



Review

Assessment of aerobic exercise capacity in obesity, which expression of oxygen uptake is the best?

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ABSTRACT

Although the impact of obesity on exercise performance is multifactorial, excessive fat mass which can impose an unfavorable burden on cardiac function and working muscle, will affect the aerobic exercise capacity. Weight loss strategies, such as bariatric surgery can obviously affect both the body composition and aerobic exercise capacity. Maximal oxygen consumption ($\dot{V}O_{2max}$) is a widely used important indicator of aerobic exercise capacity of an individual and is closely related to body weight, size and composition. An individual's aerobic exercise capacity may show different results depending on how $\dot{V}O_{2max}$ is expressed. The absolute $\dot{V}O_{2max}$ and $\dot{V}O_{2max}$ relative to body weight are the most commonly used indicators. The $\dot{V}O_{2max}$ relative to fat-free mass, lean body mass or skeletal muscle mass are not influenced by adipose tissue. The last two are more useful to precisely distinguish between individuals differing in muscle adaptation to maximum oxygen uptake. The $\dot{V}O_{2max}$ relative to body height is used for studying growth in children. With the in-depth study of exercise capacity and body composition in obesity, the relative oxygen uptake has been increasingly reinterpreted.

Introduction

Physical fitness and being overweight are generally considered incompatible, while weight-loss is associated with health and fitness.^{1–3} Aerobic exercise capacity is recognized as a strong fitness indicator and a powerful predictor of mortality^{4–9} in different populations. As an important indicator of physical fitness, aerobic exercise capacity can be best reflected by maximal oxygen uptake per minute ($\dot{V}O_{2max}$) and primarily determined by the efficiency of mechanisms supplying active muscles with oxygen from the air.¹⁰

Using the Fick Principle formula, $\dot{V}O_{2max}^{11,12} = \text{cardiac output } (CO)_{max} \times \text{peripheral arteriovenous oxygen difference } (C(a-v)O_2)_{max} = \text{heart rate } (HR)_{max} \times \text{stroke volume } (SV)_{max} \times C(a-v)O_2_{max} = \text{minute ventilation } (\dot{V}_E)_{max} \times (\text{fraction of inspiration oxygen } [FiO_2] - \text{fraction of expiration oxygen } [FeO_2])$, we recognize that $\dot{V}O_{2max}$ is determined by the respiratory system, the cardiovascular circulation and the muscle extraction/utilization of oxygen.

We need to pay attention to many factors which can affect $\dot{V}O_{2max}$, such as: body size, weight and composition,¹³ training state^{12,14,15} (type and duration of physical activity), cardiopulmonary function,^{12,16} the hemoglobin concentration in the blood,¹⁷ mitochondrial function,^{18–20}

genetic factors,^{21–23} different test methods (treadmill or cycling)^{24,25} and the protocol^{26,27} used for the assessment. The relations between fitness and cardiovascular risk factors are greatly influenced by the choice of expression (absolute, relative to body weight [BW], relative to fat-free mass [FFM]) of fitness in children and adolescents.²⁸

There is some confusion about the expression of the $\dot{V}O_{2max}$ value (absolute and relative value), when comparing individuals with different body size and composition¹⁵ (e.g., obese and normal-weight [NW] individuals, before and after bariatric surgery). To a large extent, this confusion or different interpretation of $\dot{V}O_{2max}$ results depends on the method chosen for data normalization.

Facing different research results on the determinants of aerobic exercise capacity after weight loss combined with body components analysis, how can we better interpret the values of $\dot{V}O_2$, and have more consistency and comparability in future studies?

In this paper, we discuss the modern key applications of $\dot{V}O_2$ in different expressions. The primary emphasis is on obese people, starting from the absolute value of $\dot{V}O_{2max}$ to its relative value, highlighting the recent developments on $\dot{V}O_{2max}$ corrected for body composition. For future research studies, understanding the variables in different

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expressions of $\dot{V}O_2$ will help choose, compare and discuss the variables of $\dot{V}O_2$ in obese patients following weight loss.

Literature search strategy

The literature search for this mini-review was conducted using the PubMed electronic database. The following key terms were combined, using the operators 'AND' and 'OR': [$\dot{V}O_{2max}$ OR $\dot{V}O_2$ OR absolute $\dot{V}O_{2max}$ OR relative $\dot{V}O_{2max}$ OR aerobic exercise capacity OR exercise capacity OR oxygen uptake OR maximal oxygen uptake OR performance OR fitness OR CPET] AND [obese OR obesity OR weight loss OR normal weight OR body composition OR DXA OR DEXA OR fat mass OR body fat OR TBF OR fat% OR fat percentage OR fat-free mass OR FFM OR lean mass OR LBM OR LM OR BMI OR muscle OR muscle quality] with/without AND [adults OR obese adults OR older adults OR children OR older men]. Articles involving special drug trials (except growth study) or conference abstracts were excluded.

