Original Article

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Patient adherence and outcomes under long-term oxygen therapy: A multicenter study

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Abstract:

BACKGROUND AND AIM: Long-term oxygen therapy (LTOT) improves survival and outcomes in chronic respiratory failure. This multicenter study assesses the factors affecting adherence in patients undergoing long-term oxygen therapy and evaluates its impact on the frequency of hospital visits.

METHODS: Clinical and demographic data of patients receiving LTOT who were admitted to the study centers between January 1 and June 30, 2024, were recorded. Patients who adhered to LTOT for ≥15 hours per day, including both daytime and nighttime use, were classified as fully adherent. Data from adherent patients were compared with those of non-adherent patients. Factors affecting LTOT adherence were determined using logistic regression analysis.

RESULTS: Among the 374 patients who met the inclusion criteria, 40.6% were classified as adherent to LTOT. Emergency room visits (median: 3/year) and hospital admissions (median: 1/year) were more frequent among LTOT-adherent patients over the past year. Regression analysis identified a body mass index (BMI) <25 kg/m^2 and type 2 respiratory failure as independent predictors of LTOT adherence. Among patients with type 2 respiratory failure, those with a BMI <25 kg/m^2 were found to be more likely to adhere to LTOT, with a specificity of 74.1% and a sensitivity of 44.9%. A reduction in the frequency of emergency room visits was observed in the group that adhered to LTOT for one year.

CONCLUSIONS: A BMI <25 kg/m^2 and type 2 respiratory failure can predict adherence to LTOT.

Keywords:

Long-term oxygen therapy, hospital visits, treatment adherence

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Introduction

Long-term oxygen therapy (LTOT) using oxygen concentrators is the standard approach for patients with chronic respiratory failure. The efficacy of LTOT in improving survival has been proven in cases of chronic hypoxemia (PaO_2 <55 mmHg or PaO_2 in the 56–59 mmHg range with hematocrit >55% or the presence of cor pulmonale symptoms).[1] The rationale behind this treatment is based on two studies conducted in the 1980s that demonstrated improved survival in patients receiving LTOT.[2,3] There is also evidence that LTOT has beneficial effects on depression, cognitive function, and exercise capacity.[4–6] Furthermore, it has been well established that LTOT reduces hospitalization frequency in such patients.[7] Adherence to treatment is crucial for achieving these favorable outcomes, yet despite the high costs involved, adherence to LTOT remains low.[8,9]

This multicenter study evaluates the benefits of adherence and identifies the factors influencing adherence in patients undergoing LTOT. As a secondary purpose, the study examines the impact of LTOT on hospital admissions based on a comparison of emergency room visits, hospitalizations, and intensive care unit admissions in the years before and after initiation of treatment.

Materials and Methods

All patients undergoing LTOT for at least one year in the pulmonary diseases department or outpatient clinic at the ten participating centers between January 1 and June 30, 2024, who provided informed consent for participation, were included in the study. Clinical and demographic data were recorded, including diagnosis, type of respiratory failure, arterial blood gas values, comorbidities, body mass index, smoking history, biomass and asbestos exposure, place of residence, source of LTOT supply, educational status, duration of LTOT use, reasons for non-use, and device maintenance history. In addition, the number of emergency room visits, hospital admissions, and intensive care unit admissions due to respiratory problems in the years before and after LTOT initiation were documented. Comorbidity scores were calculated using the Modified Charlson Comorbidity Index.[10] Patients were asked about their daily and weekly LTOT use, as well as their use of LTOT during nighttime sleep and daily activities, to assess adherence. Those who adhered to LTOT for ≥15 hours per day, including both daytime and nighttime use, were classified as fully adherent. Data from the adherent group were compared with those of the non-adherent group using appropriate statistical analyses. The study was approved by the Atatürk Sanatorium Training and Research Hospital Clinical Research Ethics Committee (Approval Number: 2012-KAEK-15/2842, Date: 22.11.2023) and conducted in accordance with the principles of the Declaration of Helsinki. No generative artificial intelligence was used in the writing of this article.

