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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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_1 percentage of predicted, the presence of exercise desaturation accounted for the differential mortality seen between these groups.**
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 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.** ***(CHEST 2008; 134:497–506)***

Key words: guideline adherence; pulmonary disease; chronic obstructive; supplemental oxygen

Abbreviations: BMI = 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 San Diego Shortness of Breath Questionnaire

COPD remains a major public health issue, ranking 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 pa-

Table 1—*Guidelines for Continuous Oxygen Therapy in COPD

Hypoxemia	ATS-ERS	GOLD	NCCCC-NICE
Severe	Pa_{O_2}< 7.3 kPa (55 mm Hg) or Sp_{O_2}≤ 88%	Pa_{O_2}< 7.3 kPa (55 mm Hg) or Sp_{O_2} ≤ 88%	Pa_{O_2}< 7.3 kPa
Moderate	$Pa_{O_2}$of 7.3 to 8.0 kPa (55 to 59 mm Hg) or Sp_{O_2} of 89% and at least one of the following: cor pulmonale; peripheral edema; hematocrit > 55%	Pa_{O_2} of 7.3 to 8.0 kPa (55 to 59 mm Hg) or Sp_{O_2} of 88% and at least one of the following: pulmonary hypertension; peripheral edema; hematocrit > 55%	Pa_{O_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	Pa_{O_2}≥ 8.0 kPa (60 mm Hg) or Sp_{O_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]

tients 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 specific 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 Pa_{O_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 Pa_{O_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 Pa_{O_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

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†A list of participants is given in the Appendix.
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