The absolute value of $\dot{V}O_{2max}$

Absolute $\dot{V}O_{2max}$ in obese and normal weight populations

The absolute value of $\dot{V}O_{2max}$ is one of the best indices of an individual's cardiorespiratory fitness to transport oxygen to working muscles,²⁹ which reflects the individual's intrinsic aerobic exercise capacity.^{30,31} The absolute value should be reported so that a mechanistic explanation for the changes in $\dot{V}O_{2max}$, connected to the limiting factors, can be explained.³¹ Mild to moderate obese individuals have an aerobic capacity within a normal range for a given age and sex.³² However, when evaluating differences in individuals (with different body structure and composition in daily life), the absolute value will not provide a standard which will allow a clear comparison.^{33,34} In training studies and clinical interventions, the lack of improvement in $\dot{V}O_{2max}$ with training does not mean that the training program has failed or that it has elicited no adaptations.³¹

Weight loss effect on aerobic exercise capacity

"Weight loss" is a common topic in different obese populations, and different intervention strategies (such as diet, exercise, surgery) are constantly being optimized. The improvement in exercise capacity after intervention strategies was associated with improved body composition. While increased peak oxygen uptake ($\dot{V}O_{2peak}$) relative to BW has consistently been reported after bariatric surgery, surprisingly, no study has reported enhanced an absolute $\dot{V}O_{2peak}$. Indeed, previous studies have reported either unchanged or reduced intrinsic aerobic exercise capacity.^{26,35–44} Remigio et al.⁴⁵ observed that weight loss after bariatric surgery improved exercise tolerance, although the absolute $\dot{V}O_{2max}$ was decreased.^{26,40–44} This may be related to the body mass reduction and reflect decreased energy demand to perform movements, but with no real aerobic gain.^{37,46} Weight loss may have contributed to improved exercise tolerance, which may paradoxically explain the decreased cardiopulmonary function after bariatric surgery.^{37,46,47} Stegen et al.³⁹ have provided a good summary explaining why the postoperative $\dot{V}O_{2peak}$ may be reduced or be unchanged. I have quoted this below. Depending on the presence of obesity related disorders, peak exercise capacity will evolve differently in different subjects.^{48–51} Healthy obese subjects undergoing weight loss are more likely to experience a decrease in $\dot{V}O_{2max}$ and peak work output, because of decreased muscle mass³³ and daily cardiac stress. Following weight loss, lower weight-bearing daily activities lead to less cardiac stress, so before surgery carrying more weight during daily activities may be considered as training which can stimulate muscle work and cardiac stress,³³ but after surgery, BW is lower and this effect on muscle⁴¹ and heart^{44,52} fades away. Another analogy may be, backpack

hiking can stimulate the heart and muscle more than hiking with no load and thus increase the effect of exercise.^{39,52} In contrast, many obese patients struggle with obesity related disorders such as, impaired cardiac function (impaired left ventricular function and diastolic indices),^{44,53} inefficient ventilatory work (added mass on the chest wall and increased pressure in the abdomen)⁵⁴ and decreased intramyocellular lipid oxidation,^{55,56} which are associated with reduced exercise capacity. During weight loss, cardiac and pulmonary systems will improve and will probably counteract the negative effect of a decreased muscle mass. This balance can result in a stabilization or even an improvement in maximal oxygen uptake.⁴⁴

Although we can express maximal oxygen uptake as a percent-predicted value ($\dot{V}O_{2max}\%pred$) using the same predictive value formula (ignoring the differences in corrected gender, age, height, ideal weight, and actual weight in different predicted value formulas), it may be comparable between obese and NW individuals if the equation accounts for BW, but the expression of $\dot{V}O_{2max}\%pred$ may also be confusing. For example, one person's cardiopulmonary exercise tests (CPET) shows that $\dot{V}O_{2max}\%pred$ is 95%. Maybe we can think that this value is normal and satisfactory. If you know that this result comes from a professional cyclist, his $\dot{V}O_{2max}\%pred$ 6 months ago was 130%. At this time, the 95% $\dot{V}O_{2max}\%pred$ result will be worrying that his cardiopulmonary fitness is more serious than a normal sedentary individual with 88% of $\dot{V}O_{2max}\%pred$. In this example it is inappropriate to consider the former's cardiopulmonary adaptability to be superior to the latter, based on the results of $\dot{V}O_{2max}\%pred$ alone. Therefore, the reference standard of $\dot{V}O_{2max}\%pred$ also needs to consider the difference in each benchmark.

