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The influence of appendicular skeletal muscle mass on resting metabolic equivalents in patients with cardiovascular disease: Implications for exercise training and prescription

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The metabolic equivalent (MET) is a widely used physiological concept for quantifying levels of habitual physical activity and cardiorespiratory fitness (CRF) by conveying oxygen consumption requirements of physical activities as multiples of resting or basal metabolic rate (RMR). It may also be used as a means of prescribing workload for exercise training in patient groups, including those attending cardiac rehabilitation (CR). One MET is considered equivalent to the oxygen consumed per kg of body mass at rest¹ (whilst sitting) and, due to practical issues with direct metabolic cart measurement, it is conventionally approximated as $3.5 \text{ ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$. This expression of resting energy expenditure has been incorporated within physical activity position statements and guidelines.^{2,3} However, a number of factors including age, gender, body mass (fat-free mass), cardio-metabolic health, and CRF influence RMR,⁴ which might limit the broad applicability of the conventional 1 MET at a population level. Widely prescribed cardiac medications, namely beta blockers, have also been cited to influence RMR with some inconsistent findings in males.⁵ We aimed to evaluate the potential limitations of using the estimated MET in a cohort of patients with coronary heart disease (CHD), in which we recently reported a positive association between skeletal muscle mass and peak oxygen uptake ($\dot{V}\text{O}_{2\text{peak}}$).⁶ We hypothesised that patients with lower skeletal muscle mass would also have lower RMR, determined by resting respiratory gas analysis, and this would impact on the accuracy of the aerobic exercise prescription based on METs.

In patients with diagnosed CHD, we measured resting $\dot{V}\text{O}_2$ recorded whilst lying for 15 minutes in a semi-supine position in a quiet room, following standardised instructions to avoid physical activity and limit food intake in the hours prior to testing. Patients' $\dot{V}\text{O}_2$ was continuously recorded using an Oxycon Pro metabolic gas cart (Jaeger, Hochberg, Germany). The average $\dot{V}\text{O}_2$ over the final 30 seconds of data collected was reported as the patient's RMR ($\text{ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$). Dual X-ray absorptiometry scans were conducted as previously reported.⁶ Skeletal muscle mass was expressed as appendicular lean mass (lean mass in both arms and legs) and reported as skeletal muscle index (SMI; kg m^{-2}). Maximal cardiopulmonary exercise testing using the modified Bruce protocol was

conducted as previously reported.⁶ $\dot{V}O_2$ was recorded over the last 30 seconds of each test stage, and the final 30 seconds of the symptom limited or maximal tolerance test ($\dot{V}O_{2peak}$). The $\dot{V}O_2$ at the end of stage one, and at $\dot{V}O_{2peak}$ were divided by $3.5 \text{ ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ (reference value for resting MET) to establish the estimated MET level of the stage 1 and peak exercise workload. The $\dot{V}O_2$ at the end of stage one, and at $\dot{V}O_{2peak}$ were also divided by each patient's RMR, to establish the true MET level of the graded/uphill treadmill walk.

In 70 patients with CHD (mean \pm SD; age 63.1 ± 10.0 years; male 86%; body mass 84.7 ± 13.4 kg), resting, semi-supine $\dot{V}O_2$ was lower than $3.5 \text{ ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ (mean resting $\dot{V}O_2 = 2.8 \pm 0.5 \text{ ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$; Table 1). This mean RMR is consistent with other studies in apparently healthy elderly men,⁶ and a comparable large cohort of overweight male and female patients (mean MET= $2.58 \pm 0.4 \text{ ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$) with CHD, which indicated that the $3.5 \text{ ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ significantly overestimated resting oxygen consumption by 30-35%.⁷ In our study, patients with a normal SMI had a higher resting $\dot{V}O_2$ ($2.9 \pm 0.5 \text{ ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$), than patients with a low SMI (resting $\dot{V}O_2 = 2.6 \pm 0.3 \text{ ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$).

When calculating exercise-related MET equivalents, if all patients were assumed to have a RMR of $3.5 \text{ ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$, there was no difference ($P=0.208$) in the METs required to perform stage 1 of the Mod Bruce protocol between the appendicular skeletal mass groups (low SMI group = 3.3 METs; normal SMI group = 3.6 METs). However, when a patient's RMR was used to calculate the true MET value, there was a between-group difference in METs required to perform stage 1 of the Bruce protocol (low SMI group = 5.0 METs; normal SMI group = 4.1 METs; $P=0.049$). Moreover, patients with low SMI also had a significantly lower $\dot{V}O_{2peak}$ compared to patients with normal SMI. However, patients with low SMI were older, with a total lower body mass (Table 1).

In patients with CHD, RMR was 17-26% lower than the estimated MET value of $3.5 \text{ ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$. These findings are similar to those of Savage and co-workers⁵ who showed that supine RMR was 23-36% lower, in overweight, and healthy weight patients with CHD. Our findings have important implications for exercise prescription in patients with CHD. If RMR is estimated at $3.5 \text{ ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$,

the intensity of walking over flat ground, at 2.7 km.h⁻¹ (stage 1 of the modified Bruce protocol) is 3.3 METs. However, this activity is almost 4x resting RMR in CHD patients with normal SMI, and almost 5x RMR in CHD patients with low SMI. Based on these findings we conclude that the relative intensity of physical activity is underestimated based on a conventional MET, particularly in those with lower appendicular skeletal muscle mass. It may therefore be inappropriate to estimate the intensity of exercise using existing reference values in these patients.

Further examples of how RMR can influence individual exercise prescription are as follows; If a patient has an RMR of 3.5 ml·kg⁻¹·min⁻¹, an exercise performed at a workload requiring a $\dot{V}O_2$ of 18 ml·kg⁻¹·min⁻¹ would be five times their RMR (5.1 METs).² However, an individual with a RMR of 2.6 ml·kg⁻¹·min⁻¹ (mean value in our patients with low SMI), performing the same activity would be performing it at nearly seven times their RMR, and at a vigorous intensity (6.9 METs; vigorous PA defined as >6 METs).²

Further issues arising from individual differences in RMR relate to the use of predictive equations when prescribing exercise dose. For example, the ACSM metabolic equation for walking uses the estimated resting MET value.³ Using this established ACSM equation to estimate CRF in our patient cohort would mean that estimated $\dot{V}O_{2peak}$ was 3.4% lower than actual peak $\dot{V}O_2$. This difference is 10.6% lower in patients with low SMI. This observation implies that patients with a low SMI would undertake a relatively higher dose of exercise if they were prescribed exercise as a percentage of their estimated $\dot{V}O_{2peak}$. Prescribing a higher a dose of exercise makes standardising exercise-based research studies more challenging; negatively impacting intervention compliance, and may potentially lead to increased safety concerns in these patients. We propose that accounting for individualised differences in lean mass/SMI when prescribing exercise dose may be a relevant consideration when defining CRF or prescribing exercise intensity in patients with CHD (using the METs concept). Whilst direct measurement of RMR is not possible in most exercise-based CR

programmes, skeletal muscle mass and RMR could be estimated with sufficient accuracy using bioelectrical impedance analysis/validated MET equations to identify patients with low RMR and/or SMI,¹⁰ which would allow exercise prescription to be adjusted accordingly.

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