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Continuous Oxygen Use in Nonhypoxemic Emphysema Patients Identifies a High-Risk Subset of Patients:

Retrospective Analysis of the National Emphysema Treatment Trial

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Abstract

Background: Continuous oxygen therapy is not recommended for emphysema patients who are not hypoxemic at rest, although it is often prescribed. Little is known regarding the clinical characteristics and survival of nonhypoxemic emphysema patients using continuous oxygen. Analysis of data from the National Emphysema Treatment Trial (NETT) offers insight into this population.

Methods: We analyzed demographic and clinical characteristics of 1,215 participants of NETT, stratifying by resting Pao_2 and reported oxygen use. Eight-year survival was evaluated in individuals randomized to medical therapy.

Results: At enrollment, 33.8% (n = 260) of participants nonhypoxemic at rest reported continuous oxygen use. When compared to nonhypoxemic individuals not using oxygen (n = 226), those using continuous oxygen had worse dyspnea, lower quality of life, more frequent exercise desaturation, and higher case-fatality rate. After adjusting for age, body mass index, and FEV, percentage of predicted, the presence of exercise desaturation accounted for the differential mortality seen between these group.

Conclusions: In the NETT, the use of continuous oxygen in resting nonhypoxemic emphysema patients was associated with worse disease severity and survival. The differential survival observed could nearly all be accounted for by the higher prevalence of exercise desaturation in those using

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[†]A list of participants is given in the Appendix.

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continuous oxygen, suggesting that it is not a harmful effect of oxygen therapy contributing to mortality. It remains unclear whether continuous oxygen therapy improves survival in normoxic patients with exercise desaturation.

Trial registration: Clinicaltrials.gov Identifier: NCT00000606.

Keywords

guideline adherence; pulmonary disease; chronic obstructive; supplemental oxygen

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COPD remains a major public health issue, rdnking fourth in the United States as a cause of death, with a total estimated cost of $32.1 billion in 2002.[1,2] The substantial impact of this disease on health-care cost and delivery within the United States and worldwide has stimulated development of international guidelines for the diagnosis and management of COPD.[3–5] With the exception of smoking cessation, continuous oxygen therapy, and possibly some pharmacologic regimens, few interventions have been shown to improve mortality in patients with COPD.[6–7] The Nocturnal Oxygen Therapy Trial (NOTT) and report of the Medical Research Council Working Party (MRC) evaluated long-term domiciliary oxygen therapy in patients with COPD and severe resting hypoxemia.[8,9] These studies showed that continuous oxygen therapy increased survival and improved quality of life. Based primarily on the findings of the NOTT and MRC, current guidelines recommend oxygen therapy for some patients with COPD, although spec& recommendations vary among different organizations (Table 1).

While the NOTT and MRC established the role of continuous oxygen therapy in patients with severe hypoxemia, few studies have evaluated continuous oxygen therapy in COPD patients with mild-to-moderate degrees of hypoxemia. Continuous oxygen therapy in this population has been shown to reduce the observed decline in exercise endurance but not impact survival.[10–12] It remains unclear as to the potential benefit or harm of continuous oxygen use in nonhypoxemic emphysema patients. Most guidelines do not recommend continuous oxygen therapy for patients with resting and exertional Pao_2 > 60 mm Hg (Table 1). Given the cost of therapy for COPD, it is important to understand the factors driving the use of continuous oxygen therapy in different populations of COPD patients and whether oxygen use affects survival. The National Emphysema Treatment Trial (NETT) provides an ideal data set to explore these issues. In this study, patients with severe emphysema were randomized to medical therapy or medical therapy plus lung volume reduction surgery.[13] Extensive baseline demographic and clinical measurements were collected, including resting Pao_2 and current oxygen use by self-report. Analysis of this study population provides insight into the characteristics of individuals with differing degrees of hypoxemia using continuous oxygen, and the potential effects of continuous oxygen in these individuals.

Our overall goal was to explore the relationship between mortality and use of oxygen in patients who did not meet conventional criteria. Therefore, in this study we address the following questions: Is there a survival difference in nonhypoxemic participants based on self-reported oxygen use pattern? Do clinical characteristics and survival differences exist based on self-reported oxygen use in participants exhibiting only exercise desaturation? How closely does self-reported oxygen use by NETT Participants follow current guidelines? How do the demographic and clinical characteristics of patients with resting Pao_2 > 60 mm Hg prescribed continuous oxygen compare to those reporting no oxygen use?