The relative value of $\dot{V}O_{2max}$

$\dot{V}O_{2max}$ relative to body weight

Since 1992, when Mancini et al. proposed that heart transplantation for patients with heart failure and an oxygen uptake of less than 14 ml/kg/min,⁵⁷ the $\dot{V}O_{2max}$ relative to BW has been the most commonly used method for expressing results of aerobic performance measurements. Adoption of $\dot{V}O_{2max}/BW$ as a criterion for cardiac transplantation supposes that $\dot{V}O_{2max}/BW$ is a reliable indicator of the severity of cardiac impairment.^{58–60} However, using this criterion in a clinical situation makes two fundamental assumptions which have not been systematically examined. The first is that $\dot{V}O_{2peak}$ is closely related and proportional to cardiac functional reserve.^{61–63} The second is that normalizing $\dot{V}O_{2max}$ with BW corrects the confounding influence of BW to allow a more equitable comparison between individuals of various body sizes.⁴⁷ $\dot{V}O_{2max}/BW$ is not generally considered a reliable indicator of cardiac fitness in all patients,⁴⁷ and it penalizes heavier individuals and women with a larger percent fat mass (FM).^{64,65} Obese heart failure (HF) patients with lower $\dot{V}O_{2max}/BW$ had stronger hearts capable of generating greater cardiac power than non-obese HF patients of equivalent clinical HF status.⁴⁷ Therefore, $\dot{V}O_{2max}/BW$ is not indicative of true cardiac fitness in obese patients.⁴⁷ Obese HF patients are in two distinct groups. The $\dot{V}O_{2max}/BW$ cannot be normalized to account for body size and composition, which creates a significant bias for obese individuals. $\dot{V}O_{2max}/BW$ is oftentimes lower in those who are obese when compared to NW individuals.^{66–68} When comparing obese individuals before and after bariatric surgery with NW control subjects, Browning et al.³⁷ found that the $\dot{V}O_{2max}/BW$ and O_2 pulse/BW were significantly greater in NW control subjects than in the obese individuals who underwent bariatric surgery (both before and after bariatric surgery). If $\dot{V}O_{2max}$ is expressed in absolute values and relative to BW, even when obesity is not a major factor, short athletes will have a higher $\dot{V}O_{2max}$ relative to BW than tall athletes.^{11,69} Fat does not participate in aerobic exercise, but it can be an encumbrance to increases in the bearing weight during exercise. High

BW, regardless of body composition, has a negative effect on aerobic capacity because of a significant negative correlation between $\dot{V}O_{2\max}/BW$ and BW, body mass index (BMI)²⁹ and fat mass% (% FM).^{70–75} The correlation between $\dot{V}O_{2\max}$ and %FM is higher than that between $\dot{V}O_{2\max}$ and BMI.^{29,71,76–78} High FM does not limit the $\dot{V}O_{2\max}$,⁷⁹ but men with similar body mass (BM) but better %FM seem to have significantly higher $\dot{V}O_{2\max}$.⁸⁰ Obesity in terms of %FM is a better parameter than BMI for prediction of low $\dot{V}O_{2\max}$ (negative correlation between %FM and $\dot{V}O_{2\max}/BW$).^{71,81–84} There was a lack of correlation between %FM and absolute $\dot{V}O_{2\max}$, while the relationship between body composition and $\dot{V}O_{2\max}/BW$ showed a relatively strong significant interdependence.^{85–87} This suggests that individuals with high BW have lower aerobic capacity,^{65,88} which does not reflect the difference in body composition. Actually, a high BW, as well as a high BMI, can be caused by an increased amount of body FM or increased muscle mass (i.e., lean mass [LM]), or both.^{88–95} Therefore, for two persons with similar LM and similar absolute values of $\dot{V}O_{2\max}$, if $\dot{V}O_{2\max}$ is expressed relative to BW the individual with lower body fat will display a higher aerobic performance. This means that high FM will display significantly lower values of $\dot{V}O_{2\max}/BW$.^{33,66} Heil showed that individuals with low BW were more likely to be categorized as having a low $\dot{V}O_{2\max}$.^{79,93} Similarly, the $\dot{V}O_{2\max}/BW$ of obese individuals could underestimate the real functional capacity of this population, leading to erroneously classify them as sick patients.^{96,97} At the same time, the effort test designed for patients with extreme obesity has limitations.⁵² During cycling ergometry, the $\dot{V}O_2$ will be displaced upwardly by 5.8 mL/min per kilogram of BW. For the treadmill, a predictable adjustment for BW is not possible because of multiple complex mechanical factors that are weight dependent.⁵²

$\dot{V}O_{2\max}$ relative to free-fat-mass

FFM is usually more stable than FM,^{98–103} thus $\dot{V}O_{2\max}/BW$ appeared to be more influenced by FM than FFM.²⁸ There was no correlation between absolute $\dot{V}O_{2\max}$ and FM, but there was a strong relationship between absolute $\dot{V}O_{2\max}$ and FFM,^{82,104} even in (obese and non-obese) boys,⁸¹ whereas the energy cost of weight-bearing activities is correlated to BW.¹⁰⁴ Vanderburgh et al.⁶⁵ reported a near zero relationship between $\dot{V}O_2$ and FFM, which suggests that the ratio imposes no bias across the range of FFM. Compared with BW, this suggests that FM does not contribute to individual variations in $\dot{V}O_2$.³³ Mondal et al.⁷¹ reported that FFM is positively correlated with $\dot{V}O_{2\max}/BW$ ($r = 0.3727$), although the correlation was not very strong, it suggests that the increase in FFM may be the reason for the increase in $\dot{V}O_{2\max}$.^{33,105,106} $\dot{V}O_{2\max}$ relative to FFM is truly independent of FM^{33,107} and also not subject to multicollinearity since it is unrelated to adiposity.¹⁰⁸ This may be the best indirect estimate of the metabolic function of lean (muscle) tissue.¹⁰⁹ These findings suggest that obese individuals do not have lower maximal aerobic capacity of their FFM compared with lean individuals or impaired cardiopulmonary responses to exercise.^{33,104,110,111} That means in obese individuals, the $\dot{V}O_{2\max}$ is low when related to actual BW, but usually normal when related to height or FFM.³³

