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Citation: Louvaris, Zafeiris, Langer, Daniel and Vogiatzis, Ioannis (2021) Extradaphragmatic respiratory muscle perfusion during exercise in patients with COPD: impact on dyspnea. *Jornal Brasileiro de Pneumologia*, 47 (4). e20210212. ISSN 1806-3756

Published by: Sociedade Brasileira de Pneumologia e Tisiologia

URL: <https://doi.org/10.36416/1806-3756/e20210212> <<https://doi.org/10.36416/1806-3756/e20210212>>

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# Extradiaphragmatic respiratory muscle perfusion during exercise in patients with COPD: impact on dyspnea

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## BACKGROUND

Advances in technology, such as the use of near-infrared spectroscopy to measure local respiratory muscle blood flow,<sup>(1)</sup> make it possible to investigate whether alterations in respiratory muscle perfusion during exercise contribute to the development of respiratory muscle fatigue and to associated increases in dyspnea perception in patients with COPD.

## CASE HISTORY

A 62-year-old man (BMI = 24.2 kg/m<sup>2</sup>), former smoker, was diagnosed with COPD—FEV<sub>1</sub> = 56% of predicted; FEV<sub>1</sub>/FVC = 0.37; maximum voluntary ventilation = 55 L/min (45% of predicted); static hyperinflation at rest (inspiratory capacity [IC] = 2.40 L [79% of predicted]); functional residual capacity = 6.44 L (187% of predicted); IC/TLC = 0.27; and RV/TLC = 0.47—having moderately reduced diffusion capacity (DL<sub>CO</sub> = 46% of predicted), exertional dyspnea (modified Medical Research Council scale score = 2), preserved inspiratory muscle strength (MIP = 108 cmH<sub>2</sub>O [97% of predicted]), reduced functional capacity (six-minute walk distance = 443 m [65% of predicted]), reduced peak exercise capacity (measured during a cardiopulmonary exercise test: cardiac output = 10.2 L/min; peak VO<sub>2</sub> = 1.26 L/min (59% of predicted), and reduced peak work rate (WR<sub>peak</sub> = 100 W [54% of predicted]). The patient underwent three different exercise sessions and presented with a combination of breathlessness and leg discomfort (50% in both; Borg dyspnea and leg fatigue scores = 7), which were reported to be the main reason for interrupting exercise.

## TESTING PROCEDURES

The patient performed: i) a constant-load exercise test on a cycling ergometer (CE), sustained at 80% of WR<sub>peak</sub> (80 W) to the limit of tolerance (endurance cycling time = 5 min & 30 s); ii) a normocapnic hyperpnea (NH) session sustained for 5 min at similar minute ventilation (i.e., ~51 L/min) and breathing pattern as recorded during the cycling exercise test (locomotor muscles did not compete with respiratory muscles for the available blood flow; i.e., endurance stimulus); and iii) an inspiratory loaded breathing (LB) session for 5 min against an external resistance of ~50% of MIP (i.e., 55 cmH<sub>2</sub>O; strength stimulus).<sup>(2,3)</sup>

## CLINICAL OVERVIEW

During the CE test, the patient had dynamic hyperinflation (a 970 mL reduction in IC from rest) and reported very severe leg fatigue (Borg scale score = 7). Respiratory muscle work was greater during LB than during NH and CE (Figure 1A), which resulted in larger rib cage and neck muscle activation during inspiration to overcome the additional external load imposed on the respiratory system (Figure 1B). Nevertheless, the pressure-time product of inspiration accounting for the energy cost of breathing was greater during CE and NH than during LB (158 and 165 cmH<sub>2</sub>O · s/min, respectively, vs. 49 cmH<sub>2</sub>O · s/min). Cardiac output increased from rest (4.1 L/min) during all exercise sessions, and it was greater during CE than during NH and LB (9.8 L/min vs. 5.9 and 4.9 L/min, respectively). Despite a twofold increase in cardiac output during CE, scalene, intercostal and abdominal local muscle perfusion and oxygenation were lower during NH and LB (Figures 1C and 1D). It is of note that the patient reported very severe dyspnea during CE and moderate dyspnea during NH and LB (Figure 1E).

