Cardiopulmonary exercise testing and body composition

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Shareable abstract (@ERSpublications)
Respiratory exchange ratio and work efficiency are influenced by body composition while ventilatory efficiency is not. This knowledge might have implications on CPET interpretation in a population with increasing BMI. https://bit.ly/3uVa45U

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Abstract

Background The cardiopulmonary exercise test (CPET) evaluates cardiopulmonary function. In light of the obesity epidemic, it is important to understand how body composition affects interpretation of CPET results. The aim of the present study was to assess the relationship between CPET measures, other than peak oxygen uptake, and body composition.

Method A total of 330 participants, aged 50 years, performed both a CPET and dual-energy X-ray absorptiometry (DXA). From the CPET, peak exercise respiratory exchange ratio (RER), ventilatory efficiency ($\dot{V}_E/\dot{V}_{CO_2}$ slope) and work efficiency ($\Delta\dot{V}_{O_2}/\Delta WR$) were recorded. Pearson's correlation was used to assess the association between CPET measures and selected body composition measures, including body mass index (BMI), waist circumference, fat mass, lean mass, body fat percentage and percentage trunk fat to fat mass. All analyses were done stratified by sex. A p-value <0.05 defined statistical significance.

Results RER was negatively correlated with body composition measures; the strongest correlation was observed with waist circumference in females (r= −0.36). $\dot{V}_E/\dot{V}_{CO_2}$ slope had no significant correlations with any body composition measures. $\Delta\dot{V}_{O_2}/\Delta WR$ was positively correlated with the body composition measures; the strongest correlation was observed with BMI (r=0.24). The additive role of percentage body fat and percentage trunk fat were studied in a linear regression model using waist circumference and BMI to predict the aforementioned CPET measures and no additive role was found.

Conclusion RER and $\Delta\dot{V}_{O_2}/\Delta WR$ may be influenced by body composition while $\dot{V}_E/\dot{V}_{CO_2}$ slope is not affected. Adiposity measures from DXA add no additional explanatory value to the CPET measures.

Introduction

The cardiopulmonary exercise test (CPET) is a diagnostic instrument commonly employed in clinical settings to evaluate an individual's health status. It provides insight into an individual's gas exchange during exercise, aiding in the assessment of their overall physiological status [1].

Undoubtedly, one of the most extensively researched measures from CPET is peak oxygen uptake ($\dot{V}_{O_2peak}$), a measure of the maximal amount of oxygen that an individual can consume during physical activity. This metric is typically expressed in millilitres per minute ($mL\cdot min^{-1}$). In clinical practice, $\dot{V}_{O_2peak}$ is often adjusted for body size, typically achieved by dividing the value by the individual's body weight. However, other forms of scaling, such as dividing by lean mass, are also sometimes utilised.

In addition to $\dot{V}_{O_2peak}$ there are other measures obtained from the CPET that are also used in clinical practice. Some of the more common ones are ventilatory efficiency ($\dot{V}_E/\dot{V}_{CO_2}$ slope), peak exercise respiratory exchange ratio (RER), work efficiency ($\Delta\dot{V}_{O_2}/\Delta WR$) and oxygen pulse ($\dot{V}_{O_2HR}$).

There are various methods available to measure body composition. One commonly used approach is to calculate body mass index (BMI), which can easily be determined from a person's height and weight, and has been demonstrated to provide prognostic information [2]. However, other simple measures, including waist circumference, can also provide information about regional fat distribution and may be even better predictors of cardiovascular disease [3]. Waist circumference is also frequently used as a criterion in defining metabolic syndrome [4]. However, it is possible that more detailed assessments of fat distribution, *i.e.* acquired from more advanced radiology techniques, are of even more relevance in relation to CPET measures.

In contrast to $\dot{V}_{\mathrm{O_2peak}}$, the other measures mentioned are usually not interpreted with account taken of body weight. However, they may correlate with body composition, whether this is due to a direct impact of body composition or some other factor, such as training level. Clinicians interpreting CPET results should be aware of whether these results may be affected by an individual's body composition or if other explanations should be considered.

We hypothesise that individuals with more body fat, particularly visceral fat, will have higher $\dot{V}_{\mathrm{E}}/\dot{V}_{\mathrm{CO_2}}$ slope due to its association with diastolic dysfunction and lung function impairment [5–11]. Moreover, we speculate that $\dot{V}_{\mathrm{O_2HR}}$ and $\Delta\dot{V}_{\mathrm{O_2}}/\Delta\mathrm{WR}$ may also be associated with body composition through the same mechanism.

Therefore, our aim is to explore the relationship between body composition, with special emphasis on body fat, and CPET measures, focusing on other measures less thoroughly researched than $\dot{V}_{\mathrm{O_2peak}}$. In addition to using simple and easily available measures such as BMI and waist circumference, we also analysed measures obtained from dual-energy X-ray absorptiometry (DXA), which, to the best of our knowledge, have not been tested for association with the CPET measures, except for $\dot{V}_{\mathrm{O_2peak.}}$

Methods

To investigate this, we used data from the Prospective Investigation of Obesity, Energy and Metabolism (POEM) study [12]. POEM is a research project on cardiovascular and metabolic health involving a cohort of randomly invited 50-year-olds living in Uppsala, Sweden. No exclusion criteria have been employed. A total of 502 individuals were enrolled as participants in the study.