Statistical method

Statistical analyses were conducted using IBM SPSS Statistics for Windows (Version 21.0, Armonk, NY: IBM Corp.). The conformity of variables to a normal distribution was evaluated using both visual and analytical methods. Variables were considered normally distributed if they showed visual conformity in histograms and probability plots and had a p-value >0.05 in the Kolmogorov-Smirnov test. Descriptive statistics for normally distributed variables were presented as mean±standard deviation (SD). Differences in mean values between groups were evaluated using Student's t-test. Descriptive statistics for variables that did not conform to a normal distribution were presented as median (25^{th}–75^{th} percentile) and interquartile range (IQR), while nominal variables were expressed as numbers and percentages (%). A Mann-Whitney U test was used to evaluate differences in median values. Nominal variables were analyzed using Pearson's Chi-square test or Fisher's exact test, and dependent variables using the Wilcoxon test.

Along with age and sex, variables with a p-value ≤0.25 in the univariate tests were further analyzed using logistic regression to assess their impact on LTOT adherence. Among highly correlated variables, only one was included in the model. Model fit was assessed with the Hosmer-Lemeshow test. Receiver Operating Characteristic (ROC) curve analysis was conducted to identify a significant cutoff value for Body Mass Index (BMI) in predicting LTOT adherence in patients with type 2 respiratory failure. A p-value <0.05 was considered statistically significant.

Results

Of the 442 patients who consented to participate in the study, 35 were excluded due to an LTOT usage duration of less than one year, 20 due to insufficient data, and 13

Table 1: Comparison of demographic, sociocultural, and clinical characteristics according to long-term oxygen therapy (LTOT) adherence

	LTOT-adherent (n=152) median (25th-75th percentile)		LTOT-non-adherent (n=222) median (25th-75th percentile)		p
	%	n	%	n	
Age	69 (60.3–76)		70 (63–76)	0.193	
Gender (male, %)	63.8	97	58.1	129	0.268
Smoking History (never smoker, %)	27	41	34.7	77	0.115
Smoking (pack-years)	45 (30–70)		50 (28.8–60)		0.528
Time since smoking cessation (years)	7.5 (3.6–14.5)		9 (3–18)		0.605
Modified charlson comorbidity index (CCI) score	4 (3–6)		5 (4–6)		0.059
Biomass exposure	36.8	56	37.8	84	0.845
Asbestos exposure	15.8	24	18.9	42	0.436
Living alone (%)	6.6	10	6.3	14	0.916
Device supplied by social security institution (SSI)	75	114	78.4	174	0.446
Education level					0.568
Illiterate	17.1	26	21.2	47	
Primary School	65.1	99	63.6	141	
≥High School	17.8	27	15.3	34	
BMI (kg/m^2)	25.7 (21–29.9)		26.7 (23–32.6)		**0.015**
Type 2 respiratory failure	64.9 (98)		53.6 (118)		**0.031**
pH	7.4 (7.37–7.44)		7.40 (7.38–7.45)		0.188
pO_2 (mmHg)	47.8 (41.7–52.2)		47.5 (41.3–52.2)		0.714
SpO_2	82.7 (72.2–86.3)		82 (75.6–85.6)		0.980
pCO_2 (mmHg)	50.6 (41–59)		45.9 (40.1–53.2)		**0.018**
NIMV usage	8.6	13	5.4	12	0.231
Device usage during daily life activities	69.7	106	23	51	**<0.001**
Long cannula use	55.9	85	29.7	66	**<0.001**
Regular device maintenance	70.4	107	49.5	110	**<0.001**

CI: Comorbidity index, pO_2: Partial oxygen pressure, pCO_2: Partial carbon dioxide pressure, SSI: Social security institution, NIMV: Non-invasive mechanical ventilation

who had been prescribed nighttime use only for obstructive sleep apnea syndrome (OSAS). Among the remaining 374 patients, the most common indication for prescription was chronic obstructive pulmonary disease (COPD) (80%). Only 40.6% (n=152) of the patients reported full adherence to LTOT treatment. The median daily LTOT usage was 20 hours in adherent patients compared with six hours in non-adherent patients. The majority of non-adherent patients reported that they neither felt the need to use an oxygen concentrator (55.1%) nor perceived a benefit from it (19.8%), while associated noise, headaches, nasal issues, billing costs, and power outages were reported less frequently. Body mass index was lower in the LTOT-adherent group, while rates of type 2 respiratory failure, regular device maintenance, device usage during daily activities, and pCO_2 levels at diagnosis were higher (Table 1). The prescription rate for home non-invasive mechanical ventilation and the prevalence of comorbidities between the two groups was found to be statistically comparable (Table 1, 2). LTOT-adherent patients reported more frequent emergency room visits (median: 3/year) and hospital admissions (median: 1/year) in the previous year, while in the year following the initiation of

