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Are oxygen and Non-Invasive Ventilation useful “clean doping boosters” for thoracoabdominal asynchrony during exertion in severe COPD?

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**Editorial****Are oxygen and Non-Invasive Ventilation useful “clean doping boosters” for thoracoabdominal asynchrony during exertion in severe COPD?**

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Patients with chronic obstructive pulmonary disease (COPD) experience severe mechanical constraints during physical activity, leading to dyspnea and exercise limitation.<sup>1</sup> Thoracoabdominal asynchrony (TAA) is a typical marker prevalent in patients with severe COPD and significantly contributes to exercise intolerance. This asynchrony, particularly pronounced in the lower rib cage during exercise, results in reduced chest wall volume and exercise capacity.<sup>2,3</sup> Increased ventilation during exercise in COPD patients has been associated with heightened abdominal compartment motion and a rise in asynchrony, independent of exercise intensity.<sup>4</sup>

TAA is often exacerbated during physical activity, reflecting profound ventilatory and muscular dysfunction in advanced COPD. The mechanisms underlying TAA include: a) Flow obstruction that alters the breathing pattern; b) Dynamic Hyperinflation: air trapping and increased lung volumes during expiration flatten the diaphragm, limiting its efficiency and disrupting normal respiratory mechanics; c) Diaphragmatic Dysfunction: the diaphragm becomes mechanically disadvantaged, resulting in paradoxical abdominal movements (inward abdominal motion during inspiration rather than outward); d) Increased Work of Breathing: hyperinflation and airway resistance overload respiratory muscles, including the intercostals and accessory muscles, worsening the imbalance between thoracic and abdominal compartments; e) Chest Wall Rigidity: structural changes in advanced COPD reduce chest wall compliance, further impairing coordination, and f) Ventilatory Muscle Fatigue: persistent high workloads on respiratory muscles lead to fatigue, amplifying TAA.

Patients with TAA commonly exhibit severe dyspnea, limited exercise tolerance, visible asynchrony between thoracic and abdominal movements, gas exchange abnormalities (hypercapnia and hypoxemia), and reduced oxygen delivery to muscles, contributing to early fatigue. In the study by Javier Sayas Catalán<sup>5</sup>, respiratory inductance plethysmography identified two distinct patterns of TAA during exercise in patients with advanced COPD: (1) abdomen leading (counterclockwise) and (2) thorax leading (clockwise). The abdominal paradox, characterized by inward abdominal motion during inspiration, serves as a clinical marker of severe diaphragmatic dysfunction and muscle fatigue. Patients with a pronounced clockwise pattern had greater hyperinflation, increased dyspnoea during oxygenated exercise and higher neuro-respiratory drive (NRD) as assessed by parasternal electromyography. These findings suggest compensatory activation of parasternal muscles to offset diaphragmatic inefficiency during heightened respiratory demand. The study population described by Catalán<sup>5</sup> is particularly severe and demonstrated by a low maximum workload, a high Body-mass index, Obstruction, Dyspnea and Exercise (BODE) index, severe air trapping, severe obstruction, severe hyperinflation, stable hypercapnia with dynamic hyperinflation as the main driver of exercise limitation but with preserved Maximal Inspiratory Pressure (MIP) suggesting diaphragm weakness was not the primary cause of exercise limitation.

Within pulmonary rehabilitation, some interventions may be able to mitigate this mechanism: a) Endurance training: improving respiratory pattern and reducing dynamic hyperinflation, both acutely (e.g., interval training vs continuous)<sup>6</sup> and as long-term outcome (pre-to-post variation at isovolume of exercise<sup>7</sup>; b) Inspiratory Muscle Training: using inspiratory muscle trainers to restore muscle coordination. The primary goals of all these programs include improving diaphragmatic strength, alleviating dyspnea, improving quality of life, and enhancing exercise performance<sup>8,9</sup>; c) Bronchodilator Therapy: reducing airway resistance to alleviate hyperinflation d) Oxygen Therapy: addressing hypoxemia to enhance exercise tolerance and e) Non-Invasive Ventilation (NIV): supporting inspiratory and expiratory efforts, improving synchronization during exercise, and reducing dyspnea.