The Ethics Committee of Uppsala University approved the study. Participants gave written informed consent.

Participants were required to fast overnight before undergoing various measurements and assessments at an initial visit. Measurements including height and weight were recorded. Each participant's waist circumference was measured at the level of the umbilicus. BMI was calculated as weight divided by height squared ($\mathrm{kg \cdot m^{-2}}$). Plasma lipids were measured by standard techniques at the Department of Clinical Chemistry, Uppsala University Hospital. Leisure time physical activity was given by a questionnaire. Two questions were used: "How many times a week do you engage in light activity for 30 min?" and "How many times a week do you engage in hard exercise for 30 min?". From these two questions, four groups were defined: Sedentary (light activity only, <2 times a week), Light (light activity only, >1 times a week), Moderate (hard exercise 1 or 2 times a week) and High (hard exercise >2 times a week).

Dual-energy X-ray absorptiometry

DXA (Lunar Prodigy; GE Healthcare, Chicago, IL, USA) scans were performed during the initial visit to measure body composition. All scans were done by the same nurse and with the same equipment. Following the recommendations of the International Society for Clinical Densitometry [13], triple measurements with repositioning were obtained in a sample of 15 participants to calculate the precision error. The precision error was 1.5% for total fat and 1.0% for lean mass. Automatic edge detection was used, although manual corrections were made if necessary. The validity of fat mass derived using Lunar Prodigy has been evaluated against the four-compartment model, the tool that is currently considered the gold standard method of body composition appraisal, resulting in 1.7–2.0% higher fat mass estimates with this narrow fan-beam DXA equipment [14].

Cardiopulmonary exercise test

The participants returned non-fasted, within 1 week of DXA, for a maximal CPET on a bicycle (Ergose-lect 100/200; Ergoline, Bitz, Germany). Gas exchange was measured using the breath-by-breath technique (Oxycon Pro; Erich Jaeger, Hoechberg, Germany). The start workload was 50 W for males and 30 W for females. For both sexes, the incremental load was $10\ \mathrm{W \cdot min^{-1}}$. The participants were encouraged to continue the test for as long as possible.

The CPET measures $\dot{V}_{O_2\text{peak}}$, $\dot{V}_{O_2\text{peak}}$ scaled by body weight ($\dot{V}_{O_2\text{kg}}$), $\dot{V}_{O_2\text{peak}}$ scaled by lean mass obtained from DXA ($\dot{V}_{O_2\text{lean}}$), $\dot{V}_{O_2\text{HR}}$, $\dot{V}_E/\dot{V}_{CO_2}$ slope, $\Delta\dot{V}_{O_2}/\Delta$WR and RER were used for analysis as CPET measures.

$\dot{V}_E/\dot{V}_{CO_2}$ slope was defined with regression as the slope of ventilation ($\dot{V}_E$) and carbon dioxide production ($\dot{V}_{CO_2}$) from the start of exercise to the respiratory compensation point (if achieved) [1]. $\Delta\dot{V}_{O_2}/\Delta$WR was also calculated with regression as the slope between the start of workload to maximal exertion. $\dot{V}_{O_2\text{HR}}$ was calculated as $\dot{V}_{O_2\text{peak}}$ divided by heart rate at peak exertion.

Selection of body composition measures for analysis

Various measures of body composition were available in the POEM study. We made a pre-selection of measures for analysis, settling on BMI and waist circumference as these are easily measured and commonly available in daily clinical practice.

The selection of measures from DXA was made based on the clinical reasoning of the authors and by inspecting clusters of Spearman's correlation between measures and identifying measures with low interdependency to avoid unnecessary testing. Accordingly, total fat mass, percentage body fat and total lean mass were selected as they are considered fundamental measures, and lean mass is a commonly used measure for scaling $\dot{V}_{O_2\text{peak}}$. To approximate the difference between visceral and subcutaneous fat, we used fat in the trunk divided by fat mass (percentage trunk fat) as this measure is correlated with visceral fat [15]. Because the CPET was conducted using a leg bicycle, we also sought to determine the significance of muscle mass in the legs. Therefore, we included muscle mass in the legs (lean leg), despite its high correlation with total lean mass.

Inclusion for final analysis

There were 41 individuals who either did not undergo a CPET or had non-interpretable results likely due to technical issues. One participant had a $\dot{V}_E/\dot{V}_{CO_2}$ slope that was deemed non-interpretable and was excluded from analysis only for this specific measurement. Among the participants who did undergo a CPET, 30 did not undergo DXA and were therefore also excluded. The primary reasons for individuals not to undergo a CPET were technical issues, whereas for DXA they were time constraints or body weight exceeding the DXA scanner's capability (130 kg).

To ensure the inclusion of participants with near-maximal test results, those with RER <1 and/or a peak heart rate <85% predicted were excluded from the analysis [16]. Active smokers were also excluded due to the potential impact of smoking on ventilatory parameters.

After exclusions, 330 participants were included in the analysis: 174 males and 156 females. See figure 1 for a flowchart of the process.