In the literature comparing $\dot{V}O_{2\max}$ relative to FFM during running or cycling in obese and NW individuals, the data is consistent, with no limitations^{33,112} or significant reduction in obese individuals.^{113,114} The excess FM is passive tissue during exercise, and it adversely affects aerobic performance, especially during weight-bearing activities of obese individuals. Although cycling is a non-weight-bearing activity, FM can also negatively influence cycling anaerobic performance.¹¹⁵ There is no significant relationship between fat-free thigh volume and absolute maximal power, between muscle-fiber composition or fiber area and maximal power production.¹¹⁶

Thus, $\dot{V}O_{2\max}$ relative to FFM and not BW is the preferred co-variate for comparing the aerobic capacity in children and adults of different

body size and composition.^{33,65,95,108,117} It is suggested that $\dot{V}O_2$ should be normalized by FFM, since FFM is the metabolically active tissue, and FM which is not contributing to the work being performed. When comparing the physiological ability of the tissue to maximally consume oxygen, $\dot{V}O_{2\max}$ should be presented relative to FFM. On the other hand, when looking at 'endurance' or 'performance', $\dot{V}O_{2\max}$ relative to BW should be used. When the %FM is decreased by bariatric surgery, using $\dot{V}O_{2\max}/FFM$ for comparison of maximal oxygen uptake, the difference expressed by $\dot{V}O_{2\max}/BW$ between NW and post-bariatric surgery individuals disappeared.³⁷ This difference disappeared after controlling (reduction) for %FM,³⁷ which related to a greater proportion of the cardiac output being dedicated to working skeletal muscle during walking.³⁷ Future research work is needed to assess the accuracy of the use of $\dot{V}O_{2\max}$ relative to % FM.

In previous studies, the body composition analysis in regards to bariatric surgery in obese individuals showed that FM loss after surgery is concomitant to LM loss.^{36–39,42,43,52,118–120} When there is extreme weight loss after bariatric surgery, the $\dot{V}O_{2\max}/BW$ postoperative is much smaller, which will overestimate the $\dot{V}O_2$ values and does not represent the real cardiopulmonary capacity.⁴⁵ $\dot{V}O_{2\max}$ is related to better peripheral oxygen extraction by the muscle tissues, but rapid muscle mass loss might lead to deficient metabolic utilization of oxygen, thus determining impairments in cardiopulmonary capacity.⁴⁶ In addition, FFM is made up of muscles, tendons, bones, ligaments, connective tissue, blood, nerves, inner organs, and the like. After bariatric surgery, mitochondrial respiration impairment can affect a decrease in $\dot{V}O_{2\max}/FFM$, but previous studies suggest that mitochondrial respiration is preserved after bariatric surgery.^{26,37,39,42,52} The BM increase includes simultaneous increases in LM and FM. This situation occurs most frequently in obese subjects.¹²¹ In this case, obese subjects have higher absolute power than NW persons due to not only increased adiposity, but also increased LM.

The technological advancements of the dual-energy X-ray absorptiometry (DXA) promote more discussions about $\dot{V}O_{2\max}$ focus on muscle mass. DXA is a three-compartment method that distinguishes total bone mineral content from soft tissue with high precision and accuracy, dividing the latter into fat and lean body mass.^{122,123} FFM includes bone mineral content (BMC)¹²⁴ which does not participate in aerobic exercise metabolism. Maximal aerobic capacity $\dot{V}O_{2\max}$ is a major predictor of bone mass in women.¹²⁵ We have noticed that obese populations have higher BMC than NW populations, even in age-matched children and adolescents,¹²⁶ which is likely adaptive to the greater mechanical loading that results from their higher BW.¹²⁷ There was also a positive correlation between BMI and BMC.^{128,129} Therefore, we need to focus on LM determined by DXA, which is defined as FFM minus BMC.^{123,124,130} Although, it also includes non-muscle components (e.g., blood and some interstitial fluid) and DXA-based measures of LM, it may be susceptible to greater measurement error than more direct measures of muscle mass, such as computed tomography scans. LM in the appendicular regions (i.e., upper and lower limbs) primarily represents skeletal muscle.¹³¹ Higher LM, a reflection of higher muscle mass, was associated with lower mortality and with higher physical activity.¹³⁰ LM was positively correlated to whole-body peak fat oxidation, which was positively related to $\dot{V}O_{2\max}$.¹³²

Therefore, $\dot{V}O_{2\max}$ divided by body composition, especially muscle mass, may prove useful for exercise or rehabilitation programs (e.g., trainers, obesity post-bariatric surgery) that require good aerobic performance as well as strength and power determined primarily by muscle mass. For example, during cycling, in obese subjects the higher energy involved can be attributed to moving the heavier legs and to stabilizing the trunk.^{66,133}