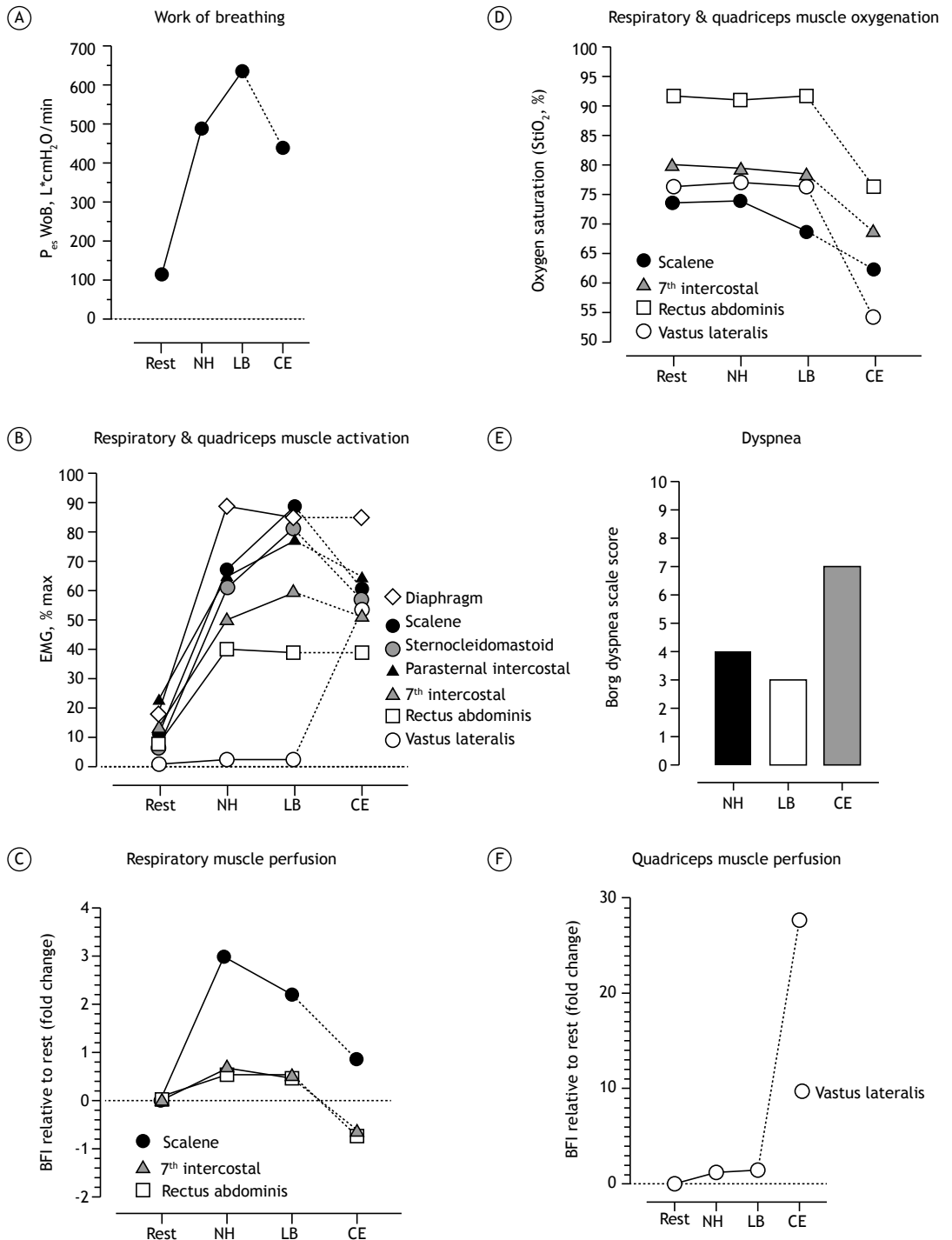
## DISCUSSION AND CLINICAL MESSAGE

Collectively, this case illustrates that extradiaphragmatic respiratory muscle underperfusion occurs during high-intensity whole-body exercise. Indeed, when high-intensity endurance and strength stimuli are imposed on respiratory muscles during NH and LB, respectively and locomotor muscles do not compete with respiratory muscles for the available blood flow, cardiac output increases proportionally to the energy cost of breathing, and intercostal, scalene and abdominal local muscle perfusion increases from rest. In contrast, during CE, the patient had a decreased respiratory muscle energy supply (Figures 1E and 1F) as indicated by the decrease in extradiaphragmatic respiratory muscle perfusion and oxygenation, whilst cardiac output was twice as high as during NH and LB. Insufficient adjustment in oxygen availability to extradiaphragmatic respiratory muscles might contribute to the development of respiratory muscle fatigue and an increase in dyspnea perception, leading to premature exercise termination.<sup>(4)</sup> In support of this mechanism, improvements in oxygen delivery to extradiaphragmatic muscles by using heliox and/

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**Figure 1.** Respiratory muscle work (A), activation of respiratory muscles and quadriceps (B), respiratory muscle perfusion (C), oxygenation response of respiratory muscles and quadriceps (D), Borg dyspnea scale score (E), and locomotor muscle perfusion (F) in a 62-year-old man with COPD. Measurements were performed at rest; during a normocapnic hyperpnea (NH) session, representing an endurance stimulus for the respiratory muscles (i.e., locomotor muscles did not compete with respiratory muscles for the available blood flow); during a loaded breathing (LB) session, representing a strength stimulus for the respiratory muscles; and during a cycling exercise (CE) test. Pes: oesophageal pressure; WoB: work of breathing; EMG: electromyography; BFI: blood flow index; and StiO<sub>2</sub>: tissue oxygen saturation.

or oxygen supplementation have been shown to be associated with less dyspnea during exercise in patients with COPD.<sup>(5)</sup> An area of specific interest for future

studies is to investigate whether specific rehabilitative interventions that have been documented to increase respiratory muscle capacity (e.g., inspiratory muscle

training)<sup>(6)</sup> can also elicit improvements in availability of respiratory muscle energy and contribute to lower dyspnea perception during whole body exercise in patients with COPD.

## AUTHOR CONTRIBUTIONS

ZL designed the study and drafted the manuscript. All authors read, revised and approved the final version of the manuscript.

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