Statistics

All statistical analyses were conducted using R version 4.2.2 (www.r-project.org). Table 1 was created with the tableone package [17], with normally distributed values described with means and standard deviations. After inspecting histograms and density curves we judged the CPET and body composition measures (stratified by sex) to be normally distributed.

The relationship between body composition and CPET parameters was assessed using Pearson's correlation, stratified by sex. All participants were 50-year-olds (standard deviation 0.1 years), therefore we did not adjust any models by age.

The correlation was classified as strong (r>0.5), moderate (r=0.3–0.5) or weak (r<0.3). We also adjusted the relationship between RER and body composition for peak heart rate using semipartial Pearson's correlations.

Multiple regression was performed using ordinary least squares with each measure from the CPET as the dependent variable. We fitted one model with only BMI and waist circumference as predictors, and a second full model with percentage body fat and percentage trunk fat as well. In this way, we could examine if there is any additional value of adiposity measures from the more expensive and not as commonly available DXA in prediction of CPET measures. Unadjusted R^2-values were used for comparison and a likelihood ratio test was done to test for statistical significance between the models. All participants were the same age and age adjustment was therefore not necessary. Model comparison tables were made with the stargazer package [18].

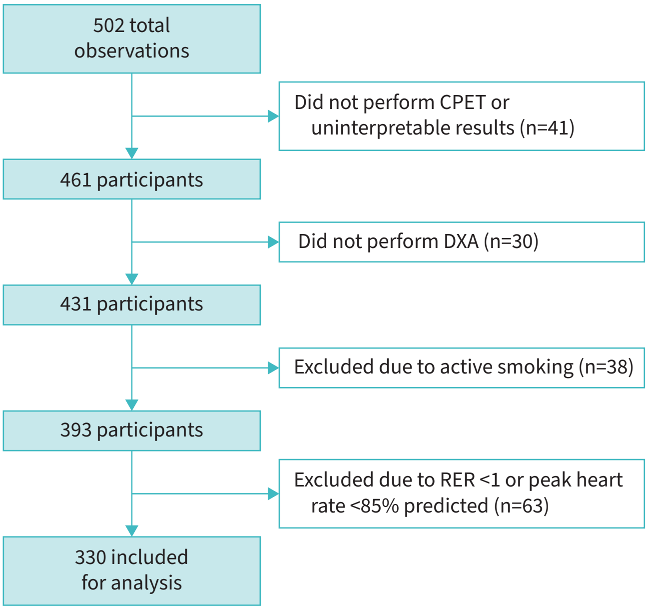

FIGURE 1 Flowchart of the steps for exclusion of participants before analysis. CPET: cardiopulmonary exercise test; DXA: dual-energy X-ray absorptiometry; RER: respiratory exchange ratio.

In all tests $p<0.05$ was considered significant.

Results

The participant characteristics are presented in table 1, separately for males and females.

Participant characteristics separated by BMI group are provided in supplementary tables S1 and S2.

There was a relatively low prevalence of participants with obesity as assessed by BMI: 19 (12.2%) females and 28 (16.1%) males. However, there was a greater prevalence of participants with a waist circumference indicating central obesity: 77 (49.4%) females and 33 (19.0%) males.

Males

Correlation coefficients and p-values between body composition and CPET measures are shown in table 2 for males.

Pearson's correlation analysis revealed a weak negative correlation between RER and all body composition measures, with the strongest correlation observed with lean leg (r= −0.23); all correlations except with total fat mass and percentage fat mass were statistically significant. The correlation pattern remained after adjustment for peak heart rate (supplementary table S3).

No statistically significant correlations were found between $\dot{V}_{\mathrm{E}}/\dot{V}_{\mathrm{CO_2}}$ slope and body composition measures.

No statistically significant correlations were found between $\Delta\dot{V}_{\mathrm{O_2}}/\Delta\mathrm{WR}$ and body composition measures.

$\dot{V}_{\mathrm{O_2peak}}$ showed a strong positive correlation with total lean mass (r=0.51) and a moderate positive correlation with lean leg (r=0.49). In addition, there was a statistically significant but weak negative correlation with fat mass.

$\dot{V}_{\mathrm{O_2HR}}$ showed a strong positive correlation with total lean mass (r=0.54) and lean leg (r=0.50). A statistically significant but weak correlation was observed with total fat mass.

Regarding $\dot{V}_{\mathrm{O_2kg}}$ there was a strong negative correlation with BMI, waist circumference and total fat mass, with the strongest correlation observed with total fat mass (r= −0.68). Furthermore, a negative moderate correlation was seen with percentage trunk fat (r= −0.23).

