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Using the HR-$\dot{V}O_2$ relationship in prescribing aerobic exercise intensity: examining the true nature of the association between HR and $\dot{V}O_2$ during incremental exercise and its transferability to steady-state exercise

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Contents

Preface

Cardiorespiratory fitness is positively associated with health status, and structured individually tailored aerobic exercise training programs are universally recommended to improve cardiorespiratory fitness.[1-4] Structuring an aerobic exercise program involves the manipulation of several parameters[5] related to both the overall training regimen (e.g., weekly exercise frequency, volume, progression, etc.) and the single exercise session (e.g., duration, intensity, etc.). Intensity is a fundamental consideration when tailoring an aerobic exercise prescription: low intensity is considered safe but may be insufficient to elicit the biological responses necessary to improve cardiorespiratory fitness,[6] whereas vigorous intensity, although effective in improving cardiorespiratory fitness, may increase the health risks associated with exercise when individuals are not accustomed to it.[5]

Aerobic exercise intensity is usually prescribed and monitored with parameters calculated using either oxygen uptake ($\dot{V}O_2$) or heart rate (HR), both of which increase with increasing aerobic exercise intensity. Studies investigating the association between $\dot{V}O_2$ and HR have generally found a linear relationship when values were expressed as percentages of maximal $\dot{V}O_2$ ($\dot{V}O_{2max}$) and maximal HR (HR_{max}), respectively.[7-11] However, the relationship between $\%\dot{V}O_{2max}$ and $\%HR_{max}$ may be affected by inter-individual differences in the maximal[12] and/or resting values. On the contrary, using the 'reserve' values, i.e., the difference between maximal and resting values, allows the correction for nonzero resting values.

The concept of reserve, which was introduced by Karvonen for HR,[13] was applied to $\dot{V}O_2$ by Swain & Leutholtz[12] in light of the previous findings of Davis & Convertino.[14] These investigations, focusing on young adults, showed that: I) the percentages of the reserve values of $\dot{V}O_2$ ($\%\dot{V}O_2R$) and HR (%HRR) did not differ significantly at four different exercise intensities;[14] II) $\%\dot{V}O_2R$ and %HRR were strongly correlated and their regression was not distinguishable from the line of identity, i.e., slope = 1 and intercept = 0.[12] Subsequent studies confirmed that $\%\dot{V}O_2R$ and %HRR regressions did not differ significantly from the line of identity in healthy subjects,[15, 16] in myocardial infarction,[17] obese,[18] and diabetic[19] patients or in elite amateur and professional cyclists.[20]

The actual association between $\%\dot{V}O_2R$ and %HRR, however, has always been questionable. Indeed, in 1998, Swain et al.[21] found that regression parameters differed significantly from those of the identity line in healthy adults, and the same discrepancies have since been found in children and adolescents,[22] in overweight and obese pregnant women,[23] and in obese,[24] CHF,[16, 17] CAD,[17] and heart transplant[25] patients. Cunha et al.[26] obtained mixed results in healthy adults, and found that the $\%\dot{V}O_2R$-%HRR relationship was significantly affected by the exercise testing protocol that was used. Importantly, they also found that %HRR was more closely associated with $\%\dot{V}O_{2max}$ than it was with $\%\dot{V}O_2R$,[26] confirming the results of a previous study.[22] The conflicting nature of the aforementioned results have often been attributed to methodological biases, namely the different methods used to assess the resting and maximal values of $\dot{V}O_2$ and HR and the differences among the incremental exercise protocols adopted.[26] Nonetheless, since 1998[27] the regression between $\%VO_2R$ and %HRR has been widely accepted as non-significantly different from the line of identity. Indeed, the latest position stand of the American College of Sports Medicine (ACSM)[6] are also based on the 1:1 relationship between the percentages of the HRR and $\dot{V}O_2R$, and therefore recommend using the reserve values in prescribing aerobic intensity during steady-state exercise.

To date, the nature of the association between HR and $\dot{V}O_2$ and their true relationship, either during incremental or steady-state exercise, have yet to be examined properly. Therefore, the overall aim of the present work was to investigate the HR-$\dot{V}O_2$ relationships under different exercise conditions, overcoming the methodological limitations of the studies reported in the literature. We conducted four separate investigations. In the first two, we focused on incremental exercise, whereas in the following two studies the issue of the transferability of the HRR-$\dot{V}O_2R$ relationship from incremental to steady-state exercise was addressed.

