Is ventilatory efficiency the next new thing in prehabilitation?

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The concept of “prehabilitation” is of increasing interest in surgery, and a reliable means of assessing the response to an exercise program is therefore useful. Cardiopulmonary exercise testing measures physical function to predict major outcomes after surgery.¹ Peak oxygen consumption (VO_{2peak}) is a component measurement of cardiopulmonary exercise testing used to determine operability for lung cancer.^{2,3}

Ventilatory efficiency describes the relationship between minute ventilation (VE) and CO_2 production (V_{CO_2}), which is an additional measure obtained from cardiopulmonary exercise testing. If VE rises quickly relative to V_{CO_2} production during exercise (to maintain the arterial $Paco_2$), then the VE/V_{CO_2} slope increases. An elevated slope (>35) is an independent prognostic factor in lung resection,⁴ heart failure,⁵ and chronic obstructive pulmonary disease.⁶ In their article in this issue of the *Journal*, Gravier and colleagues⁷ determine whether VE/V_{CO_2} can be improved with an exercise program.

Gravier and colleagues⁷ report their findings on patients undergoing a prehabilitation program. They retrospectively reviewed high-risk patients in an exercise program to determine whether there was a change in VE/V_{CO_2} slope after the program and, if so, whether this change was related to VO_{2peak} .

Gravier and colleagues⁷ found no change in the slope, but the VO_{2peak} increased, and there was a moderate correlation between the change in VE/V_{CO_2} slope and change in the VO_{2peak} . They conclude that the slope did not change with the exercise program, even though other measures, such as VO_{2peak} and maximum power reached (W_{peak}), changed in the expected direction.

If ventilatory efficiency is an independent predictor of major outcomes in various disease states and reflects a separate biologic phenomenon not reflected by VO_{2peak} or W_{peak} , it could serve as a target for improvement with an exercise program or a target of further study to alter prognosis. Gravier and colleagues⁷ did as well as possible with the material

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Central Message

Ventilatory efficiency may be useful to determine the response to “prehabilitation.” It remains unknown, however, whether improving ventilatory efficiency will improve important patient outcomes.

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available to them, but there are 2 issues that limit our confidence in their conclusions.

First, their study population was heterogeneous. The subjects included not only those with demonstrated limitation of pulmonary function ($VO_{2peak} < 20$ mL/kg/min) but also those thought to be at increased risk because of other comorbidities. Perhaps those with limitation in function could be expected to demonstrate improvement; however, it is not necessarily the case that the other risk group will respond similarly. Of the 50 subjects, 13 (26%) were undergoing neoadjuvant therapy (NAC). This cohort both may start at a different functional baseline from the cohort without neoadjuvant therapy and may respond differently to the intervention.

Second, Gravier and colleagues⁷ concluded that there is no relationship between slope and exercise after comparing the medians of the slope. They did, however, find a significant correlation between changes in VE/V_{CO_2} slope and VO_{2peak} . This correlation is a more sensitive analysis, because it uses all the data points available, rather than comparing medians (as they did in their other analyses showing no difference) and takes advantage of the variability in the data. According to this more sensitive analysis, the results of Gravier and colleagues⁷ could be interpreted to mean that there is indeed a change in the slope.

Ventilation efficiency may offer a new target for improvement in prehabilitation; however, a prospective study with a clearly characterized and homogeneous patient

population with a consistently applied intervention will be required before any conclusions can be drawn about whether prehabilitation can increase ventilatory efficiency. More importantly, it remains to be seen whether improving ventilatory efficiency will result in improvement in important patient outcomes.

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