TABLE 1 Basic characteristics, separated by sex

	Male (n=174)	Female (n=156)
Height, cm	180.8±7.3	166.6±6.2
Weight, kg	86.4±11.5	70.8±13.5
BMI, $\mathrm{kg \cdot m^{-2}}$	26.5±3.4	25.6±4.9
BMI group		
BMI <25 $\mathrm{kg \cdot m^{-2}}$	67 (38.5)	83 (53.2)
BMI 25–30 $\mathrm{kg \cdot m^{-2}}$	79 (45.4)	54 (34.6)
BMI >30 $\mathrm{kg \cdot m^{-2}}$	28 (16.1)	19 (12.2)
Waist circumference, cm	94.5±9.1	89.1±11.4
Central obesity[#]	33 (19.0)	77 (49.4)
Total fat mass, kg	21.9±8.3	25.9±10.5
Percentage body fat, %	24.8±6.9	35.5±8.1
Fat in the trunk, kg	13.7±5.3	13.0±5.7
Percentage trunk fat, %	61.8±4.9	49.6±5.1
Total lean mass, kg	61.0±5.7	42.0±4.8
Lean leg, kg	20.4±2.3	13.7±1.9
$\dot{V}_{\mathrm{O_2peak}}$, $\mathrm{mL \cdot min^{-1}}$	2896.3±502.8	1898.5±344.4
$\dot{V}_{\mathrm{O_2kg}}$, $\mathrm{mL \cdot kg^{-1} \cdot min^{-1}}$	34.0±7.1	27.5±6.1
$\dot{V}_{\mathrm{O_2lean}}$, $\mathrm{mL \cdot kg^{-1} \cdot min^{-1}}$	47.5±7.2	45.4±7.4
$\dot{V}_{\mathrm{O_2HR}}$, $\mathrm{mL \cdot beat^{-1}}$	17.0±2.8	11.3±2.2
$\dot{V}_{\mathrm{E}}/\dot{V}_{\mathrm{CO_2}}$ slope	27.6±3.5	25.7±4.0
RER	1.1±0.1	1.1±0.1
$\Delta\dot{V}_{\mathrm{O_2}}/\Delta\mathrm{WR}$, $\mathrm{mL \cdot min^{-1} \cdot W^{-1}}$	11.4±1.2	10.2±1.0
Peak workload, W	230.7±41.6	158.4±32.1
Peak heart rate, $\mathrm{beats \cdot min^{-1}}$	170.8±12.0	167.7±10.4
Physical activity group[¶]		
Sedentary	26 (15.0)	11 (7.1)
Light	29 (16.8)	34 (22.1)
Moderate	60 (34.7)	56 (36.4)
High	58 (33.5)	53 (34.4)
Diabetes	2 (1.1)	2 (1.3)
Antihypertensive treatment	12 (6.9)	8 (5.1)
Total cholesterol, $\mathrm{mmol \cdot L^{-1}}$	5.4±1.0	5.2±0.9
LDL-cholesterol, $\mathrm{mmol \cdot L^{-1}}$	3.6±0.9	3.2±0.8

Data are presented as mean±SD or n (%). BMI: body mass index; lean leg: total lean mass in legs; $\dot{V}_{\mathrm{O_2peak}}$: peak oxygen uptake; $\dot{V}_{\mathrm{O_2kg}}$: peak oxygen uptake divided by body weight; $\dot{V}_{\mathrm{O_2lean}}$: peak oxygen uptake divided by lean mass; $\dot{V}_{\mathrm{O_2HR}}$: peak oxygen uptake divided by peak heart rate; $\dot{V}_{\mathrm{E}}$: minute ventilation; $\dot{V}_{\mathrm{CO_2}}$: carbon dioxide production; $\dot{V}_{\mathrm{E}}/\dot{V}_{\mathrm{CO_2}}$ slope: ventilatory efficiency; RER: respiratory exchange ratio; $\dot{V}_{\mathrm{O_2}}$: oxygen uptake; WR: work rate; $\Delta\dot{V}_{\mathrm{O_2}}/\Delta\mathrm{WR}$: work efficiency; LDL: low-density lipoprotein. [#]: central obesity was defined as waist circumference ⩾102 cm in males and ⩾88 cm in females; [¶]: three participants had missing physical activity data.

Finally, there was a moderate negative correlation between $\dot{V}_{\mathrm{O_2lean}}$ and BMI, waist circumference and fat mass, with the strongest correlation observed with total fat mass (r= −0.31).

Females

Correlation coefficients and p-values between body composition and CPET measures are shown in table 3 for females.

RER exhibited weak to moderate negative correlation with all body composition measures, with the strongest correlation observed with waist circumference (r= −0.36) (figure 2); all correlations except with percentage trunk fat were statistically significant. After adjustment for peak heart rate, the correlation pattern for RER remained (supplementary table S4).

No statistically significant correlations were found between $\dot{V}_{\mathrm{E}}/\dot{V}_{\mathrm{CO_2}}$ slope and body composition measures.

$\Delta\dot{V}_{\mathrm{O_2}}/\Delta\mathrm{WR}$ showed a statistically significant but weak positive correlation with BMI, waist circumference and total fat mass, with the strongest correlation observed with BMI (r=0.24) (figure 3).

$\dot{V}_{\mathrm{O_2peak}}$ exhibited a strong positive correlation with total lean mass and lean leg (r=0.57 for both).