$\dot{V}O_{2\max}$ relative to lean mass

Another suggested method for normalization is expressing $\dot{V}O_{2\max}$

relative to LM^{65,95,117} which may be a better way to make an estimation in this condition. LM and leg muscle mass (LMM) is positively correlated with absolute $\dot{V}O_{2max}$, which is confirmed by previous studies that high muscle mass (i.e., the main component of LM) resulted in increased $\dot{V}O_2$,^{25,33,79,134} and indicates the importance of the training state.⁷⁹ Individuals with similar absolute $\dot{V}O_{2max}$ may have significantly different $\dot{V}O_{2max}$ relative to BW, but may have similar $\dot{V}O_{2max}$ relative to LM.⁷⁹ There was no difference in $\dot{V}O_{2max}/LM$ between obese and non-obese children.¹³⁵ At the same time, this method of normalization shows that body composition does not affect $\dot{V}O_{2max}$ relative to LM because there is no significant correlation of $\dot{V}O_{2max}$ with BW, body composition, or BMI,^{79,115} This is an indicator of the physiological status of the cardio-respiratory system in terms of the oxidative demands of the body and does not seem to be influenced by excess FM.⁶⁶ For this reason, it is recommended to provide $\dot{V}O_{2max}$ relative to LM for comparing $\dot{V}O_{2max}$ values in individuals with different body composition, not relative to total BM.³³ Overweight or obese individuals, demonstrated that obese persons displayed similar absolute $\dot{V}O_{2max}$ and $\dot{V}O_{2max}$ relative to LM compared to individuals with normal body composition.^{33,136} In addition, previous research indicates that $\dot{V}O_{2max}$ corrected for LM improves the prognostic resolution of aerobic capacity in patients with heart failure.^{137,138}

Active muscle mass involved during exercise is highly associated with $\dot{V}O_{2max}$.²⁵ This relationship may partially explain age-related decline in $\dot{V}O_{2max}$.²⁵ Theoretically, cycling would recruit primarily only leg muscles, but other muscle groups (e.g., respiratory muscles) will also be recruited during cycling, therefore its aerobic capacity can be expressed by $\dot{V}O_{2max}/LMM$. The more muscles involved in exercise, the greater the contribution of the muscle pump to venous return and the increasing muscle mass helps increase CO. For the same individual, $\dot{V}O_{2max}$ during running has been shown to be on average 5%–8% higher than for bicycling,¹³⁹ and 20% higher during a test on the treadmill rather than on a cycloergometer.¹⁴⁰

Therefore, in this section, we also need to discuss the topic of “muscle quality”. The broad concept describing muscle quality should include glucose metabolism, oxidative damage, protein metabolism, intramuscular adipose tissue, capillary density, structural composition, contractility and fatigability.¹⁴¹ In addition, muscle quality may be built on the functions of muscle tissue such as force production, metabolism, thermoregulation and signaling/myokine production. Therefore, muscle quality is inextricably linked to the primary functions of skeletal muscle¹⁴² and is defined as the force generated by each volumetric unit of muscle tissue, which is related to muscle mass, static muscle strength, dynamic muscle strength and muscle endurance.¹⁴³ In other words, muscle quality would then be ultimately determined by the degree that muscle tissue fulfills its roles, but there is no consensus on the best way to measure muscle quality.^{142,143} Muscle architecture, composition, metabolism, fat infiltration, fibrosis, and neural activation are among the multiple factors potentially influencing muscle quality.¹⁴⁴ Muscular activity is the major source for mechanical loading of the skeleton and there is a significant relationship between bone density and muscle mass or strength.¹²⁵ The capacity to generate force relative to the mass/volume of contractile tissue (calculated as a ratio of peak force and a measure of body size, regional LM, or cross-sectional area) is a frequently used method and preferred approach to characterizing muscle quality.^{143–149} This method could be useful to comprehensively quantify physiological changes in skeletal muscle.¹⁴³ While strength alone quantifies the amount of force a muscle can generate, larger muscles are not necessarily stronger. In some situation a smaller muscle may be more effective due to more contractile proteins, less fat infiltration, or other physiological properties that can alter the quality of the muscle.^{149–151} This method

more likely reflects static muscle strength or dynamic muscle strength of one or more muscles, not the dynamic aerobic endurance capacity of several groups of muscles (muscle endurance). During hard cycling the lower limbs have multiple groups of muscles which need to be continuously expanded and contracted to complete and coordinate with each other, which results in a relatively complicated movement. This raises the question can $\dot{V}O_{2max}$ relative to LM or LMM be a better indicator to reflect muscle endurance?

Muscle mass is strongly coupled with muscle strength during the course of maturation through young adulthood,¹⁴² but the relationship between muscle mass and strength decreases in magnitude as one ages.^{152,153} The age-related loss of muscle strength may occur more rapidly than the loss of LM,^{152,153} and the adverse changes in muscle quality may precede a loss of muscle mass.¹⁴² The $\dot{V}O_{2max}/LM$ and $\dot{V}O_{2max}/LMM$ were both associated with age.²⁵ $\dot{V}O_2/LM$ has more relationship with bone density and back strength.¹²⁵ The $\dot{V}O_{2max}/skeletal\ muscle\ mass\ (SMM)$ may be considered as an indication of the “aerobic muscle quality” of the athlete's skeletal muscle, which refers to the amount of oxygen consumed per SMM.^{15,154} There is a strong negative correlation between %FM and $\dot{V}O_{2max}/SMM$, and positive relationship between SMM and absolute $\dot{V}O_{2max}$ in athletes, including sumo wrestling and untrained controls.¹⁵⁴ When the “ceiling” is reached, the increase in SMM will not result in an additional increase in absolute $\dot{V}O_{2max}$.¹⁵⁴ Pollock et al.¹⁵⁵ indicated that resistance training should not be regarded as the main training method to improve $\dot{V}O_{2max}$, but it has important value for increasing muscle strength and endurance, FFM and physical function.^{156,157} However, SMM in the study of Beekley et al. was not obtained by DXA, but calculated by an equation,¹⁵⁸ based on FFM using the subcutaneous fat measurements from ultrasound.¹⁵⁹ Although there was a negative correlation between BW and $\dot{V}O_2$ per unit of BW,^{65,160} it is not equal in heavier persons having a relatively lower oxygen uptake and hence, low aerobic capacity,^{65,88,160} when compared to lighter subjects who may have a low $\dot{V}O_{2max}$.⁹³ Like $\dot{V}O_{2max}/FFM$, $\dot{V}O_{2max}/SMM$ is not influenced by adipose tissue.¹⁰⁷ The $\dot{V}O_{2max}/LM$ or $\dot{V}O_{2max}/SMM$ can be useful as a tool to more precisely distinguish between groups or individuals differing in muscle adaptation to maximum oxygen uptake, and provide equivalent information about maximum aerobic capacity in athletes,¹⁵ but is less reported in obesity studies. In the exercise and diet study by Kitzman et al.,¹⁶¹ muscle quality was calculated as leg power/thigh muscle area (Watts/cm²) from magnetic resonance imaging (MRI). They used the absolute $\dot{V}O_{2peak}$ and $\dot{V}O_{2peak}$ related to LM, to LMM and muscle area by MRI (ml/cm²muscle/min) to evaluated the exercise performance. The field on muscle quality and aerobic exercise capacity needs further exploration.