Regarding endurance training, it is well known from the literature that high-intensity training programs have been shown to be superior to low-intensity training programmes. The mechanical and ventilatory limitations of the most severe patients described above do not always allow for high intensity training programmes. As both oxygen therapy and NIV have been shown to improve dyspnea and exercise tolerance<sup>10,11</sup> it is reasonable to expect that these programs can act as "boosters" on exercise as well as "clean doping" tools during exercise, promoting a normalization of breathing pattern during exertion.

Oxygen therapy reduces ventilatory drive and respiratory muscle workload by improving oxygen delivery to muscles, delaying the onset of dyspnea and respiratory muscle fatigue, and might indirectly mitigate TAA. Studies have shown that oxygen therapy enhances exercise capacity and reduces ventilatory demand in hypoxemic patients. However, its efficacy is less pronounced in non-hypoxemic individuals or those with mild hypoxemia, as responses depend on factors such as exercise intensity, delivery method, and disease characteristics. Further research is needed to better delineate the patient populations most likely to benefit from oxygen therapy during exercise.

NIV reduces respiratory muscle workload and stabilizes chest wall and diaphragm mechanics, improving thoracoabdominal coordination.<sup>12</sup> Its application during exercise has been associated with improved ventilation, reduced dyspnea, and enhanced performance, particularly in patients with severe COPD. Studies suggest that NIV enables higher training intensity, yielding greater physiological benefits, especially in patients with significant hyperinflation. However, limitations include variability in individual

responses, the need for acclimatization to NIV, and logistical challenges in applying NIV to activities of daily living (ADLs).<sup>10,11</sup>

The interesting Catalán's study<sup>5</sup> describes the absence of superiority of one intervention over another (oxygen therapy, NIV, high-flow therapy). The lack of a control group exercising without NIV support and oxygen therapy, prevents the results from detecting the add-on effect of these therapies on "basal" TAA. However, the results show that patients with clockwise TAA patterns experienced greater dyspnea relief under NIV, suggesting potential benefits in patients with severe diaphragmatic dysfunction. In this direction, respiratory inductance plethysmography may provide a non-invasive tool for identifying patients most likely to respond to tailored interventions, including high-pressure NIV settings. In addition, it could help to ensure proper NIV settings during exercise based on recorded asynchronies and could be an effective tool for the follow-up of patients, tracking changes in the breathing pattern during physical effort.

To the best of our knowledge, it is reasonable to offer oxygen therapy and NIV to subgroups of patients with advanced COPD, with and without hypercapnia, with hyperinflation, with clear ventilatory limitation, and with severe diaphragmatic dysfunction and abdominal paradox breathing. **Table 1** summarizes future physiological and clinical research areas on TAA should be prioritized to reach personalized therapies to optimize patient outcomes.

**Table 1 Key areas of future investigation**

Physiological perspective	Clinical setting
<i>Pathophysiology and Mechanisms:</i> exploring the role of dynamic hyperinflation, muscle dysfunction, and fatigue in TAA	<i>Prognostic Value:</i> determining whether the severity of TAA can predict disease progression, exacerbation frequency, or mortality
<i>Neurophysiological Mechanisms:</i> studying the influence of central neural drive and feedback mechanisms on thoracoabdominal coordination	<i>Comorbidities:</i> assessing the impact of conditions such as obesity, kyphoscoliosis, and musculoskeletal abnormalities on TAA;

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*Rehabilitation Strategies:* investigating task-specific training, pharmacological therapies, and optimal NIV settings for managing TAA

*Advanced Monitoring Implementation:* integrating imaging, wearable technologies, and artificial intelligence (AI) with plethysmography and exercise data to identify predictors of TAA;

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*Long-Term Implications:* understanding the effects of TAA on respiratory muscle structure, cardiovascular health, and overall function

*Telemedicine:* developing remote assessment tools to support long-term monitoring of TAA.

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*Prevention Strategies:* identifying methods to prevent TAA in early-stage COPD or other respiratory conditions to improve patient outcomes.

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In summary, TAA during physical exercise is a significant factor contributing to exercise intolerance in patients with severe COPD. Pulmonary rehabilitation professionals must consider this aspect and manage it effectively to improve patient outcomes. Specific monitoring tools, such as plethysmography, can help better personalize care, including the administration of oxygen and the use of NIV during exertion. Continued research into TAA's pathophysiology, monitoring, and management is essential for improving patient care and quality of life.

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### **Conflict of Interests**

The authors declare not to have any conflicts of interest that may be considered to influence directly or indirectly the content of the manuscript

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