Peak VO_2 in Obesity: Is It Worth the Effort?

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Pluricellular animals have developed the availability to extract oxygen from the atmosphere in order to produce the energy necessary for locomotion. In humans, oxygen consumption can increase 10 fold from rest to maximal exercise (peak VO_2) and even up to 20 fold in athletes. This adaptation takes place within a few minutes and involves an increase in cardiac output (Q_c) together with an enhanced oxygen extraction from the muscles [1]. Normal values have been established, usually expressed as absolute O_2 consumption in L/min. However, in order to compare the performance of different individuals, peak VO_2 is often also presented as a normalized to body weight value in $\text{mL/kg} \times \text{min}$. This formulation is associated with some difficulty as VO_2 generally does not vary linearly with body mass [2]. Although obese individuals usually have a higher absolute muscle mass than lean subjects, they exhibit a lower economy during exercise, with a higher O_2 consumption for any work load [3]. This remains so on a cycle ergometer, despite that this type of exercise is less demanding for obese than the treadmill test since the excess weight is impacted less by gravity [4]. Therefore, for the same workload, obese subjects must either increase their Q_c and/or the tissue extraction for oxygen compared to nonobese individuals.

In this issue of *Respiration*, Brunani and colleagues present additional data on comparative exercise physiology in obese and lean individuals [5]. Maximal cycle-ergometer exercise was performed by 17 obese and 15 lean male subjects, matched by age and height. As expected, the maximal workload was lower in obese subjects, but peak VO_2 expressed in L/min was similar, confirming the lower energy efficiency in obese individuals. More interestingly, when VO_2 was adjusted to total body weight or to fat-free mass, peak VO_2 ($\text{mL/kg} \times \text{min}$) remained lower in obese individuals. The investigators then estimated peripheral O_2 consumption by measuring end-tidal PO_2 (PETO_2). When normalized to muscle mass, PETO_2 was also lower in obese subjects, indicating an increased tissue extraction for oxygen. This increased oxygen extraction was paralleled by a decrease in venous plasma endothelin-1 (ET-1), suggesting a role for this vasoactive peptide in the regulation of the muscular microcirculation in obese individuals. In addition, a drop in nitric oxide (NO) level was observed in lean but not in obese subjects at mid-intensity exercise. Therefore, vasoactive (ET-1) and vasodilating mediators (NO) seem to play a role in the muscular adaptive response to exercise, with an adaptive regulatory mechanism for elevated body weight. This in-

vestigation obviously leaves several unanswered questions. (1) What is the mechanism involved in this regulation? The very fast response of ET-1 is not compatible with a downregulation at the gene expression level, but could involve a decrease in cellular release, an inhibition of enzymatic activation of the precursor for ET-1, or an enhanced scavenging of the active molecule. (2) Is there a real causal relationship between modulation of these two vasoactive mediators and the level of peripheral O₂ extraction? To answer the latter question, experiments with inhibitors, such as endothelin receptor antagonist and phosphodiesterase V inhibitor, may unravel the physiological pathways involved. In addition, we may question if this change in vasoactive homeostasis is a consequence of obesity itself or is correlated to some features

of premetabolic syndrome. It should be noted that Brunani and colleagues excluded diabetic and hypertensive subjects from their young obese cohort. However, subtle endothelial dysfunction and altered insulin metabolism may predate any clinical features in this population for several years [6].

In clinical practice it is often a challenge to evaluate the level of exercise capacity in an obese subject. This is in part due to ambiguity in the prediction equations available that may or may not include body weight [7, 8]. Peak VO₂ normalized to body weight even increases the uncertainty. Brunani and colleagues remind us that the excess weight in obese subjects is not just a passive load but has a significant impact on muscular and vascular homeostasis during exercise.

References

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