In Studies 1 and 2, the relationship between HR and $\dot{V}O_2$ and the potential influence of an individual's particular characteristics on those relationships, were investigated using the large heterogenous dataset provided by the HERITAGE Family Study[28]. The main aims of the first study (Study 1) were to identify the actual relationship between %HRR and $\%\dot{V}O_2R$ and between %HRR and $\%\dot{V}O_{2max}$ and to assess if those relationships are equal to the identity line (i.e., intercept = 0 and slope = 1). The results of Study 1 showed that both the %HRR-$\%\dot{V}O_2R$ and %HRR-$\%\dot{V}O_{2max}$ relationships (i.e., the individual linear regressions derived from an incremental exercise test) were different from the identity line (i.e., $y = x$). Importantly, the intercepts and the slopes of the regressions, for both relationships, presented high standard deviations (SD). This indicates high variability among individuals and can lead to substantial error when the relationship is used to predict HR and/or $\dot{V}O_2$ values for a single subject. We hypothesized that the high variability found in Study 1 may be the result of the heterogeneity of the HERITAGE study participants (age, gender, fat mass, cardiorespiratory fitness, etc.). Study 2 was therefore designed to assess the potential confounding effect of several characteristics of the HERITAGE study participants on the relationship (i.e., slopes and intercepts) between the percentages of the HRR and $\dot{V}O_2R$. Hence, the aim of Study 2 was to use those variables as predictors to increase the accuracy of the %HRR vs. % $\dot{V}O_2R$ relationship.

The final two studies encompassed in this work aimed to assess if the HR-$\dot{V}O_2$ relationships currently adopted can be used in steady-state exercise conditions. Indeed, the relationships between HR and $\dot{V}O_2$ are based on studies that used incremental exercise protocols, yet these relationships based on such protocols are commonly used in prescribing the intensity of steady-state aerobic exercise.[5] This is a controversial topic[29-31] since during prolonged steady-state exercise several acute physiological adjustments occur, such as cardiovascular drift and $\dot{V}O_2$ slow component,[29] which can affect the relationships found during incremental exercise. Therefore, in STUDY 3 the reliability of the 1:1 relationship between %HRR and $\%\dot{V}O_2R$ and the transferability of $\%HRR\text{-}\%\dot{V}O_2R$ relationship from incremental to steady-state exercise were investigated using the results of the steady-state tests of the HERITAGE study, which were performed at a fixed power output and a fixed relative exercise intensity. The maximum duration of the steady-state exercises in STUDY 3 was 15 minutes. Since exercise duration and intensity are possible confounding effects of the HR-$\dot{V}O_2$ relationship,[29] STUDY 4 was designed to assess if different intensities and durations of steady-state aerobic exercise can affect the $\%HRR\text{-}\%\dot{V}O_2R$ relationship.

The findings of the present work may be used to either confirm or revise the current physical activity guidelines for prescribing aerobic exercise intensity, which could result in more tailored and therefore effective aerobic exercise training prescriptions.

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STUDY 1

The percentages of heart rate reserve and oxygen uptake reserve are not equivalent during incremental exercise and the percentages of heart rate reserve more closely reflect those of maximal oxygen uptake rather than oxygen uptake reserve

Introduction

Cardiorespiratory fitness is positively associated with health status, and structured and individually tailored aerobic exercise training programs are universally recommended to improve cardiorespiratory fitness .[1-4] Structuring an aerobic exercise program involves the manipulation of several parameters[5] related to both the overall training regimen (e.g., weekly exercise frequency, volume, progression, etc.) and the single exercise session (e.g., duration, intensity, etc.). Intensity is a fundamental consideration when tailoring an aerobic exercise prescription: low intensity is considered safe but may be insufficient to elicit the biological responses necessary to improve cardiorespiratory fitness,[6] whereas vigorous intensity, although effective in improving cardiorespiratory fitness, may increase the health risks associated with exercise when individuals are not accustomed to it.[5]

Aerobic exercise intensity is usually prescribed and monitored with parameters calculated using either oxygen uptake ($\dot{V}O_2$) or heart rate (HR), both of which increase with increasing aerobic exercise intensity. Studies investigating the association between $\dot{V}O_2$ and HR have generally found a linear relationship when values were expressed as percentages of maximal $\dot{V}O_2$ ($\dot{V}O_{2max}$) and maximal HR (HR_{max}), respectively.[7-11] However, the relationship between $\%\dot{V}O_{2max}$ and $\%HR_{max}$ may be affected by inter-individual differences in the maximal[12] and/or resting values. On the contrary, using the 'reserve' values, i.e., the difference between maximal and resting values, allows the correction for nonzero resting values. The concept of reserve, which was introduced by Karvonen for HR,[13] was applied to $\dot{V}O_2$ by Swain & Leutholtz[12] in light of previous findings of Davis & Convertino.[14] These investigations, focusing on young adults, showed that: i) the percentages of the reserve values of $\dot{V}O_2$ ($\%\dot{V}O_2R$) and HR (%HRR) did not differ significantly at four different exercise intensities;[14] ii) $\%\dot{V}O_2R$ and %HRR were strongly correlated and their regression was not distinguishable from the line of identity, i.e., slope = 1 and intercept = 0.[12] Subsequent studies confirmed that %$\dot{V}O_2R$ and %HRR regressions did not significantly differ from the line of identity in healthy subjects,[15, 16] in myocardial infarction,[17] obese,[18] and diabetic[19] patients or in elite amateur and professional cyclists.[20]