Materials and Methods

Patient Selection

Data for this study were extracted from the initial and follow-up data of patients enrolled in the NETT. The design and methods of the NETT are published elsewhere.[14] Briefly, former smokers with severe emphysema who were deemed to be candidates for lung volume reduction surgery were enrolled in 6 to 10 weeks of pulmonary rehabilitation. Oxygen therapy, when necessary, was prescribed by the rehabilitation center or primary care physician. After rehabilitation, the treatment plan including oxygen prescription was approved, by a NETT physician. Baseline measurements were obtained within 2 weeks of completing pulmonary rehabilitation but prior to randomization in the study. These measurements included resting room air arterial blood gas analysis and oxygen use by self-report. Three separate exercise tests were performed. A treadmill exercise test with pulse oximetry, performed by walking on a treadmill at one mile per hour for 3 min and then two to three miles per hour for 4 min, was used to test for exercise desaturation. Exercise desaturation was defined as oxygen saturation by pulse oximetry (Spo_2) < 90% at any point during this test. A 6-inin walk test on supplemental oxygen (if needed based on treadmill walking) was conducted. Finally, a graded maximal cycle ergometry on 30% oxygen was performed to determine maximum exercise capacity. Short-acting bronchodilators were used at least 15 min and no more than 4 h before testing of oxygen desaturation. In order to assess severity and persistence of resting room air desaturation, two criteria were used. In the first S min of a resting period, desaturation was defined as presence of room air $Spo_2 \leq$ 85% at any time. After 5 min of rest, desaturation was considered to be present if the Spo_2 was < 90%. Self-administered questionnaires were used to assess disease-specific quality of life (St. George Respiratory Questionnaire [SGRQ]), general health-related quality of life (Quality of Well-Being Score [QWB]), and dyspnea (University of California San Diego Shortness of Breath Questionnaire [UCSD-SOBQ]). Eligible patients were then randomized to medical therapy or medical therapy plus lung volume reduction surgery. Each patient's medical management was reviewed on an annual basis by one of the NETT pulmonologists and recommendations made to the treating physician based on American Thoracic Society guidelines. However, there was no requirement that changes he made consistent with these recommendations. The NETT study protocol was approved by local institutional review boards, and all patients provided informed consent.

Data Analysis

Of the 1,218 participants enrolled in the NETT, 3 patients were excluded from this data analysis because of missing baseline Pao_2 measurements. For the purpose of this report, normoxia was defined as Pao_2 > 60 mm Hg. For analysis, subjects were categorized based on postrehabilitation resting room air Pao_2 and reported oxygen use at baseline postrehabilitation assessment. Because of the heterogeneous indications, usage patterns, and lack of detailed information about oxygen use duration in the participants (n = 283) using oxygen intermittently (rest, sleep, or exertion, but not all three), we evaluated their survival but otherwise did not include them in the analysis. Participants randomized to medical therapy were followed up for vital status until August 31, 2006, 8 years after trial initiation (n = 394). In order to avoid the confounding effect of lung volume reduction surgery, we did not include patients randomized to surgical therapy when evaluating survival. Clinical and demographic characteristics between groups were compared using *t* tests for continuous variables and Fisher exact tests for categorical variables. Kaplan-Meier curves were generated and compared for those individuals randomized to medical therapy, classified into two groups: resting $Pao_2 > 60$ mm Hg using continuous oxygen and $Pao_2 > 60$ mm Hg not using oxygen. A modified BODE (body mass index [BMI], obstruction, dyspnea; exercise capacity) [mBODE] score was calculated using the formula of Martinez et al.[15] Because of multiple comparison, a p value of 0.01 was used to determine significance among groups treated with different oxygen therapies. Cox proportional hazard models were used to test for survival differences between groups, adjusting for known predictors of mortality (age, BMI, FEV_1 percentage of predicted). Additional models included adjustment for exercise desaturation on 6-min walk test. All analyses were performed using statistical software (SAS version 9.1; SAS Institute; Cay, NC; and freeware R version 2.3.1; R Foundation for Statistical Computing; Vienna, Austria).