TABLE 2 Pearson's correlation coefficients (r) and corresponding p-values between measures from cardiopulmonary exercise test measures and body composition measures: males

	RER		$\dot{V}_E/\dot{V}_{CO_2}$ slope		$\Delta\dot{V}_{O_2}/\Delta$WR		$\dot{V}_{O_2peak}$		$\dot{V}_{O_2HR}$		$\dot{V}_{O_2kg}$		$\dot{V}_{O_2lean}$	
	r	p-value	r	p-value	r	p-value	r	p-value	r	p-value	r	p-value	r	p-value
BMI	−0.16	0.04	0.08	0.29	0.14	0.07	−0.10	0.21	−0.07	0.33	−0.56	<0.001	−0.30	<0.001
Waist circumference	−0.16	0.04	0.08	0.27	0.13	0.08	−0.08	0.29	−0.05	0.47	−0.6	<0.001	−0.28	<0.001
Total fat mass	−0.13	0.08	0.08	0.29	0.12	0.12	−0.18	0.02	−0.18	0.02	−0.68	<0.001	−0.31	<0.001
Percentage fat mass	−0.08	0.31	0.07	0.33	0.08	0.31	−0.36	<0.001	−0.36	<0.001	−0.72	<0.001	−0.33	<0.001
Percentage trunk fat	−0.18	0.02	0.07	0.35	0.08	0.26	−0.04	0.57	<0.01	0.95	−0.23	0.003	−0.14	0.07
Total lean mass	−0.22	0.003	0.09	0.24	0.1	0.19	0.51	<0.001	0.54	<0.001	0.05	0.52	−0.01	0.86
Lean leg	−0.23	0.002	0.03	0.70	0.07	0.35	0.49	<0.001	0.50	<0.001	0.01	0.88	0.01	0.94

BMI: body mass index; lean leg: total lean mass in legs; $\dot{V}_{O_2peak}$: peak oxygen uptake; $\dot{V}_{O_2kg}$: peak oxygen uptake divided by body weight; $\dot{V}_{O_2lean}$: peak oxygen uptake divided by lean mass; $\dot{V}_{O_2HR}$: peak oxygen uptake divided by peak heart rate; $\dot{V}_E$: minute ventilation; $\dot{V}_{CO_2}$: carbon dioxide production; $\dot{V}_E/\dot{V}_{CO_2}$ slope: ventilatory efficiency; RER: respiratory exchange ratio; $\dot{V}_{O_2}$: oxygen uptake; WR: work rate; $\Delta\dot{V}_{O_2}/\Delta$WR: work efficiency.

$\dot{V}_{O_2HR}$ was found to have a strong positive correlation with total lean mass and lean leg (r=0.58 for both). Statistically significant but weak positive correlations were observed with BMI and waist circumference.

$\dot{V}_{O_2kg}$ showed a strong negative correlation with BMI, waist circumference, total fat mass and percentage trunk fat, with the strongest correlation observed with percentage fat mass (r= −0.69).

Lastly, $\dot{V}_{O_2lean}$ showed weak but statistically significant negative correlations with BMI, waist circumference, total fat mass and percentage trunk fat, with the strongest correlation observed with percentage trunk fat (r=0.24).

Multiple regression

There was no statistically significant added value of DXA regarding RER, $\dot{V}_E/\dot{V}_{CO_2}$ slope and $\Delta\dot{V}_{O_2}/\Delta$WR in either sex.

There was a statistically significant added value of DXA regarding $\dot{V}_{O_2lean}$ in females and $\dot{V}_{O_2peak}$, $\dot{V}_{O_2HR}$ and $\dot{V}_{O_2kg}$ in both sexes. It should be noted that the R^2 in the full model for $\dot{V}_{O_2lean}$ in females was very modest (0.080).

In contrast, the increases in R^2 for $\dot{V}_{O_2peak}$, $\dot{V}_{O_2HR}$ and $\dot{V}_{O_2kg}$ were more pronounced, and the full models showed a more robust significance; the largest increase in R^2 was observed for $\dot{V}_{O_2HR}$ in males (0.010 to 0.232).

TABLE 3 Pearson's correlation coefficients (r) and corresponding p-values between measures from cardiopulmonary exercise test measures and body composition measures: females

	RER		$\dot{V}_E/\dot{V}_{CO_2}$ slope		$\Delta\dot{V}_{O_2}/\Delta$WR		$\dot{V}_{O_2peak}$		$\dot{V}_{O_2HR}$		$\dot{V}_{O_2kg}$		$\dot{V}_{O_2lean}$	
	r	p-value	r	p-value	r	p-value	r	p-value	r	p-value	r	p-value	r	p-value
BMI	−0.35	<0.001	0.09	0.24	0.24	0.003	0.14	0.08	0.20	0.01	−0.58	<0.001	−0.17	0.03
Waist circumference	−0.36	<0.001	0.07	0.41	0.22	0.005	0.13	0.12	0.20	0.01	−0.6	<0.001	−0.19	0.02
Total fat mass	−0.30	<0.001	0.13	0.12	0.23	0.003	0.07	0.36	0.14	0.09	−0.66	<0.001	−0.16	0.04
Percentage fat mass	−0.21	0.007	0.12	0.13	0.19	0.02	−0.10	0.22	−0.05	0.55	−0.69	<0.001	−0.13	0.10
Percentage trunk fat	−0.14	0.09	0.07	0.36	0.04	0.65	−0.04	0.58	−0.04	0.63	−0.33	<0.001	−0.24	0.003
Total lean mass	−0.32	<0.001	0.14	0.09	0.18	0.03	0.57	<0.001	0.58	<0.001	−0.04	0.62	−0.05	0.53
Lean leg	−0.32	<0.001	0.11	0.17	0.17	0.04	0.57	<0.001	0.58	<0.001	−0.04	0.64	−0.01	0.90

