



# Avoidance of hypoxemia in COPD is essential

Sebastián Rodríguez-Llamazares<sup>1</sup>, Ileri Thiri6n-Romero<sup>1</sup>,  
Rogelio Pérez-Padilla<sup>1</sup>

Since the publication of a relevant clinical trial by the Nocturnal Oxygen Therapy Trial Group<sup>(1)</sup> and a similar trial supported by the Medical Research Council,<sup>(2)</sup> it has been accepted that long-term oxygen therapy (LTOT) in patients with COPD and daytime hypoxemia significantly reduces mortality. LTOT has now become a standard treatment not only for COPD but also for other respiratory diseases. In the two aforementioned studies<sup>(1,2)</sup> as well as in one recent meta-analysis,<sup>(3)</sup> it was clarified that the number of hours of daily oxygen use also determines survival. For example, 12 hours of daily oxygen therapy<sup>(1)</sup> provided little survival benefit over no oxygen therapy,<sup>(2)</sup> whereas more than 15 hours of daily oxygen therapy provided a clear survival benefit.

It is of note that no further improvement in survival has been demonstrated with the use of LTOT if oxygenation is slightly higher than that defined in the aforementioned trials.<sup>(1,2)</sup> Although most organizations accept the prescription of oxygen when there is hypoxemia during exercise and sleep, recent randomized controlled trials<sup>(4,5)</sup> have been unable to prove that supplemental oxygen for patients with nocturnal hypoxemia or moderate hypoxemia alone impacts clinical outcomes.

Sleep studies in patients with COPD have shown that peak hypoxemia occurs during rapid eye movement sleep and has a direct relationship with daytime PaO<sub>2</sub>. In the presence of sleep apnea, episodic desaturation also develops and complicates any established hypoxemia.<sup>(6)</sup> In the present issue of the *Jornal Brasileiro de Pneumologia* (JBP) Prados et al.<sup>(7)</sup> reported that COPD patients who had severe nocturnal hypoxemia, especially during rapid eye movement sleep, had a greater left ventricular mass and more risk factors, such as slightly higher diastolic blood pressure and mean blood pressure, as well as higher BMI and lower daytime oxygenation. These findings justify additional clinical trials and studies centered on how to prevent, identify, and treat nocturnal hypoxemia in COPD patients with and without sleep apnea.

Hypoxemia in COPD patients contributes to severe organ damage, including (mostly mild to moderate) pulmonary hypertension<sup>(8)</sup>; polycythemia; systemic inflammation; neurocognitive dysfunction; and skeletal muscle failure.<sup>(9)</sup> Therefore, hypoxemia itself becomes a primary pathophysiological mechanism. Also in the present issue of the JBP Marcondes et al.<sup>(10)</sup> showed higher mortality in patients with more severe COPD and more hypoxemia, despite more hours of daily oxygen therapy and a self-reported adherence of 73%. Therefore, it is essential to avoid hypoxemia in patients with COPD or other lung diseases by improving adherence to treatment, including long-term oxygen therapy with or without CPAP in patients with sleep apnea. This is especially true in patients with severe baseline hypoxemia, such as those receiving oxygen therapy 24 h/day. Nonadherence to oxygen therapy can cause much more damage in such cases than in those of patients with less severe hypoxemia.

For years, the only interventions capable of improving survival in COPD patients were smoking cessation and the use of oxygen in the event of hypoxemia, and they remain the most relevant. In most cases, despite repeated efforts, a proportion of patients with COPD persist smoking: 27% in the Prados et al. study<sup>(7)</sup> and 17% in the study by Marcondes et al.<sup>(10)</sup> This has been reported worldwide, especially in patients recruited for controlled clinical trials of inhaled drugs, approximately 40% of whom keep smoking. Given that smoking is a persistent risk for premature death, disease, and worsening of COPD, it is imperative to promote smoking cessation.

In conclusion, patients with COPD often fail to adhere to treatment and health recommendations, such as diet and exercise. Therefore, any strategies to improve treatment adherence should be a priority. The studies cited here remind us to strengthen efforts to control hypoxemia and to monitor adherence to treatments, especially those that impact survival and modify the natural course of COPD.

## REFERENCES

1. Continuous or nocturnal oxygen therapy in hypoxemic chronic obstructive lung disease: a clinical trial. Nocturnal Oxygen Therapy Trial Group. *Ann Intern Med.* 1980;93(3):391-398. <https://doi.org/10.7326/0003-4819-93-3-391>
2. Long term domiciliary oxygen therapy in chronic hypoxic cor pulmonale complicating chronic bronchitis and emphysema. Report of the Medical Research Council Working Party. *Lancet.* 1981;1(8222):681-686. [https://doi.org/10.1016/S0140-6736\(81\)91970-X](https://doi.org/10.1016/S0140-6736(81)91970-X)
3. Cranston JM, Crockett AJ, Moss JR, Alpers JH. Domiciliary oxygen for chronic obstructive pulmonary disease. *Cochrane Database Syst Rev.* 2005;2005(4):CD001744. <https://doi.org/10.1002/14651858.CD001744.pub2>
4. Lacasse Y, Sériès F, Corbeil F, Baltzan M, Paradis B, Simão P, et al. Randomized Trial of Nocturnal Oxygen in Chronic Obstructive Pulmonary Disease. *N Engl J Med.* 2020;383(12):1129-1138. <https://doi.org/10.1056/NEJMoa2013219>
5. Long-Term Oxygen Treatment Trial Research Group, Albert RK, Au DH, Blackford AL, Casaburi R, Cooper JA Jr, et al. A Randomized Trial of Long-Term Oxygen for COPD with Moderate Desaturation. *N Engl J Med.* 2016;375(17):1617-1627. <https://doi.org/10.1056/NEJMoa1604344>
6. McNicholas WT, Hansson D, Schiza S, Grote L. Sleep in chronic respiratory disease: COPD and hypoventilation disorders. *Eur Respir Rev.* 2019;28(153):190064. <https://doi.org/10.1183/16000617.0064-2019>

7. Prados VO, Lima T, Silva LTD, Matos IC, Maya ACL, Silva Júnior JLR, et al. Evaluation of the left ventricle in patients with COPD and nocturnal hypoxemia. *J Bras Pneumol.* 2020;46(6):e20190136. <https://doi.org/10.36416/1806-3756/e20190136>
8. Scharf SM, Iqbal M, Keller C, Criner G, Lee S, Fessler HE, et al. Hemodynamic characterization of patients with severe emphysema. *Am J Respir Crit Care Med.* 2002;166(3):314-322. <https://doi.org/10.1164/rccm.2107027>
9. Kent BD, Mitchell PD, McNicholas WT. Hypoxemia in patients with COPD: cause, effects, and disease progression. *Int J Chron Obstruct Pulmon Dis.* 2011;6:199-208. <https://doi.org/10.2147/COPD.S10611>
10. Marcondes VK, Kuwazuru TS, Silva LPCE, Cezare TJ, Franco EAT, Prudente R, et al. 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. *J Bras Pneumol.* 2020;46(6):e20190158. <https://doi.org/10.36416/1806-3756/e20190158>