Results

Oxygen Use at Enrollment

At enrollment, 769 of the 1,215 participants had a resting baseline room air $Pao_2 > 60$ mm Hg (Table 2). Of these, 33.8% reported continuous oxygen use, while 29.4% reported no oxygen use. The remaining 283 participants (36.8%) reported oxygen use for either rest, exercise, or sleep, but not all three (intermittent use). Resting baseline room Pao_2 values (mean ± SD) for the three groups were 67.9 ± 6.5 mm Hg (continuous use), 70.3 ± 6.7 mm Hg (intermittent use), and 73.5 ± 7.8 mm Hg (no oxygen use); $p < 0.0001$ between groups (Kruskal Wallis test).

Baseline Demographics and Clinical Characteristics

We compared demographic and clinical characteristics of normoxic individuals using continuous oxygen to those not using oxygen (Table 3). Those using continuous oxygen had more advanced disease as evidenced by lower FEV_1, FEV_1 percentage of predicted, FVC, 6-min walk distance, and ergometry exercise. They also had worse dyspnea, lower quality of life, higher mBODE scores, and more frequent exercise desaturation. The continuous oxygen group was slightly younger with a higher BMI, prognostic variables generally considered favorable in COPD.

Survival in Participants Enrolled in the Medical Therapy Arm

Limiting the analysis to participants randomized to medical therapy, we compared survival in normoxic participants using continuous oxygen normoxic participants not using oxygen (Fig 1). The case-fatality rate was substantially higher in normoxic individuals using continuous oxygen at the time of enrollment when compared to those reporting no oxygen use (61.4% vs 48.6%). The survival curve for normoxic patients using intermittent oxygen was intermediate between those using continuous oxygen and those using no supplemental oxygen (data not shown). The unadjusted hazard ratio for the groups using continuous oxygen and no oxygen was 1.63 ($p = 0.005$), with worse survival in those using continuous oxygen. In order to explore whether clinical prognostic indicators accounted for this difference in survival, we incorporated other variables into the proportional hazards model. After adjusting for BMI, age, arid FEV_1 percentage of predicted, the difference between the two groups was no longer significant, with a hazard ratio of 1.38 ($p = 0.078$; Fig 1). The differential mortality was further attenuated by incorporating the presence of exercise desaturation into the model, with a resultant hazard ratio of 1.14 ($p = 056$).

Normoxic Participants With Exercise Desaturation

Because exercise desaturation was highly correlated with mortality, we wanted to understand die characteristics and survival of those using continuous oxygen and demonstrating exercise desaturation (Table 4, Fig 2). Among the 471 participants with resting normoxia and exercise desaturation, 44.5% were using continuous oxygen, 38.6% were using oxygen intermittently, and 16.7% reported no oxygen use. More severe disease was seen in those using continuous oxygen, as demonstrated by lower FEV_1, FEV_1 percentage of predicted, FVC, FVC percentage of predicted, 6-min walk distance, ergometer exercise, and indexes of dyspnea and overall quality of life. Despite these differences, oxygen use was not associated with differences in survival in individuals randomized to medical therapy demonstrating resting normoxia and exercise desaturation (p = not significant for pair-wise comparisons by log-rank test) [Fig 2]. Thus, patients who had exercise desaturation had similar mortality regardless of whether they were using continuous, intermittent, or no oxygen.

Discussion

The main finding in this exploratory study is that use of oxygen in normoxic patients identifies a high-risk group of emphysema patients. Norimoxic participants using continuous oxygen demonstrated more frequent exercise desaturation, lower spirometric values, poorer exercise performance, more dyspnea, and worse survival. These observations indicate that normoxic individuals using continuous oxygen were a population with more severe disease. While the increased mortality in those using oxygen could be caused directly by the use of oxygen, the observed difference in mortality could be partially accounted for by adjusting for FEV_1, age, and BMI. This suggests that patient characteristics rather than oxygen use contributed to the observed increase in mortality. Therefore, oxygen use appears to be a surrogate marker for other risk factors for mortality.