$\dot{V}O_{2max}$ relative to body height

When $\dot{V}O_{2max}$ was compared to height, body mass and lean body mass it was apparent that the almost linear relationship with height was the most precise in children.¹⁶² Body height (BH) was more related to FFM ($r = 0.66$) than fat ($r = 0.009$) and accounts for growth and/or age.¹⁶³ Therefore, BH may be a factor to consider when scaling $\dot{V}O_{2max}$ for growth and body size.^{88,117,164} $\dot{V}O_{2max}$ relative to BH does not incorporate potential differences in muscle mass with change in height.²⁸ Although BH does not affect one's endurance capabilities,⁷⁹ it can affect total muscle mass. $\dot{V}O_{2max}/BH$ is rarely used, but is usually normal in obese individuals.³³ When discussing the aerobic capacity for patients who have had bariatric surgery (before and after) and/or when compared to matched controls, this normalizing method does not add any value, but it may make sense to use this method in growing children or adolescents. Saho et al.¹⁶⁵ found that the correlation of $\dot{V}O_{2max}/BH$ with physical

Table 1
Summary sheet regarding the advantages and disadvantages of different $\dot{V}O_{2max}$ measures.

| Variable | Advantage | Disadvantages |
|---|---|--|
| Absolute value of $\dot{V}O_{2max}$ ($L \cdot \text{min}^{-1}$) | <ul style="list-style-type: none"> - Recognized and widely used. - Reflects the intrinsic aerobic capacity.^{30,31} | <ul style="list-style-type: none"> - Cannot reflect the impact of body composition on maximal aerobic exercise capacity. - The absolute $\dot{V}O_{2max}$ in studying children is clearly not supported, because both height and weight have been shown to relate highly with $\dot{V}O_{2max}$ and serves to control for the effects of growth in children.¹⁷³ |
| Relative value of $\dot{V}O_{2max}$ | | |
| - $\dot{V}O_{2max}/BW$ ($\text{ml} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$) | <ul style="list-style-type: none"> - Easy calculated. - The most commonly used index of maximal aerobic power to compare both adult subjects and children with different body mass.¹⁶² - There was a negative correlation between BW and $\dot{V}O_{2max}/BW$.^{65,160} The $\dot{V}O_{2max}/BW$ evaluates the ability of an individual to perform exhaustive work (i.e., aerobic ‘performance’, weight-bearing aerobic capacity).³⁴ - The $\dot{V}O_{2max}/LM$ should also be considered when we examine the performance of the cardiorespiratory fitness.¹³⁵ | <ul style="list-style-type: none"> - $\dot{V}O_{2max}/BW$ has been shown to unduly penalize heavier subjects.⁶⁵ Because higher FM, as a part of BW, is due to inherent limitations of $\dot{V}O_2$ being scaled with BW by the power factor ratio of 1.⁶⁵ - Differences in $\dot{V}O_{2max}/BW$ appear to be clearer either in children or in adults varying greatly in body composition.³³ - Due to the different regression slopes before and after weight loss, the $\dot{V}O_{2max}/BW$ is not a good tool for data comparison.³³ - $\dot{V}O_{2max}/BW$ can't reflect the changes in both dimensional and functional capacities due to the growth in children.¹⁶² - Predicts better performance than the absolute $\dot{V}O_{2max}$ in competitions lasting from 60 to 90 s to several hours.¹⁷⁸ |
| - $\dot{V}O_{2max}/FFM$ ($\text{ml} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$) | <ul style="list-style-type: none"> - There was a near zero relationship between $\dot{V}O_2$ and FFM, thus the $\dot{V}O_{2max}/FFM$ imposes no bias across the range of FFM.⁶⁵ - Stronger bivariate correlation with FFM compared with BW, and the lack of a significant partial correlation with FM which contribute to no individual variation in $\dot{V}O_2$.³³ - $\dot{V}O_{2max}/FFM$ is independent of FM.^{33,107} - $\dot{V}O_{2max}/FFM$ and not $\dot{V}O_{2max}/BW$ is the preferred co-variate for comparing children and adults of different body size and body composition, even after weight loss and overweight women.³³ - May be the best indirect estimate of the metabolic capacity of the muscle.²⁸ | <ul style="list-style-type: none"> - FFM depends on body composition measurement tools (such as: bioelectrical impedance, DXA). - $\dot{V}O_{2max}/FFM$ during running or cycling in obese and NW individuals is not consistent.^{112, 113, 179-185} - May not be the best technique to scale $\dot{V}O_{2max}$ to relate to cardiometabolic risk factors in children.²⁸ |
