needed for such cases. Multiple studies have proven EBUS-TBNA to be an effective means of providing adequate samples for molecular analysis (2–5). In most of these studies, EBUS-TBNA was, in fact, performed under moderate sedation. The number of samples required from a lymph node to obtain adequate material for molecular testing remains unclear. The only available study is a retrospective review from Yarmus and colleagues that evaluated 85 patients with adenocarcinoma of the lung who underwent EBUS-TBNA (6). Molecular analysis was successfully performed in 93.5% of the cases with a median of four needle passes. In our study, we routinely performed between three and six passes per lymph node in both groups without difficulty, sampling a similar amount of targets in both groups (1). On the basis of the current literature showing that EBUS-TBNA performed under moderate sedation can provide enough material for molecular testing, and the study from Yarmus and coworkers showing that four needle passes may provide sufficient material, I respectfully disagree with Dr. Song's suggestion of the need of general anesthesia for such cases. I do, however, recognize that the influence of the type of sedation on the ability to obtain adequate material for molecular testing with EBUS-TBNA remains unclear and needs to be studied in prospective trials. ■

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Effects of Mild Chronic Obstructive Pulmonary Disease on Gas Exchange during Cycling and Walking

To the Editor:

Elbehairy and colleagues provided insightful rationale to the gas exchange abnormalities observed in patients with mild chronic obstructive pulmonary disease (COPD) during cycling exercise (1). Interestingly, some of those findings in mild COPD have also been described using self-paced assessments such as the 6-minute-walk test (2). The 6-minute-walk test is widely used by clinicians, and the addition of a portable telemetric system allows a more comprehensive assessment of a patient's response to exertion (3). We have demonstrated that in patients with mild COPD, gas exchange abnormalities (high minute ventilation to carbon dioxide production ratio and oxygen saturation drop) started at minute 1 and persisted through the duration of the test (2). This was accompanied by attenuated increases in tidal volume and a decrease in inspiratory capacity of 0.26 L, similar to what was observed during cycling (1). This mechanical constraint was accompanied by an increase in expiratory flow limitation (73.8% of tidal volume overlap). Although Elbehairy and colleagues observed similar oxygen saturation at rest and exercise peak (1), we found that oxygen saturation decreased over the duration of the 6-minute-walk test, going from 95% at rest to 91% at 6 minutes. These contrasting findings may be attributed to differential respiratory muscle activity. Body positioning during cycling may improve diaphragm force and facilitate additional engagement of the accessory muscles of respiration (4). The aggregate of these affects may lead to greater lung expansion and lower V/Q mismatch than what is observed during walking.

Calverley, in his accompanying editorial (5), stated that both functional and structural "changes in COPD happen well before we become aware of them as clinicians." Although the authors stated that computed tomographic (CT) measures of parenchymal destruction were performed, no results were reported. It would be of interest for the *Journal* readership to know some CT findings, and in particular functional–structural relationships. In our study (2), which included a CT assessment as well, those patients with the greatest emphysema and narrowest airway lumen had the greatest expiratory flow limitation and decrease in inspiratory capacity, suggesting that even mild emphysema (median, 9.1%) is related to the mechanical constraints observed in patients with mild COPD. ■

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Reply

From the Authors:

We thank Dr. Alejandro Diaz and Dr. Orlando Diaz for their interest in our recent article, which examined the effect of mild chronic obstructive pulmonary disease (COPD) on pulmonary gas exchange during cycle exercise (1). Our results contrasted with those of their previous study (2), in which significant arterial oxygen desaturation (Sa_{O_2} decreased by ~5%) was reported during the 6-minute-walk test in a group of dyspneic patients with mild COPD. Arterial oxyhemoglobin desaturation during exercise in COPD is thought to reflect the effect of a fall in mixed venous oxygen pressure ($P\bar{v}_{O_2}$) on lung units with low ventilation-perfusion ratios and shunt. The question arises: Does cycle exercise underestimate abnormalities in gas exchange during walking in mild COPD? It is noteworthy that the lack of arterial O_2 desaturation in our study patients obscured actual improvement in arterial O_2 pressure during exercise (Pa_{O_2} increased by 11 mm Hg), as previously reported by Barberà and colleagues (3). Notwithstanding intersubject heterogeneity and possible differences in the baseline physiological impairment between the two mild COPD study groups, the contrasting results raise the issue of the influence of exercise modality (cycling vs. walking) on respiratory muscle recruitment patterns and pulmonary gas exchange and in mild COPD.

To explain this difference in Sa_{O_2} between studies, Diaz and Diaz postulated that "body positioning during cycling may improve diaphragm force and facilitate additional engagement of the accessory respiratory muscles of respiration." This hypothesis could be tested by comparing pulmonary gas exchange, metabolic parameters, ventilatory mechanics, and respiratory muscle activity during incremental cycle and treadmill walking tests, using a matched linearized rise in work rate. Indeed, using this approach in more advanced COPD, previous studies have provided evidence that greater Sa_{O_2} at a given work rate or oxygen consumption during cycling versus treadmill was explained by higher alveolar ventilation as a result of earlier metabolic acidosis; that is, earlier onset of anaerobic glycolysis in the relatively overstressed quadriceps muscle during cycling (4, 5). We have confirmed these findings in patients with COPD with mild to moderate obesity and also reported greater neuromuscular efficiency of the diaphragm, greater diaphragmatic use, and less expiratory muscle activity during cycling compared with treadmill walking in this group (6). The extent to which these intermodality differences in respiratory muscle recruitment directly contributed to differences in ventilation-perfusion matching and Sa_{O_2} for a given ventilation would be difficult to determine with precision but merits further study. The evidence currently points to differences in chemostimulation between exercise modalities as the main explanation for the disparity in Sa_{O_2} between tests.

Computed tomography emphysema scoring was reported in our original article: $15 \pm 11\%$ (mean $\pm$ SD) of the patients' lungs were assessed as low attenuation areas (< -950 Hounsfield units) (1). On average, airway wall area expressed as a percentage of total airway area was $84 \pm 3\%$, and airway wall thickness assessed as the square root of the wall area of a standardized airway with an internal perimeter of 10 mm was 1.5 ± 0.3 mm. Because of the small sample size, structure–function correlations between emphysema scores and physiological dead space and between airway wall thickness and increased expiratory flow limitation were not reported. However, we did make the observation, as others have done, that high physiological dead space at rest and during exercise was present in patients with minimal or no structural emphysema, as quantified by computed tomography imaging. This suggests that mechanisms other than alveolar-capillary destruction contribute to gas exchange inefficiency in mild COPD. The mechanisms and clinical consequences of reduced pulmonary blood flow relative to ventilation in patients with mild COPD without emphysema would seem to be a fruitful area for future study. ■

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