A significant proportion of the risk of death could be accounted for in the hazard model by the presence of exercise desaturation. Because the presence of exercise desaturation correlated strongly with continuous oxygen use in normoxic individuals, the ability to confidently infer die impact of exercise desaturation on survival is limited. There are several potential explanations for why exercise desaturation may be a strong predictor of mortality in COPD patients with resting normoxia. Given the frequent presence of comorbidities in individuals with COPD,[7] acute desaturation with exercise may pose imminent threat by increasing the risk of cardiac dysrhythmias and ischemia. Other insults such as pneumonia or acute exacerbations of COPD may induce more frequent or more severe hypoxemia. Exercise desaturation may be a marker of more extensive, undiagnosed pulmonary hypertension, which is associated with shorter survival in COPD patients.[19] Exercise desaturation has been shown previously to correlate with severity of pulmonary vascular disease in COPD patients with no or mild resting hypoxemia.[20] Although it is unclear which of these mechanisms is playing a role in the poorer survival observed in those with exercise desaturation, our analysis suggests that exercise desaturation is a predictor of mortality in patients with severe emphysema and resting normoxia. This conclusion supports the findings of Takigawa and colleagues,[21] who reported on the ability of oxygen desaturation during 6-min walk test to predict mortality in a group of 144 COPD patients. Previous analysis of the NETT cohort demonstrated that increased mortality was independently associated with use of oxygen supplementation.[15] The present study extends the analysis of Martinez et al[15] by analyzing only the subgroup that was normoxic at rest. Our findings add exercise desaturation to the list of factors impacting mortality in this population. Although oxygen supplementation may be helpful in patients with exercise desaturation, we did not see a significant difference in survival based on oxygen use. Because the retrospective nature of our analysis limits full evaluation of causal mechanisms, the potential benefit of continuous oxygen therapy in emphysema patients with resting normoxia and exercise desaturation needs further evaluation in a prospective randomized manner.

A second finding of this study is that 21.4% of the 1,215 NETT participants reported oxygen use outside of current guidelines despite having been recently enrolled in supervised pulmonary rehabilitation. This observation highlights the challenge of monitoring oxygen prescription and use. While one could speculate that the patient's clinical status changed from the time of physician assessment at rehabilitation discharge to the baseline Pao_2 measurement, this is unlikely given that the Pao_2 assessment occurred within 2 weeks of discharge from rehabilitation. Higher altitudes could have impacted on the appropriateness of oxygen use, but of the 49 participants enrolled at a high altitude site (Denver, CO), only 1 of the 4 patients with a baseline Pao_2 > 60 mm Hg reported continuous oxygen use. Several centers enrolled patients from large recruitment areas with wide variations in altitude, which may have led to differing degrees of hypoxia at home compared to the screening site, resulting in oxygen prescriptions that were appropriate at home, but not when visiting the study center. Using participant home zip codes and reference altitudes for those zip codes, we found no trend in guideline adherence associated with altitude in a center with a large recruitment area of various topography (Seattle, WA).

What could explain the use of continuous oxygen in normoxic participants? Physician may be inclined to treat a patient with worsening functional status and quality of life more aggressively. Physicians may attempt to minimize symptoms of dyspnea and exercise intolerance by prescribing continuous oxygen therapy for this subset of patients despite lack of indication by Pao_2 measurements. There is support for this approach because oxygen therapy can yield higher training intensity and improve exercise tolerance in nonhypoxic patients with COPD.[22] Alternatively, physicians may have responded to requests for oxygen from patients with worsening functional status and quality of life. We do not have data regarding the specific rationale and indication for individual oxygen prescription in NETT participants. Moreover, it seems likely that oxygen prescriptions changed over time, and this may have influenced survival, either positively or negatively. Another limitation of this study is that we relied on patient self-report of oxygen use, which may have underestimated actual oxygen use. This has been well documented for continuous oxygen use, and may also apply to patients who report intermittent oxygen use.[23] Despite this, this study observes that within a group of normoxic emphysema patients, physicians recognized a sicker subset of individuals and prescribed them continuous oxygen therapy.

In conclusion, this study shows that continuous oxygen use in a population of patients with severe emphysema and resting normoxia is common. The use of continuous oxygen identifies a high-risk subset of emphysema patients. Exercise desaturation is a substantial contributor to mortality in this population. The findings of this study highlight the ongoing need for prospective trials focusing on the use of oxygen therapy in emphysema patients not meeting conventional criteria for continuous oxygen use.

