Oxygen Consumption: Another Key Component in Predicting Ventilator Weaning Success

To the Editor:

I read with great interest the article by Bellani *et al.*[1] and praise their important work in the field of weaning from mechanical ventilation. More than anything, I question how the authors formed the hypothesis that oxygen consumption ($\dot{V}O_2$) increases more in patients unable to sustain decreasing ventilatory assistance. In a landmark article by Jubran *et al.*,[2] weaning failure was associated with increased oxygen extraction and decreased oxygen delivery. In the same article, the measured $\dot{V}O_2$ increased in both the success and failure from weaning groups, with a lower increase in the success group. In contrast, Zakynthinos *et al.*[3] demonstrated that patients who cannot be weaned have one of two hemodynamic and oxygen use profiles. (1) Those who fail without increasing $\dot{V}O_2$ demonstrate increased oxygen extraction and decreased oxygen delivery. (2) In those who fail and increase their $\dot{V}O_2$, the increase mainly occurs secondary to increased oxygen extraction. Direct measures of mixed venous oxygen saturation are increased in the first group and decreased in the second group, supporting their findings. Given the complex physiologic nature of respiratory weaning and weaning failure, it is widely believed that failure to wean occurs secondary to decreased oxygen delivery and increased oxygen extraction. Given the proposal of 1870 by Fick,[4] a decrease in cardiac output in combination with an increase in the arteriovenous oxygen content difference would yield a relatively stable $\dot{V}O_2$. Combining these data with those of Bellani *et al.*, it is clear that the weaning process is complex and highly variable between patients. Overall, this work supports previous studies demonstrating that there are patients who fail weaning in the absence of increased $\dot{V}O_2$.

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A High Significance Level after Analysis of Covariance in a Small-group Study?

To the Editor:

In the study by Bellani *et al.*,[1] changes of oxygen consumption ($\dot{V}O_2$) in patients, who succeeded or failed in weaning from mechanical ventilation support, were addressed. The authors rejected their original hypothesis and constructed a new theory after they analyzed their results. However, some statistical issues should first be clarified by them to better support their discussion and conclusion.

There were two main findings in their study. (1) There were no significant differences in the maximum $\dot{V}O_2$ readings between the success and the failure groups during the weaning pressure support trials. In addition, the minimum $\dot{V}O_2$ readings (when adequate pressure support was provided) in the failure group were significantly higher than in the success group ($P < 0.05$). (2) The authors further analyzed the group and pressure support effects on patients' successive $\dot{V}O_2$ data. By analysis of covariance (cited as a two-way ANOVA by the authors), significant differences were found both in the group and pressure support effects at $P < 0.001$. Accordingly, the authors concluded that the patients able to successfully complete their weaning trials were those who reacted to the decrease of ventilatory assistance with a greater increase in $\dot{V}O_2$.

A paradox exists between these two results. The statistical values increased significantly after the analysis of covariance. With an increasing P value, their analysis of covariance model probably omitted the patients' effects.[2] In other words, they probably treated a patient's successive $\dot{V}O_2$ data (these data were related) as independent $\dot{V}O_2$ data from different patients. Thus, their statistical values reached levels of less than 0.001 in such a small-group study (16 patients in the success group and 12 in the failure group). This criticism seems reasonable, especially after considering the diverse $\dot{V}O_2$ trend patterns in response to the withdrawal of pressure support (as shown in their second figure). The diverse patterns would add complexity to the determination of the pressure support effect and should decrease, rather than increase, the statistical significance.

Another statistical issue is that the authors used a correlation coefficient to access the reproducibility of $\dot{V}O_2$ measurements. The correlation coefficient is misleading. The Bland–Altman analysis is much more appropriate for assessing reproducibility.[3]