The actual association between %$\dot{V}O_2R$ and %HRR, however, has been questioned in other reports. Swain et al.[21] in 1998, found that regression parameters differed significantly from those of the identity line in healthy adults and, subsequently, the same discrepancies have been found in children and adolescents,[22] in overweight and obese pregnant women,[23] and in obese,[24] CHF,[16, 17]CAD,[17] and heart transplant recipient[25] patients. Cunha et al.[26] obtained mixed results in healthy adults, and found that the %$\dot{V}O_2R$-%HRR relationship was significantly affected by the exercise testing protocol used. Importantly, they also found that %HRR was more closely associated with %$\dot{V}O_{2max}$ than it was with %$\dot{V}O_2R$,[26] confirming the results of a previous study.[22]

Nonetheless, since 1998[27] the regression between %$\dot{V}O_2R$ and %HRR has been widely accepted as non-significantly different from the line of identity, as reported in the latest position stand by the ACSM.[5] Therefore, the main aim of the present study was to assess the actual relationships between %HRR and %$\dot{V}O_2R$ and between %HRR and %$\dot{V}O_{2max}$ using the large dataset of the HERITAGE Family Study.[28]

Methods

Sample

The sample of the present investigation was composed of 741 members of Caucasian and African American families participating in the pre-training assessments of the HERITAGE Study (see Bouchard et al.[28] for details regarding ethical approval, inclusion and exclusion criteria, and study design).

All the subjects enrolled in the HERITAGE study, ranging in age from 17 to 65, were healthy, i.e., with no significant medical conditions or diseases. They were sedentary, i.e., they had not engaged in regular physical activity in the previous 6 months, and were not taking any medications that could affect resting and/or exercise HR.

HERITAGE study assessments

The design of the HERITAGE study included several exercise and non-exercise tests performed before and after an aerobic exercise training intervention. In the present study, only baseline (body weight and pre-exercise HR) and exercise testing ($\dot{V}O_{2max}$ tests) data of selected pre-training assessments were used (see below).

Body weight and pre-exercise heart rate

Body mass was measured to the nearest 0.1 kg using a balance beam scale. Resting HR (HR_{rest}) was measured both immediately before the exercise test and at the end of a 5-min rest period with the subject sitting quietly in a chair.

Maximal oxygen uptake

Participants' $\dot{V}O_{2max}$ was defined based on the results of two cardiorespiratory fitness tests. First, a continuous, incremental exercise test to exhaustion (T1) was performed on a cycle ergometer (model 800S – Sensor Medics, Yorba Linda, CA, USA) connected to a mixing-chamber metabolic cart (model 2900 – Sensor Medics, Yorba Linda, CA, USA). In the first 3-min stage, participants pedalled at 50 W, then the resistance of the ergometer was increased by 25 W every 2 minutes until volitional exhaustion (in older, smaller, or less fit subjects, starting the test with a lower power output and/or making smaller increases every 2 minutes was permitted). At least 48 hours later, a submaximal, steady-state exercise test, followed by a progressive test to maximum (T2) was performed. After the first phase of the test (which is not relevant to the present investigation but involved having the subjects exercise at a steady-state intensity of about 60% of the $\dot{V}O_{2max}$ measured in T1), participants peddled for 3 minutes at the power output corresponding to 80% of the $\dot{V}O_{2max}$ measured in T1. Thereafter, a 2-min stage at the highest power output attained in T1 was performed, and the resistance was then increased, if necessary, by the same increment used in T1, every 2 minutes until volitional exhaustion. Since the cycle ergometer was able to keep the PO constant regardless of the pedalling frequency, each participant was allowed to choose his/her own "comfortable" cadence (usually around 60 rpm), which was noted and used in both T1 and T2.

In both tests, $\dot{V}O_2$ (along with other gas exchange variables that were not used in the present investigation) was determined every 20 seconds and retained for subsequent analysis as the average of the last three 20-s values of each stage, whereas HR was measured continuously by means of ECG (in order to confirm HR, ECG rhythm strips were taken within the last 15 seconds of each stage and at maximum).