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Abbreviations:

RMI	body mass index
mBODE	modified body mass index, obstruction, dyspnea; exercise capacity
MRC	Medical Research Council Working Party
NETT	National Emphysema Treatment Trial
NOTT	Nocturnal Oxygen Treatment Trial
QWB	quality of well-being score
SGRQ	St. George Respiratory Questionnaire
Spo_2	oxygen saturation by pulse oximetry
UCSD-SOBQ	University of California Sari Diego Shortness of Breath Questionnaire

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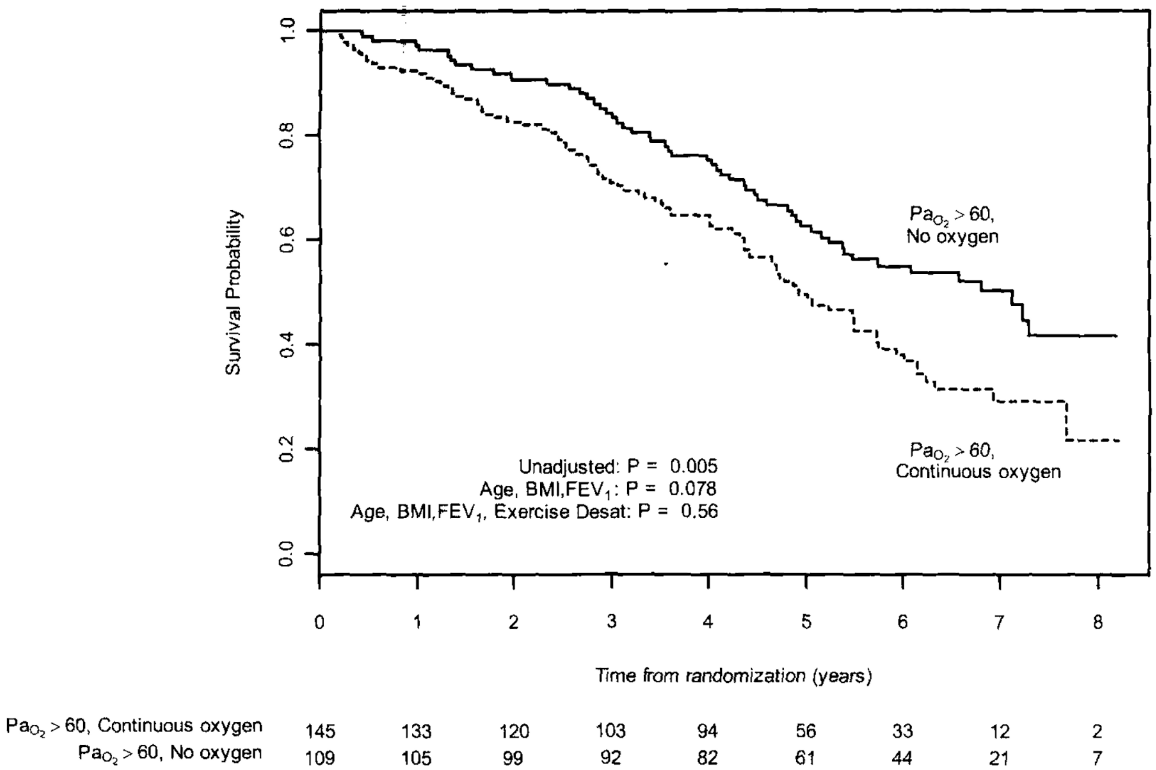

Figure 1.

Multivariate 8-year survival analysis in normoxic participants randomized to medical therapy, startified bv oxygen use; p values are calculated from Cox models that adjust for BMI. age, FEV_1 percentage of predicted, and exercise desaturation (Desat).

