Reply to: "Ventilatory efficiency in athletes, asthma and obesity": different ventilatory phenotypes during exercise in obesity?

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Reply to N. Borasio and co-workers:

We thank N. Borasio and co-workers for their correspondence bringing attention to their recent publications [1, 2]. The ventilatory response to exercise in patients with obesity is clearly an area of interest, as their original research articles [1, 2], along with others [3], have been published after our review article "Ventilatory efficiency in athletes, asthma and obesity" [4] was first submitted for publication.

Ventilatory efficiency after bariatric surgery: recent findings by Borasio *et al.* [2] in patients with a baseline body mass index of 43.6±5.3 $kg \cdot m^{-2}$ show that the minute ventilation (V'_E)–carbon dioxide production (V'_{CO_2}) slope was reduced following sleeve gastrectomy, while the submaximal partial pressure of end-tidal carbon dioxide (P_{ETCO_2}) at anaerobic threshold and V'_E/V'_{CO_2} at the respiratory compensation point (*i.e.* nadir) were unchanged. The V'_E/V'_{CO_2} ratio at peak exercise was not specifically reported, but can be calculated using V'_E, V'_{CO_2} and respiratory exchange ratio data reported in the published tables [2]. Using these data, the V'_E/V'_{CO_2} ratio at peak exercise appears slightly reduced after sleeve gastrectomy as compared to baseline (30.5 *versus* 29.1).

In their correspondence letter, the authors state that the V'_E/V'_{CO_2} ratio at peak exercise may be used as a clinical marker to better understand the underlying mechanisms of exercise intolerance. While we agree that V'_E/V'_{CO_2} ratio at peak exercise may be useful when evaluating responses following interventions like bariatric surgery, we want to clarify that it is not an appropriate evaluation of ventilatory efficiency, due to the instability of arterial carbon dioxide tension (P_{CO_2}) (and P_{ETCO_2}) at peak exercise, largely due to respiratory compensation at heavy metabolic demands [5–7]. To our knowledge, the prognostic utility of V'_E/V'_{CO_2} in this disease population has not been established.

Combined obesity and obstructive sleep apnoea (OSA): N. Borasio and co-workers bring up the important point that there is limited research on the ventilatory response to exercise in patients with obesity and OSA and propose that OSA can contribute to further worsening exercise tolerance in obesity. Their recently published work found that patients with concomitant obesity and OSA show evidence of blunted V'_E and higher P_{ETCO_2} at peak exercise, as compared to those without OSA and individuals with OSA receiving night-time nasal continuous positive airway pressure treatment [1]. These data are suggestive of mechanical constraint; however, additional work is required to determine the precise mechanism behind these responses.

In their correspondence, the authors suggest evaluating ΔP_{ETCO_2} (calculated as the difference between the maximum value obtained during exercise *versus* the value at peak exercise) and proposed that a threshold value may be a predictor of OSA in patients with morbid obesity. We are cautious to use P_{ETCO_2} as a clinical marker because of a lack of accuracy and suggest that temperature corrected arterial P_{CO_2} is preferred in evaluating alveolar ventilation as P_{ETCO_2} is prone to errors [5–7]. Specifically, P_{ETCO_2} may be higher than alveolar and arterial P_{CO_2} in health and obesity [8, 9], since during exercise more carbon dioxide diffuses into the alveoli as lung volumes decrease during a continued exhalation. Therefore, expiratory P_{CO_2} increases toward mixed-venous P_{CO_2} faster during exercise than at rest [5–7].

Shareable abstract (@ERSpublications)
The ventilatory response to exercise may improve after 1) bariatric surgery in morbid obesity, and 2) CPAP treatment in obesity with obstructive sleep apnoea, but the prognostic utility of minute ventilation/CO_2 production in these patients is unclear. https://bit.ly/3Gl6rHW

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We thank N. Borasio and co-workers for bringing attention to their interesting work [1, 2]. We look forward to future studies evaluating the ventilatory response to exercise in patients with obesity and various comorbidities.

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