Table 2: Distribution of comorbidities

	LTOT-adherent (n=152) 40.6%		LTOT-non-adherent (n=222) 59.4%		p
	%	n	%	n	
CAD	29.6	45	30.2	67	0.905
CHF	19.7	30	24.8	55	0.253
Hypertension	24.1	67	45.1	102	0.722
Diabetes mellitus	27	41	28.8	64	0.695
Lung cancer	5.3	8	6.8	15	0.555
Extrapulmonary cancer	5.9	9	4.5	10	0.540
PTE	3.3	5	4.1	9	0.702
Bronchiectasis	3.3	5	3.2	7	1.000
BPH	3.3	5	2.3	5	0.536
OSAS	3.3	5	3.2	7	1.000
CRF	1.3	2	4.5	10	0.133
Neurological disorder[1]	7.2	11	4.5	10	0.260
Psychiatric disorder[2]	2	3	0.9	2	0.400
Rheumatologic disorder[3]	0.7	1	3.6	8	0.089
COPD	79.6	121	80.2	178	0.892
Asthma	6.6	10	7.2	16	0.814
ILD	7.9	12	5.9	13	0.438
OHS	0.7	1	0.9	2	1.000

[1]: Parkinson's disease, cerebrovascular disease (CVD), dementia, and epilepsy, [2]: Anxiety disorder and depression, [3]: Rheumatoid arthritis (RA) and vasculitis. BPH: Benign prostatic hyperplasia, CRF: Chronic renal failure, CAD: Coronary artery disease, CHF: Congestive heart failure, COPD: Chronic obstructive pulmonary disease, ILD: Interstitial lung disease, OHS: Obesity hypoventilation syndrome, OSA: Obstructive sleep apnea syndrome, PTE: Pulmonary thromboembolism

Table 3: Distribution of hospital visits according to long-term oxygen therapy (LTOT) adherence

	LTOT-adherent (n=152) median	Mean	LTOT-non-adherent (n=222) median	Mean	p
1 year before LTOT					
Emergency room	3 (1–5)	4.7	2 (1–4)	3.0	0.007
Ward	1 (1–2)	1.9	1 (0–2)	1.3	0.039
ICU	0 (0–1)	0.4	0 (0–1)	0.3	0.461
1 year after LTOT					
Emergency room	2 (0–4)	3.7	2 (0–3)	2.5	0.150
Ward	1 (0–2)	1.9	0 (0–1)	0.9	<0.001
ICU	0 (0–1)	0.5	0 (0–0)	0.2	<0.001

ICU: Intensive care unit

Table 4: Comparison of changes in hospital visits following long-term oxygen therapy (LTOT) usage

	1 year before LTOT	1 year after LTOT	p
Total			
ER	3.68±4.8	2.99±4.4	<0.001
Ward	1.60±2.2	1.30±2.2	<0.001
ICU	0.35±0.72	0.32±0.68	0.511
Adherent			
ER	4.65±5.9	3.66±5.4	<0.001
Ward	1.99±2.8	1.90±2.8	0.174
ICU	0.41±0.9	0.47±0.8	0.379
Non-adherent			
ER	3.02±3.8	2.54±3.4	0.002
Ward	1.33±1.5	0.90±1.4	<0.001
ICU	0.31±0.6	0.22±0.6	0.059

ER: Emergency room, ICU: Intensive care unit

Table 5: Evaluation of factors influencing long-term oxygen therapy (LTOT) adherence using logistic regression analysis

	Variables in the Equation				
	B	Sig.	Exp(B)	95% CI for Exp(B)	
				Lower	Upper
Age	-0.009	0.349	0.991	0.972	1.010
Gender (female vs. male)	-0.004	0.986	0.996	0.621	1.597
Chronic kidney disease	-0.975	0.225	0.377	0.078	1.824
Body mass index	-0.043	0.014	0.958	0.926	0.991
Respiratory failure (Type 1 vs. Type 2)	0.543	0.019	1.721	1.095	2.703
Number of emergency room visits in the last year before LTOT initiation	0.052	0.136	1.053	0.984	1.128
Number of hospital admissions in the last year before LTOT initiation	0.054	0.507	1.056	0.899	1.240