BMI: body mass index; lean leg: total lean mass in legs; $\dot{V}_{O_2peak}$: peak oxygen uptake; $\dot{V}_{O_2kg}$: peak oxygen uptake divided by body weight; $\dot{V}_{O_2lean}$: peak oxygen uptake divided by lean mass; $\dot{V}_{O_2HR}$: peak oxygen uptake divided by peak heart rate; $\dot{V}_E$: minute ventilation; $\dot{V}_{CO_2}$: carbon dioxide production; $\dot{V}_E/\dot{V}_{CO_2}$ slope: ventilatory efficiency; RER: respiratory exchange ratio; $\dot{V}_{O_2}$: oxygen uptake; WR: work rate; $\Delta\dot{V}_{O_2}/\Delta$WR: work efficiency.

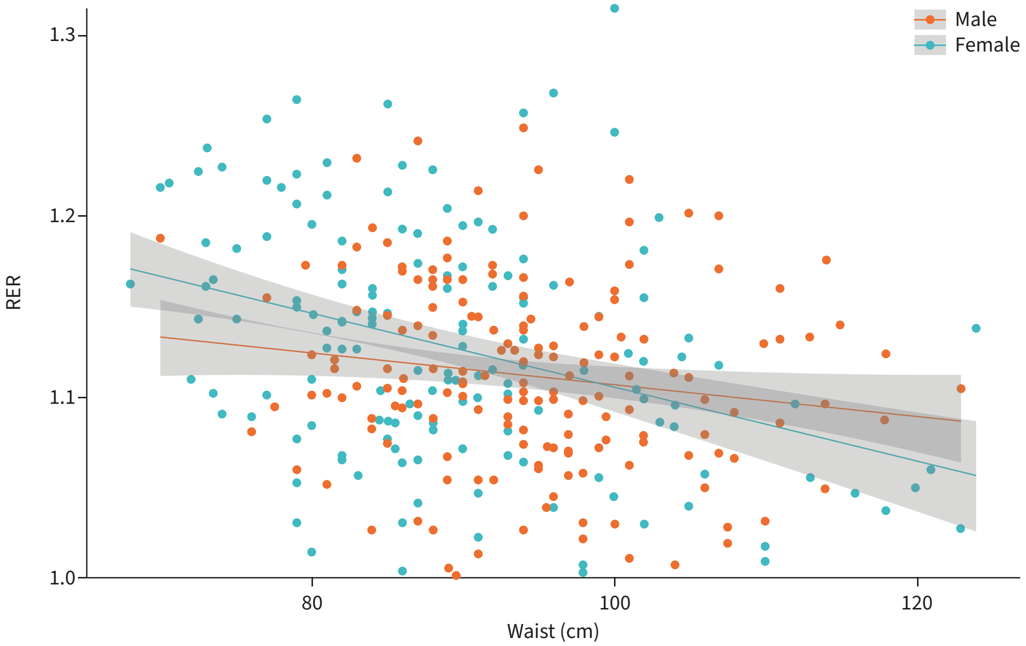

FIGURE 2 Scatter plot of respiratory exchange ratio (RER) and waist circumference. Linear regression lines stratified by sex. Grey area shows 95% confidence interval.

The R^2-values and the results of the likelihood ratio test are presented in table 4. Supplementary tables S5 and S6 present detailed results of the models for $\dot{V}_{O_2peak}$ and $\dot{V}_{O_2kg}$.

Interaction test

Multiplicative interaction terms between sex and body composition measures to predict $\Delta\dot{V}_{O_2}/\Delta WR$ did not show statistical significance for any of the models (supplementary table S7).