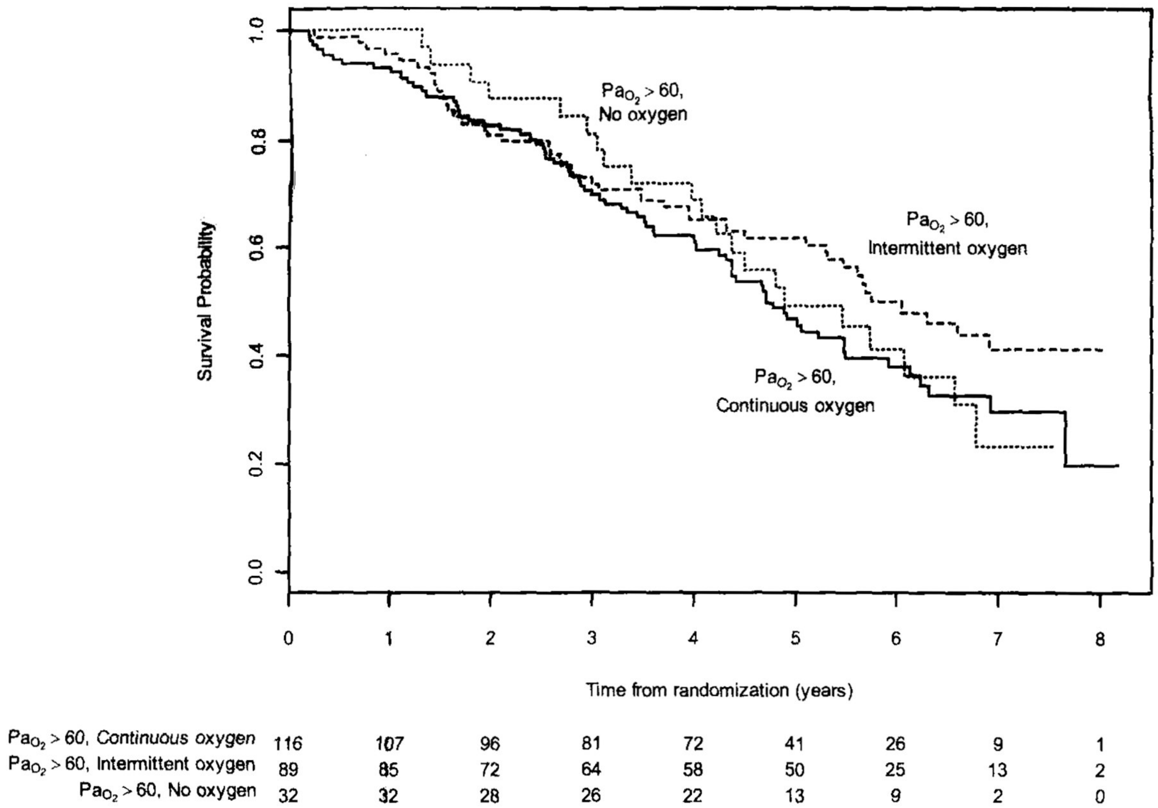

Figure 2.

Multivariate 8-year survival analysis for participants with resting normoxia and exercise desaturation, randomized to medical therapy. Groups are stratified by oxygen use.

Table 1–

Guidelines for Continuous Oxygen Therapy in COPD*

Hypoxemia	ATS-ERS	GOLD	NCCCC-NICE
Severe	Pao_2< 7.3 kPa (55 mm Hg) or SpO_2≤ 88%	Pao_2< 7.3 kPa (55 mm Hg) or Spo_2 ≤ 88%	Pao_2< 7.3 kPa
Moderate	$Pao_2$of 7.3 to 8.0 kPa (55 to 59 mm Hg) or Spo_2 of 89% and at least one of the following: cor pulmonale; peripheral edema; hematocrit > 55%	Pao_2 of 7.3 to 8.0 kPa (55 to 59 mm Hg) or Spo_2 of 88% and at least one of the following: pulmonary hypertension; peripheral edema; hematocrit > 55%	Pao_2 of 7.3 to 8.0 kPa (55–59 mm Hg) and at least one of the following: pulmonary hypertension; peripheral edema; secondary polycythemia; nocturnal desaturation > 30% of sleep
None	Pao_2≥ 8.0 kPa (60 mm Hg) or SpO_2> 90% with severe nocturnal desaturation and lung-related dyspnea responsive to oxygen	No recommendation given	No recommendation given

*ATS-ERS = American Thoracic Society-European Thoracic Society;[3] GOLD = Global Initiative for Chronic Obstructive Lung Disease;[4] NCCCC-NICE = National Collaborating Centre for Chronic Conditions-National Institute for Health and Clinical Excellence.[5]

Table 2–

Oxygen Use at Enrollment (n = 1,215)*

	Baseline Pao_2, mm Hg		
Oxygen Use	**≤ 55**	**56 to 60**	**>60**
None	4 (1.5)	7 (3.9)	226 (29.4)
Intermittent	22 (8.3)	43 (23.6)	283 (36.8)
Continuous	238 (90.2)	132 (72.5)	260 (33.8)

*Data are presented as No. (% of patients in similar Pao_2 group).