B: Regression coefficient, Sig.: Significance level of regression coefficient, CI: Confidence interval

LTOT, the non-adherent group had lower hospital (median: 0.9/year vs. 1.9/year) and ICU admission rates (median: 0.2/year vs. 0.5/year) than the adherent group (Table 3). A comparison of hospital visits after the initiation of LTOT revealed a reduction in emergency room visits in the adherent group, while the non-adherent group exhibited a statistically significant decrease in both emergency room visits and hospital admissions (Table 4). A logistic regression analysis identified low BMI and the presence of type 2 respiratory failure as independent factors associated with LTOT adherence (Table 5), while ROC curve analysis demonstrated that BMI had diagnostic value in predicting LTOT adherence among patients with type 2 respiratory failure (area under the curve [AUC]: 0.63, 95% confidence interval [CI]: 0.56–0.71, p=0.001). Using a cut-off value of 25 kg/m^2, BMI predicted LTOT adherence with a specificity of 74.1% and a sensitivity of 44.9%. In patients with type 2 respiratory failure and a BMI <25 kg/m^2, LTOT adherence could be determined with a positive predictive value of 59.5% and a negative predictive value of 61.4% [Fig. 1].

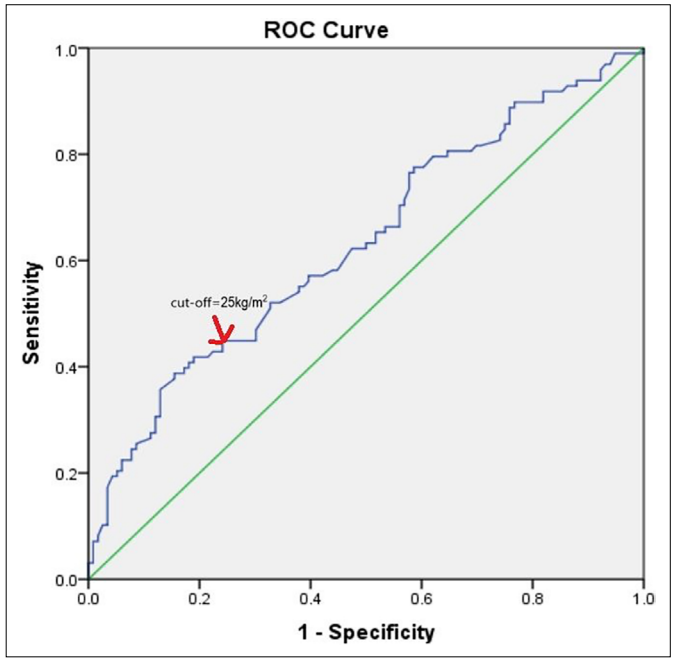

Figure 1: Receiver operating characteristic (ROC) curve analysis: The cut-off value for body mass index in predicting treatment adherence was set at 25 kg/m^2

Discussion

In the present study, while LTOT was associated with a reduction in emergency visits, no significant differences were observed in hospital or ICU admissions among adherent patients. Furthermore, LTOT adherence was found to be associated with low BMI and type 2 respiratory failure rather than comorbidities or sociodemographic characteristics. In patients with type 2 respiratory failure and a BMI <25 kg/m^2, LTOT adherence could be predicted with a specificity of 74.1% and a sensitivity of 44.9%.