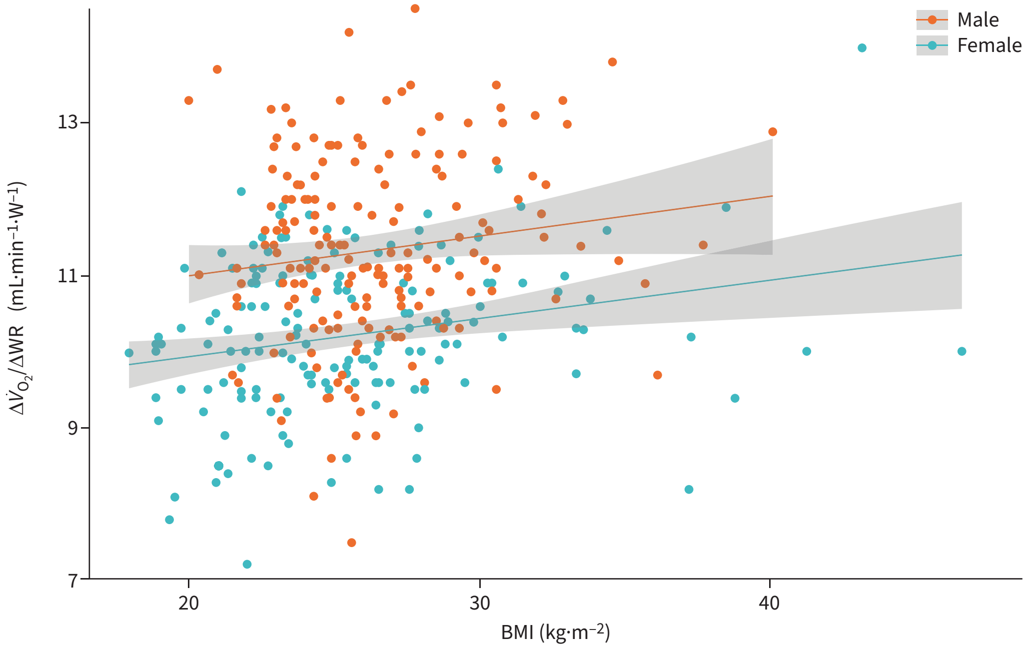

FIGURE 3 Scatter plot of work efficiency (increase in oxygen uptake to work rate increment ($\Delta\dot{V}_{O_2}/\Delta WR$)) and body mass index (BMI). Linear regression lines stratified by sex. Grey area shows 95% confidence interval.

TABLE 4 Comparison between the reduced model (model 1) with waist circumference and body mass index and the full model (model 2) including dual-energy X-ray absorptiometry measures for predicting cardiopulmonary exercise test measures

	Male			Female		
	R^2 (Model 1)	R^2 (Model 2)	χ^2 (p-value)	R^2 (Model 1)	R^2 (Model 2)	χ^2 (p-value)
RER	0.025	0.042	3.07 (0.215)	0.132	0.157	4.47 (0.107)
$\dot{V}_E/\dot{V}_{CO_2}$ slope	0.006	0.010	0.77 (0.679)	0.011	0.025	2.41 (0.299)
$\Delta\dot{V}_{O_2}/\Delta WR$	0.017	0.018	0.17 (0.918)	0.058	0.061	0.42 (0.809)
$\dot{V}_{O_2peak}$	0.014	0.209	38.24 (<0.001)	0.012	0.167	26.62 (<0.001)
$\dot{V}_{O_2HR}$	0.010	0.232	44.20 (<0.001)	0.035	0.216	32.39 (<0.001)
$\dot{V}_{O_2kg}$	0.402	0.514	36.20 (<0.001)	0.378	0.507	36.35 (<0.001)
$\dot{V}_{O_2lean}$	0.093	0.113	3.90 (0.142)	0.039	0.080	6.80 (0.033)

R^2: unadjusted coefficient of determination. χ^2: Chi-squared value obtained from likelihood ratio test for model comparison; RER: respiratory exchange ratio; $\dot{V}_E$: minute ventilation; $\dot{V}_{CO_2}$: carbon dioxide production; $\dot{V}_E/\dot{V}_{CO_2}$ slope: ventilatory efficiency; $\dot{V}_{O_2}$: oxygen uptake; WR: work rate; $\Delta\dot{V}_{O_2}/\Delta WR$: work efficiency; $\dot{V}_{O_2peak}$: peak oxygen uptake; $\dot{V}_{O_2HR}$: peak oxygen uptake divided by peak heart rate; $\dot{V}_{O_2kg}$: peak oxygen uptake divided by body weight; $\dot{V}_{O_2lean}$: peak oxygen uptake divided by lean mass.

Discussion

The main findings of our study were that the correlations between CPET measures, apart from $\dot{V}_{O_2peak}$ and its scaled versions, and body composition were in general weak. There was no apparent correlation between body composition and $\dot{V}_E/\dot{V}_{CO_2}$ slope, and there was no additional value of DXA in predicting CPET measures, except for $\dot{V}_{O_2peak}$ and its scaled versions.

The correlations between CPET measures, apart from $\dot{V}_{O_2peak}$ and its scaled versions, and body composition were in general weak. In both males and females, RER had negative correlations with all body composition measures. Despite our exclusion of participants with signs of submaximal effort, it might be speculated that the observed correlations could be attributed to lower effort levels. It is possible that individuals with larger body size and greater adiposity are less habituated to exercise, which could make it more difficult for them to attain their maximum effort. However, adjusted models for peak heart rate showed similar results. There are also previous studies that have indicated lower RER in participants with obesity [19, 20]. This may be clinically relevant as RER above a certain cut-off is used as a proxy for optimal CPET.

Our findings indicate that in females, but not in males, there is a weak correlation between $\Delta\dot{V}_{O_2}/\Delta WR$ and all body composition measures except percentage trunk fat. However, when testing for interaction between the sexes, no statistically significant differences were found. The relationship between the rate of oxygen uptake ($\dot{V}_{O_2}$) and workload has previously been regarded to be shifted upwards in individuals with higher body weight, *i.e.* a higher intercept and higher oxygen uptake per workload. However, it has been reported that the slope of the relationship, $\Delta\dot{V}_{O_2}/\Delta WR$, is independent of body weight [1, 21, 22].