Table 3–

Demographic and Clinical Characteristics at Enrollment*

Characteristics	Resting PaO_2> 60 mm Hg and Continuous Oxygen (n = 260)	Resting Pao_2> 60 mm Hg and No Oxygen (n = 226)	p Value
Age, yr	65.5 ± 6.4	66.7 ± 6.5	0.04
Race			
White	247 (95)	214 (95)	> 0.99
Nonwhite	13 (5)	12 (5)	
Gender			
Female	101 (39)	72 (32)	0.13
Male	159 (61)	154 (68)	
Pack-yr†	63.9 ± 30.1	63.8 ± 33.4	0.97
Income, $			
< 15,000	54 (21)	40 (18)	0.37
15,000–29,999	90 (35)	76 (35)	
30,000–49,000	76 (29)	65 (29)	
≥ 50,000	34 (13)	41 (18)	
Missing/no answer	6 (2)	1 (0.5)	
BMI, kg/m^2	25,1 ± 3.8	24.1 ± 3.2	0.002
FEV_1, L	0.75 ± 0.22	0.89 ± 0.26	< 0.0001
FEV_1, % predicted‡	25.8 ± 6.8	29.8 ± 7.4	< 0.0001
FVC, L	2.5 ± 0.8	2.8 ± 0.8	0.0002
FVC, % predicted‡	65.7 ± 14.7	70.9 + 15.0	0.0002
TLC, L	7.7 ± 1.6	7.8 ± 1.5	0.17
TLC, % predicted§	127.5 ± 15.0	127.1 ± 13.6	0.72
RV, L	5.0 ± 1.2	4.9 + 1.1	0.23
RV, % predicted§	226.1 ± 48.8	214.8 ± 42.9	0.002
IC, L	1.7 ± 0.6	1.9 ± 0.6	< 0.0001
IC, % predicted	60.1 ± 17.3	66.8 ± 17.3	< 0.0001
DLCO, mL/min/mm Hg	7.7 ± 3.5	9.9 ± 3.4	0.25
DLCO, % predicted‖	27.8 ± 11.6	30.4 ± 6.6	0.64

Characteristics	Resting PaO_2> 60 mm Hg and Continuous Oxygen (n = 260)	Resting Pao_2> 60 mm Hg and No Oxygen (n = 226)	p Value
6-min walk distance, feet	1143 ± 292	1363 ± 305	< 0.0001
Maximum exercise, W	37.1 ± 21.1	47.3 ± 22.8	< 0.0001
Exercise desaturation			
Present	210 (81)	79 (35)	< 0.0001
Absent	50 (19)	147 (65)	
UCSD-SOBQ[¶]	68.2 ± 17.8	55.6 ± 19.6	< 0.0001
QWB[#]	0.55 ± 0.13	0.58 ± 0.10	0.008
SGRQ[**]			
Symptoms	58.8 ± 20.4	56.0 ± 20.0	0.14
Activity	81.7 ± 12.8	75.0 ± 15.0	< 0.0001
Impact	40.2 ± 16.5	34.4 ± 14.5	< 0.0001
Total	55.9 ± 13.3	50.4 ± 12.5	< 0.0001
mBODE score[††]			
0–2	5 (1.9)	18 (8.0)	< 0.0001
3–4	67 (25.8)	115(51.1)	
5–6	112 (43.1)	71 (31.6)	
7–10	76 (29.2)	21 (9.3)	

[*] Values are given as mean ± SD or No. (%). TLC = total lung capacity; RV = residual volume; IC = inspiratory capacity; Dlco = diffusing capacity of the lung for carbon monoxide.

[†] No. of cigarettes smoked daily on average/20 times total years smoked.

[‡] Predicted values calculated from Crapo et al.[16]

[§] Predicted values calculated from Crapo et al.[17]

[||] Predicted values calculated from Crapo Morris.[18]

[¶] The UCSD-SOBQ is a 24-item questionnaire regarding dyspnea. Scores range from 0 to 120 with higher scores indicating more dyspnea.

[#] The QWB scale is a 77-item questionnaire focusing on generic health-related quality of life. Scores range from 0 to 1, with higher scores indicate better quality of life.

[**] The SGRQ is a 51-item questionnaire focusing on respiratory symptoms and quality of life. Scores range from 0 to 100, with higher scores indicating worse health-related quality of life.

[††] The mBODE is a composite 11-point score.