| - $\dot{V}O_{2max}/LM$ and - $\dot{V}O_{2max}/LMM$ ($\text{ml} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$) | <ul style="list-style-type: none"> - Active muscle mass involved during exercise is highly associated with $\dot{V}O_{2max}$.²⁵ Therefore, $\dot{V}O_{2max}/LMM$ may be better for cycling, and $\dot{V}O_{2max}/LM$ for rowing.²⁵ - The $\dot{V}O_{2max}/LM$ and $\dot{V}O_{2max}/LMM$, were both associated with age.²⁵ - Muscular activity is the major source of mechanical loading of the skeleton, there is a significant relationship between bone density and muscle mass or strength.¹²⁵ Therefore, $\dot{V}O_{2max}/LM$ present more relationship with bone density and back strength.¹²⁵ - $\dot{V}O_{2max}/SMM$ is not influenced by adipose tissue.¹⁰⁷ - The $\dot{V}O_{2max}/SMM$ may be considered as an index of “aerobic muscle quality”,^{15,154} together with $\dot{V}O_{2max}/LBM$ or can be useful as a tool to more precisely distinguish between groups or individuals differing in muscle adaptation to maximum oxygen uptake, and provide equivalent information about maximum aerobic capacity in athletes.¹⁵ | <ul style="list-style-type: none"> - The accuracy of LM and LMM and SMM depends on body composition measurement tools (e.g., magnetic resonance imaging, DXA), and quality control. - Not a commonly used indicator. |
| - $\dot{V}O_{2max}/BH$ ($\text{ml} \cdot \text{cm}^{-1} \cdot \text{min}^{-1}$) | <ul style="list-style-type: none"> - Easy calculated. - Used for growth study in children. - Does not incorporate potential differences in muscle mass with change in height.²⁸ | <ul style="list-style-type: none"> - Rarely used and less reported. - Does not reflect the impact of body composition and gender differences (boys and girls). - May not be the best technique to scale $\dot{V}O_{2max}$ to relate to cardiometabolic risk factors in children.²⁸ |
| - $\dot{V}O_{2max}/BSA$ ($L \cdot \text{m}^{-2} \cdot \text{min}^{-1}$) | <ul style="list-style-type: none"> - Easy calculated. - Used in children and/or growth study. | <ul style="list-style-type: none"> - Rarely used and less reported. - May not be the best technique to scale $\dot{V}O_{2max}$ to relate to cardiometabolic risk factors in children.²⁸ - Does not take into consideration the disproportionate increases in muscle mass with increasing body size during sexual maturation.¹⁶³ |

Abbreviations: $\dot{V}O_2$: oxygen consumption; BW: body weight; FFM: fat-free mass; NW: normal weight; LM: lean mass; LMM: leg muscle mass; DXA: dual-energy X-ray absorptiometry; BH: body height; BSA: body surface area.

growth variables is high and positive in boys, but low and negative in girls.

$\dot{V}O_{2max}$ relative to body surface area

$\dot{V}O_{2max}$ relative to body surface area (BSA) appeared to be more related to body fat than FFM and does not take into consideration the disproportionate increases in muscle mass with increasing body size during sexual maturation.¹⁶³ In addition, $\dot{V}O_{2max}/BSA$ adjusted for ancestry, sex, height and body fat could provide some information on the relationship between blood pressure and $\dot{V}O_{2max}$.²⁸

Comparing $\dot{V}O_{2max}/BH$ and $\dot{V}O_{2max}/BSA$, scaling per centimeter of height adjusts for growth and is generally related to age and blood

pressure,¹⁶⁶ but scaled to BSA could be problematic because the BSA-to-mass ratio declines as children age.¹⁶⁷

$\dot{V}O_{2max}$ in adults, older adults and children

In adults, the absolute $\dot{V}O_{2max}$ was similar between obese and NW subjects,^{37,168} but $\dot{V}O_{2max}/BW$,^{37,168–170} $\dot{V}O_{2max}/FFM$ ³⁷ and $\dot{V}O_{2max}/LM$ ¹⁶⁸ were lower in obese subjects. In older untrained adults, aging inevitably affects body fat and exercise capacity. The $\dot{V}O_{2max}$ was negatively correlated with age in older obese adults.⁷⁰ Compared with lean men, obese older men had similar absolute $\dot{V}O_{2max}$ and $\dot{V}O_{2max}/FFM$, but a lower $\dot{V}O_{2max}/BW$ due to greater body fat.¹⁷¹ The $\dot{V}O_{2max}/FFM$, $\dot{V}O_{2max}/LM$ and $\dot{V}O_{2max}/SMM$ are not influenced by adipose tissue.¹⁰⁷ The $\dot{V}O_{2max}/LM$ or $\dot{V}O_{2max}/SMM$ can be useful as a

tool to more precisely distinguish between groups or individuals differing in muscle adaptation to maximum oxygen uptake,¹⁵ but is less reported in obesity studies.