Our study did not show any relationship between $\dot{V}_E/\dot{V}_{CO_2}$ slope and body composition. There are several previous studies that have examined the association between obesity and $\dot{V}_E/\dot{V}_{CO_2}$ slope and did not find any associations [20, 21, 23]. However, one study demonstrated that females with severe obesity had a higher $\dot{V}_E/\dot{V}_{CO_2}$ slope than physically active females without obesity [24]. Research has established a relationship between fat mass and visceral fat with diastolic dysfunction [9, 10]. In addition, these factors have also been found to affect lung function, especially function residual capacity [5–8, 11]. Thus, it might be plausible that fat mass or visceral fat can have an impact on $\dot{V}_E/\dot{V}_{CO_2}$ slope, which is commonly elevated in patients with heart failure or lung disease. Our study did not show such an effect. Based on our results, it is important to highlight that a high $\dot{V}_E/\dot{V}_{CO_2}$ slope should therefore not be attributed to variations in body composition; other possible explanations should be taken into consideration.

The added value of DXA in predicting CPET measures, except for $\dot{V}_{O_2peak}$ and its scaled versions, was non-existent or low. As RER, $\dot{V}_E/\dot{V}_{CO_2}$ slope and $\Delta\dot{V}_{O_2}/\Delta WR$ only had very weak correlations with all body composition measures, the explanatory values (R^2-values) of the multiple regression models were also low and became not significantly higher when including adiposity measures from DXA. This suggests that adiposity measures from the more expensive, time-consuming and more technically demanding DXA method were not able to provide additional explanatory value above waist circumference and BMI. This strengthens the findings that these measures are less dependent on body composition.

In both males and females, $\dot{V}_{O_2peak}$ had the strongest correlation with lean mass. This is consistent with previous studies [25–28]. Lean mass and lean leg exhibited similar correlation patterns, and based on our analysis can essentially be used interchangeably. As a consequence of all participants being the same age and therefore having the same expected maximum heart rate, the correlation patterns between $\dot{V}_{O_2peak}$ and $\dot{V}_{O_2HR}$ were found to be nearly identical.

In our study, $\dot{V}_{O_2kg}$ was strongly correlated with BMI and body fat-related measures. Furthermore, the inclusion of measures from DXA in the regression models for predicting $\dot{V}_{O_2kg}$ could explain approximately an additional 30% of the variance, in both males and females. Scaling by body weight has been suggested to result in overcorrection in larger individuals and our results provide support for this notion [24, 28–30]. Allometric methods have been proposed as an alternative approach, in which the denominator, typically body weight, is raised to a power (*e.g.* 2/3) [29–32]. However, one study with a large sample size (more than 300 000 individuals) did not identify any clear advantage of allometric scaling compared with ordinary ratio scaling in predicting cardiovascular disease risk and all-cause mortality [33]. Scaling $\dot{V}_{O_2peak}$ by total lean mass has also been suggested to be a better alternative to assess cardiorespiratory fitness as skeletal muscle mass is to a large extent responsible for the increased metabolic demands during exercise [1]. This method does not seem to be as biased in larger individuals [25, 26, 29, 30, 34]. In addition, scaling by lean mass has in one study been shown to be a better predictor of all-cause mortality than scaling by body weight [35]. In our study, the absence of any correlation between $\dot{V}_{O_2lean}$ and lean mass supports there being no bias with this form of scaling for individuals with larger lean mass. This is also consistent with studies of allometric scaling methods which suggest that the exponent for scaling by lean mass is close to 1 [32]. However, the negative correlation between $\dot{V}_{O_2lean}$ and most of the fat measures, including percentage trunk fat, is noteworthy. A likely explanation for this observation is an association between higher levels of body fat, including visceral fat, and lower levels of physical activity.

Strengths and limitations

A major strength of our study is that we had a relatively large sample of participants who underwent both DXA and CPET. A potential limitation of our study is that only 14% of the study population were obese, based on BMI. However, this reflected the random population sample of study participants and therefore results should be representative for the Uppsala population of 50-year-old individuals. It is possible that some effects may not be linear and may be apparent only in individuals from high BMI categories. In an attempt to assess the impact of visceral fat, we used waist circumference and percentage trunk fat. However, these markers are not optimal, as they depend on both visceral and subcutaneous fat. This limitation arises from the fact that DXA is unable to measure visceral fat directly. Therefore, a study utilising computed tomography or magnetic resonance imaging to quantify visceral fat would add further knowledge about its impact on CPET measures. Lastly, all analyses were cross-sectional and we can therefore only report correlations; no conclusions can be drawn with regard to causality.

Conclusions

Several key findings have emerged from this study. First, the correlations between CPET and body composition, except for $\dot{V}_{O_2peak}$ and its scaled versions, are in general weak. Second, we observed that $\dot{V}_E/\dot{V}_{CO_2}$ slope did not vary significantly with differences in body composition. Therefore, clinicians should avoid attributing a high $\dot{V}_E/\dot{V}_{CO_2}$ slope to variations in body composition and explore other potential explanations. Finally, adiposity measures from DXA offer very limited added value in predicting CPET measures, except for $\dot{V}_{O_2peak}$ and its scaled versions, compared with only BMI and waist circumference.

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