Table 4–

Characteristics of Individuals With Resting Normoxia and Exercise Desaturation*

Characteristics	Continuous Oxygen (n = 210)	Intermittent Oxygen (n = 182)	No Oxygen (n = 79)	p Value		
				Continuous vs Intermittent	Continuous vs None	Intermittent vs None
Age, yr	65.5 ± 6.2	66.9 ± 5.9	66.2 ± 5.9	0.02	0.40	0.33
Race						
White	202 (96.2)	170 (61.5)	75 (94.9)	0.25	0.74	0.78
Nonwhite	8 (3.8)	12 (6.6)	4(5.1)			
Gender						
Female	84 (40.0)	70 (38.5)	25 (31.7)	0.84	0.22	0.33
Male	126 (60.0)	112 (61.5)	54 (68.4)			
Pack-yr	64.0 ± 27.1	62.0 ± 29.3	67.4 ± 36.2	0.49	0.39	0.21
Income, $						
< 15,000	41 (19.5)	33 (18.1)	17 (21.5)	0.12	0.93	0.71
15,000–29,999	74 (35.2)	54 (29.7)	24 (30.4)			
30,000–49,000	62 (29.5)	54 (29.7)	25 (31.7)			
≥ 50,000	29 (13.8)	41 (22.5)	13 (16.5)			
Missing/no answer	4 (1.9)	0 (0.0)	0 (0.0)			
BM1, kg/m^2	25.3 ± 3.8	24.5 ± 3.4	24.3 ± 3.1	0.03	0.05	0.77
FEV_1, L	0.73 ± 0.22	0.77 ± 0.21	0.86 ± 0.28	0.03	< 0.0001	0.004
FEV_1, % predicted	25.1 ± 6.6	27.7 ± 6.8	28.3 ± 8.3	0.002	0.001	0.28
FVC, L	2.4 ± 0.78	2.5 ± 0.78	2.7 ± 0.84	0.17	0.005	0.08
FVC, % predicted	64.1 ± 14.3	68.0 ± 15.4	68.1 + 15.7	0.01	0.04	0.94
TLC, L	7.7 ± 1.6	7.7 ± 1.5	8.1 ± 1.6	0.68	0.06	0.10
TLC, % predicted	127.6 ± 15.5	129.1 ± 13.0	127.8 ± 12.9	0.31	0.90	0.48
RV, L	5.1 ± 1.2	5.0 ± 1.1	5.1 ± 1.2	0.40	0.95	0.47
RV, % predicted	228.2 ± 49.6	221.4 ± 43.7	221.7 ± 49.7	0.15	0.32	0.96
IC, L	1.6 ± 0.60	1.8 ± 0.56	1.9 ± 0.63	0.05	0.0002	0.02
IC, % predicted	58.8 ± 17.3	63.4 ± 16.4	66.1 ± 16.7	0.008	0.001	0.22
DLCO, mL/min/mm Hg	7.2 ± 3.4	8.3 ± 2.5	9.4 ± 3.7	0.49	0.32	0.58
DLCO, % predicted	25.4 ± 10.9	29.7 ± 7.9	28.8 ± 6.3	0.39	0.58	0.84

Characteristics	Continuous Oxygen (n = 210)	Intermittent Oxygen (n = 182)	No Oxygen (n = 79)	p Value		
				Continuous vs Intermittent	Continuous vs None	Intermittent vs None
6-min walk distance, feet	347.9 ± 87.8	395.3 ± 95.2	400.8 ± 100	< 0.0001	< 0.0001	0.67
Maximum exercise, W	36.7 ± 21.0	42.0 ± 19.8	45.1 ± 23.7	0.01	0.004	0.27
UCSD-SOBQ	68.2 ± 16.9	60.6 ± 16.8	57.7 ± 19.4	< 0.0001	< 0.0001	0.23
QWB	0.55 ± 0.12	0.59 ± 0.11	0.57 ±0.10	0.002	0.28	0.16
SGRQ						
Symptoms	58.5 ± 20.0	53.5 ± 18.7	54.7 ± 18.8	0.01	0.15	0.64
Activity	81.9 ± 12.3	79.8 + 13.1	78.1 ± 13.7	0.10	0.02	0.35
Impact	39.6 ± 15.9	35.4 ± 15.2	35.9 ± 14.4	0.01	0.08	0.80
Total	55.6 ± 12.7	51.9 ± 12.0	51.9 ± 12.3	0.004	0.03	0.98
mBODE score						
0–2	2 (1.0)	6 (3.3)	7 (8.9)	< 0.0001	< 0.0001	0.30
3–4	55 (26.2)	84 (46.2)	33 (41.8)			
5–6	92 (43.8)	66 (36.3)	27 (34.2)			
7–10	61 (29.1)	26 (14.3)	12 (15.2)			

*Date we presented as mean ± SD or No. See Table 3 for expansion of abbreviations and definitions.