In addition to increased survival, LTOT has been associated with positive outcomes in exercise capacity, cognitive function, hospitalization frequency, sleep quality, depression, and overall quality of life.[2,3,11] LTOT has also been shown to lower hematocrit levels in secondary polycythemia and reduce the progression of pulmonary hypertension.[12,13] It is reported that 1,500–2,000 oxygen concentrators are prescribed annually in our country.[8] In the present study, COPD was the most common indication for LTOT prescription, accounting for 80% of cases. According to both local and global data, COPD ranks first among the indications for LTOT initiation, with a prevalence ranging from 71% to 87%.[14–17]

The effectiveness of LTOT in achieving positive outcomes relies on treatment adherence, therapy duration, and the correction of hypoxemia. In a study by Kurtar et al.[14] examining 220 patients in Türkiye, adherence to LTOT was reported to be 29%. Treatment adherence has been reported in the range of 17–70% in different studies.[11,14] In the present study, only 40.6% of patients prescribed an oxygen concentrator were found to adhere to their treatment regimens, with approximately 75% of non-adherent patients reporting either no further need for treatment or a lack of perceived benefit from it. Kurtar et al.[14] also reported that the primary reason for ineffective use was a perceived lack of necessity. The medical necessity of LTOT should be reassessed in certain patient groups to optimize resource utilization.

In the present study, a BMI below 25 kg/m^2 and the presence of type 2 respiratory failure were identified as independent factors influencing LTOT adherence. LTOT adherence is affected not only by disease characteristics (such as severity and treatment complexity) but also by the demographic and cognitive status of the patient and their family.[11] Misconceptions that long-term treatment may cause dependency or reduce effectiveness, along with fear of social stigma, also contribute to lower treatment adherence.[9] Several studies have also reported that increased disease severity and airway obstruction, along with decreased oxygenation, are associated with better adherence to oxygen therapy.[14,15,18,19] Although age, sex, education level, and social status have been shown to influence adherence,[8] the present study found no significant impact of these factors on treatment adherence. Evidence suggests that the determinants of LTOT non-adherence include advanced age, male sex, low health literacy, misinterpretation of treatment recommendations, lack of communication, advanced-stage COPD, high PaO_2 levels in room air, active smoking, poor functional status, and side effects associated with oxygen therapy.[9,20] The results of the present study indicate that LTOT adherence can be predicted with 74.1% specificity in patients with type 2 respiratory failure and a BMI <25 kg/m^2. The authors of the present study therefore believe that patients with type 1 respiratory failure and those with type 2 respiratory failure with a BMI ≥25 kg/m^2 should be more closely monitored for LTOT adherence.

Previous reports indicate that hospitalization frequency is significantly reduced in COPD patients who adhere to LTOT regimens.[7] However, in the present study, non-adherent patients with a median daily usage of six hours on the provided oxygen concentrator had lower hospital and intensive care unit (ICU) admission rates than the adherent group, along with a statistically significant reduction in emergency room visits and hospital admissions. It is thought that the need for oxygen concentrators among non-adherent patients may have diminished over the short term. In addition to a placebo effect, prescribing LTOT may have increased patients' understanding of the severity of their disease, their compliance with other treatments, and their ability to cope with the disease and its exacerbations. No assessment of patients' adherence to pharmacological therapies or their access to non-pharmacological treatments, such as pulmonary rehabilitation and vaccinations, was made in the present study, which can be considered a limitation. Relying on self-reported data for the measurement of device adherence may also be considered a limitation. However, the difference in median usage between the study and control groups is large enough (20 hours vs. 6 hours) to indicate correct patient categorization. In the present study, compliance with the regular device maintenance requirements was significantly higher in the adherent group than in the non-adherent group (70.4% vs. 49.5%, p<0.001). In the study by Atiş et al.,[8] regular technical support was provided to

75% of patients, while in the study by Kurtar et al.,[14] the rate of patients who received maintenance conducted by the medical device company was reported as 16%.

In conclusion, the low rate of regular device maintenance among non-adherent patients can increase the risk of device-related infections in this group. A BMI below 25 kg/m^2 and type 2 respiratory failure can predict the adherence of patients to their LTOT regimens, and the presence of type 2 respiratory failure should be considered when predicting LTOT adherence. The authors believe that patients prescribed oxygen concentrators should be periodically screened for their ongoing need of LTOT to optimize resource utilization. Such follow-ups could be organized through home healthcare services and/or telemedicine programs.[21,22]

Ethics Committee Approval

The study was approved by the Atatürk Sanatorium Training and Research Hospital Clinical Research Ethics Committee (No: 2012-KAEK-15/2842, Date: 22/11/2023).

Informed Consent

Written informed consent was obtained from the patients.

Conflicts of Interest

The authors have no conflicts of interest to declare.

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Author Contributions

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