In children, it is necessary to consider the influence of growth on both body fat and exercise capacity. The absolute value of $\dot{V}O_{2max}$ was positively correlated with BW and LM.¹³⁵ In normal children, absolute $\dot{V}O_{2max}$ increases roughly proportional to body size.¹⁷² The use of L/min as the unit of expression for $\dot{V}O_{2max}$ in studying children is clearly not supported, because both height and weight have been shown to relate highly with $\dot{V}O_{2max}$ and serve as a control for the effects of growth in children.¹⁷³ As known, $\dot{V}O_{2max}/BW$ is also the most commonly used index of maximal aerobic power to compare both adult subjects and children with a different body mass.¹⁶² $\dot{V}O_{2max}/BW$ remains stable throughout childhood and adolescence in males, while for females, it decreases throughout childhood and adolescence,^{173,174} but, $\dot{V}O_{2max}/BW$ can't reflect the changes in both dimensional and functional capacities due to the growth in children.¹⁶² The linear relationship between absolute $\dot{V}O_{2max}$ and BH and square of height was still evident in children, even at pre and post-pubertal stages.¹⁶² Therefore, compared with non-obese (boys), the obese have higher absolute $\dot{V}O_{2max}$ and $\dot{V}O_{2max}/BSA$, but lower $\dot{V}O_{2max}/BW$ ¹⁷⁵ and similar $\dot{V}O_{2max}/LM$.¹³⁵ There were no significant differences in $\dot{V}O_{2max}$ between the BW categories in girls. The lower overall $\dot{V}O_{2max}$ may be related to a grossly reduced oxygen utilization by adipose tissue during exercise.¹³⁵ The relationship between $\dot{V}O_{2max}$ and endurance performance is not as strong in children as in adults. This may be due to less reliable references between children and adults.¹⁷³

The above content describes the absolute and relative value of $\dot{V}O_{2max}$ in detail. Table 1 summarizes the advantages and disadvantages of different $\dot{V}O_{2max}$ measures.

$\dot{V}O_2$ at the first ventilatory threshold

Over-weight and obese individuals do not have an impaired $\dot{V}O_{2max}$, but have a reduced sub-maximal aerobic capacity.³³ After bariatric surgery, the $\dot{V}O_2$ at the first ventilatory threshold (VT1) was found to be impaired.^{26,35,44} The VT1 was determined by the V-slope and is considered to be a body mass-independent parameter as carbon dioxide production ($\dot{V}CO_2$) and $\dot{V}O_2$ are both corrected for BW.^{26,176} This reflects the activity level which triggers dyspnea and is related to quality of life. The implication is that it is physiologically more difficult for the obese individual to do the same amount of work as a NW person, at least in weight-bearing activities. This may explain why obese individuals perceive walking to be difficult, even at low intensities. Lower muscle mass and oxidative capacity can lead to a deconditioned profile with a low absolute $\dot{V}O_{2max}$ and VT1.^{18,26} VT1 is reduced in deconditioning situations when the purely aerobic performance of the muscle is reduced due to poor oxygen transport, muscular deconditioning or muscle mass loss.²⁶ Aerobic capacity can be evaluated using a maximal incremental bicycle ergometer test, where the VT1 reflects true aerobic capacity and where $\dot{V}O_{2max}$ reflects exercise capacity (maximal aerobic capacity).³⁹ Maximal oxygen uptake is determined by the oxygen transport system (pulmonary, cardiac and vascular system) and the oxidative capacity of the skeletal muscle (O_2 use in the mitochondria). The VT1 is mostly determined by the maximum oxygen uptake in subjects without severe complications.³⁹

Conclusion

Numerous studies further indicate that $\dot{V}O_{2max}$ is ahead of traditional risk factors and has been described as prognostically more important than adiposity.¹⁷⁷ The absolute $\dot{V}O_{2max}$ reflects the individual's intrinsic aerobic exercise capacity and the relative $\dot{V}O_{2max}$ reflects more the

exercise capacity during weight-bearing exercise. The $\dot{V}O_{2max}$ relative to fat-free mass, lean body mass or skeletal muscle mass is not influenced by adipose tissue, and the last two can be more useful to precisely distinguish between individuals differing in muscle adaptation versus maximum oxygen uptake. In obese individuals, the $\dot{V}O_{2max}$ is low when related to actual BW, but usually normal when related to height or FFM. Surgical weight loss does not improve the absolute $\dot{V}O_{2max}$, but a general consensus exists on the positive effect on $\dot{V}O_{2max}$ relative to body weight. Active muscle mass involved during exercise is highly associated with $\dot{V}O_{2max}$, therefore the $\dot{V}O_{2max}$ relative to lean body mass or skeletal muscle mass may be a better indicator to reflect muscle endurance in obese individuals, combined with the first ventilatory threshold which is considered to be a body mass-independent parameter and reflects the daily activity level.

Submission statement

This manuscript has not been published and is not under consideration for publication elsewhere.

Authors' contributions

NZ performed the review, drafted and revised the paper.

Conflict of interest

There are no conflicts of interest associated with this publication.

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