbidity index). However, the same study identified characteristics associated with non-adherent patients: greater use of health services, less assessments of disease severity (lung function, symptoms and comorbidities), more physical activity, less dependence, less fragility and better quality of life. Another French study of 930 patients found that 31.9% of patients reduced the duration of oxygen use because they believed that the therapy was ineffective.[27]

Our study did not identify the influence of adherence to LTOT on mortality, but we found that patients who needed to use 24h/day had a higher risk of mortality when compared to those who use 12h/day. However, by comparing groups, we observed that patients who need 24h/day present more severe COPD, which is associated with a higher risk of mortality. In the scientific literature, a recent study by Ahmadi et al.[28] with 2,249 patients with severe COPD, found no difference between the use of 15 to 16 h/day compared to use for more than 15 h/day.

The present study has limitations such as a failure to assess hospitalizations and exacerbations that may have influenced adherence and, consequently, mortality. Thus, other studies that take into account the influence of these variables must be carried out. The patients' follow-up time was also short, and cannot be definitive for longer periods. We did not identify any great variation in quality of life between adherent and non-adherent groups, which demonstrates the need to increase the sample size so that we can in fact confirm the null hypothesis of the study.

In conclusion, the present study showed that adherence to LTOT and the type of prescription were not associated with mortality rates. The clinical characteristics of the patients were not associated with adherence to LTOT and a high mortality rate was identified in patients with COPD using LTOT in five years.

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REFERENCES

1. SBPT: Sociedade Brasileira de Pneumologia e Tisiologia. II Consenso Brasileiro sobre Doença Pulmonar Obstrutiva Crônica - DPOC - 2004: orientações terapêuticas de acordo com os estádios da DPOC. J Bras Pneumol. 2004;30:5-15.
2. NOTT: Nocturnal Oxygen Therapy Trial Group. Continuous or nocturnal oxygen therapy in hypoxemic chronic obstructive lung disease. Ann Intern Med. 1980;93(3):391-8. http://dx.doi.org/10.7326/0003-4819-93-3-391. PMid:6776858.
3. Medical Research Council (MRC). Long-term domiciliary oxygen therapy in chronic hypoxic cor pulmonale complicating chronic bronchitis and emphysema. Lancet. 1981;1(8222):681-6. PMid:6110912.
4. GOLD: Global Initiative for Chronic Obstructive Pulmonary Disease. Global strategy for diagnosis, management, and prevention of COPD, 2019 report [Internet]. Bethesda: GOLD; 2018 [cited 2019 Feb 5]. Available from: https://goldcopd.org/wp-content/uploads/2018/11/GOLD-2019-v1.7-FINAL-14Nov2018-WMS.pdf
5. Coleta KD, Silveira LVA, Lima DF, Rampinelli EA, Godoy I, Godoy I. Predictors of first-year survival in patients with advanced COPD treated using long-term oxygen therapy. Respir Med. 2008;102(4):512-8. http://dx.doi.org/10.1016/j.rmed.2007.12.003. PMid:18191558.
6. Lima DF, Coleta KD, Tanni SE, Silveira LVA, Godoy I, Godoy I. Potentially modifiable predictors of mortality in patients treated with long-term oxygen therapy. Respir Med. 2011;105(3):470-6. http://dx.doi.org/10.1016/j.rmed.2010.08.012. PMid:20846839.
7. Ringbaek TJ, Lange P. Trends in long-term oxygen therapy for COPD in Denmark from 2001 to 2010. Respir Med. 2014;108(3):511-6. http://dx.doi.org/10.1016/j.rmed.2013.10.025. PMid:24275146.
8. Machado MCL, Krishnan JA, Buist SA, Bilderback AL, Fazolo GP, Santarosa MG, et al. Sex differences in survival of oxygen-dependent patients with chronic obstructive pulmonary disease. Am J Respir Crit Care Med. 2006;174(5):524-9. http://dx.doi.org/10.1164/rccm.200507-1057OC. PMid:16778158.
9. Cullen DL. Long term oxygen therapy adherence and COPD: what we don't know. Chron Respir Dis. 2006;3(4):217-22. http://dx.doi.org/10.1177/1479972306070506. PMid:17190126.
10. Verduri A, Ballerin L, Simoni M, Cellini M, Vagnoni E, Roversi P, et al. Poor adherence to guidelines for long-term oxygen therapy (LTOT) in two Italian university hospitals. Intern Emerg Med. 2014;9(3):319-24. http://dx.doi.org/10.1007/s11739-012-0898-2. PMid:23329404.

11. Hernandez C, Aibar J, Batlle J, Cabrero DG, Soler N, Duran-tauleria E, et al. Assessment of health status and program performance in patients on long-term oxygen therapy. Respir Med. 2015;109(4):500-9. http://dx.doi.org/10.1016/j.rmed.2015.01.005. PMid:25771036.
12. Bourbeau J, Bartlett SJ. Patient adherence in COPD. Thorax. 2008;63(9):831-8. http://dx.doi.org/10.1136/thx.2007.086041. PMid:18728206.
13. Earnest MA. Explaining adherence to supplemental oxygen therapy. J Gen Intern Med. 2002;17(10):749-55. http://dx.doi.org/10.1046/j.1525-1497.2002.20218.x. PMid:12390550.
14. Neri M, Melani AS, Miorelli AM, Zanchetta D, Bertocco E, Cinti C, et al. Long-term oxygen therapy in chronic respiratory failure: A Multicenter Italian Study on Oxygen Therapy Adherence (MISOTA). Respir Med. 2006;100(5):795-806. http://dx.doi.org/10.1016/j.rmed.2005.09.018. PMid:16242926.
15. Cornford CS. Lay beliefs of patients using domiciliary oxygen: a qualitative study from general practice. Br J Gen Pract. 2000;50(459):791-3. PMid:11127167.
16. Katsenos S, Constantopoulos SH. Long-Term Oxygen Therapy in COPD: factors affecting and ways of improving patient compliance. Pulm Med. 2011;2011:325362. http://dx.doi.org/10.1155/2011/325362. PMid:21941649.
17. Miller MR, Hankinson J, Brusasco V, Burgos F, Casaburi R, Coates A, et al. Standardisation of spirometry. Eur Respir J. 2005;26(2):319-38. http://dx.doi.org/10.1183/09031936.05.00034805. PMid:16055882.
18. Souza TC, Jardim JR, Jones P. Validação do questionário do Hospital Saint George na Doença respiratória (SGRQ) em pacientes portadores de doença pulmonar obstrutiva crônica no Brasil. J Pneumol. 2000;26(3):119-28. http://dx.doi.org/10.1590/S0102-35862000000300004.
19. Mahler DA, Weinberg DH, Wells CK, Feinstein AR. The measurement of dyspnea: contents, interobserver agreement, and physiologic correlates of two new clinical indexes. Chest. 1984;85(6):751-8. http://dx.doi.org/10.1378/chest.85.6.751. PMid:6723384.
20. Kovelis D, Segretti NO, Probst VS, Lareau SC, Brunetto AF, Pitta F. Validation of the Modified Pulmonary Functional Status and Dyspnea Questionnaire and the Medical Research Council scale for use in Brazilian patients with chronic obstructive pulmonary disease. J Bras Pneumol. 2008;34(12):1008-18. http://dx.doi.org/10.1590/S1806-37132008001200005. PMid:19180335.
21. Bratås O, Gronning K, Forbord T. Psychometric properties of the hospital anxiety and depression scale and the general health questionnaire-20 in COPD inpatients. Scand J Caring Sci. 2014;28(2):413-20. http://dx.doi.org/10.1111/scs.12054. PMid:23713548.
22. Lee RG, Bitchell TC, Foerster J, Athens JW, Lukens J. Wintrobe: hematologia clinica. 9th ed. São Paulo: Manole; 1998.
23. Ekström M, Ahmadi Z, Larsson H, Nilsson T, Wahlberg J, Ström KE, et al. A nationwide structure for valid long-term oxygen therapy: 29-year prospective data in Sweden. International Journal of COPD. 2017;12:3159-69. http://dx.doi.org/10.2147/COPD.S140264. PMid:29133978.
24. Albert RK, Au DH, Blackford AL, Casaburi R, Cooper JA Jr, Criner GJ, et al. A randomized trial of long-term oxygen for COPD with moderate desaturation. N Engl J Med. 2016;375(17):1617-27. http://dx.doi.org/10.1056/NEJMoa1604344. PMid:27783918.
25. Ahmadi Z, Bornefalk-Hermansson A, Franklin KA, Midgren B, Ekström MP. Hypo- and hypercapnia predict mortality in oxygen-dependent chronic obstructive pulmonary disease: a population-based prospective study. Respir Res. 2014;15(1):30. http://dx.doi.org/10.1186/1465-9921-15-30. PMid:24625018.
26. Kayhan F, Ilik F, Karamanli H, Pazarli AC, Kayhan A. Major depression in long-term oxygentherapy dependent Chronic Obstructive Pulmonary Disease. Perspect Psychiatr Care. 2018;54(1):6-10. http://dx.doi.org/10.1111/ppc.12169. PMid:27220917.
27. Pépin JL, Barjhoux CE, Deschaux C, Brambilla C. Long-term oxygen therapy at home: compliance with medical prescription and effective use of therapy. Chest. 1996;109(5):1144-50. http://dx.doi.org/10.1378/chest.109.5.1144. PMid:8625658.
28. Ahmadi Z, Sundh J, Bornefalk-Hermansson A, Ekström M. Long-term oxygen therapy 24 vs 15 h/day and mortality in chronic obstructive pulmonary disease. PLoS One. 2016;11(9):e0163293. http://dx.doi.org/10.1371/journal.pone.0163293. PMid:27649490.