The criteria used for the attainment of $\dot{V}O_{2max}$ were: a *plateau* in $\dot{V}O_2$ (a change <100 mL·min^{-1} in the last three consecutive 20-s intervals); a HR within 10 bpm of the age-predicted HR_{max}; a respiratory exchange ratio >1.1. All participants met at least one of these criteria in one of the two tests,[29] but most subjects met two or more.[30] Hence, when the $\dot{V}O_2$ peak of only one test met at least one criterion, it was assumed to be the $\dot{V}O_{2max}$. When both T1 and T2 $\dot{V}O_2$ peaks met the criteria and the values were within 5% of each other, their average was calculated and assumed to be the $\dot{V}O_{2max}$; otherwise, the highest value was assumed to be the $\dot{V}O_{2max}$[29] HR_{max} was assumed to be the highest value attained during either of the two maximal exercise tests.

Study dataset implementation

Before performing the calculations necessary to implement the dataset used in the present study, the HERITAGE study data were screened and filtered.

HERITAGE study dataset screening and filtering

Since only a few subjects were under the age of 17, only the records of the participants who were 17 or older were retained. Moreover, participants whose records had missing data in the $\dot{V}O_{2max}$ (and/or body weight), HR_{rest}, or HR_{max} fields were excluded. Subsequently, each stage of the T1 was inspected and deleted if either the $\dot{V}O_2$ or the HR fields were missing. Finally, the data integrity of all the above-mentioned variables was assessed by means of range checks: when implausible physiological data were found, the whole participant record and/or the relevant stage/s of the T1 were excluded (see Figure 1 for details).

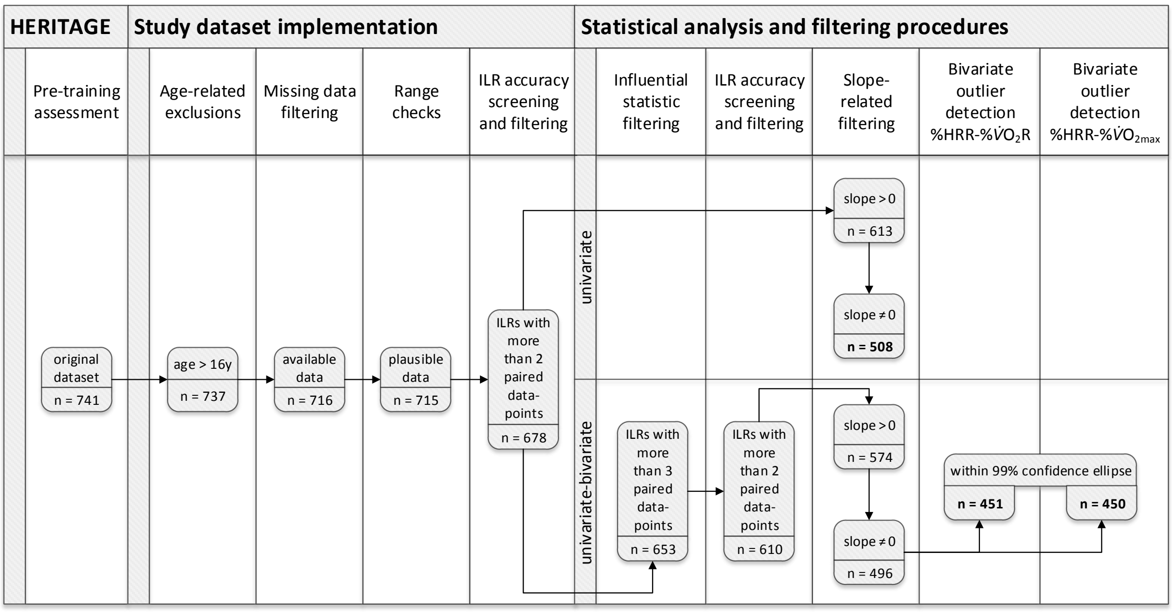

Figure 1. Flowchart illustrating the number of subjects (n) retained after each step of the screening and filtering procedures applied to the original HERITAGE Family Study dataset. ILR, individual linear regression.

Data preparation and processing

Each $\dot{V}O_2$ and HR recorded for each stage of the T1 was computed as a percentage of both the reserve and maximal values using, respectively, the following two formulae: i) 100 x (recorded value – resting value) / (maximal value – resting value); ii) 100 x recorded value / maximal value. In the calculation of %$\dot{V}O_2R$, the $\dot{V}O_{2max}$ was retrieved from the HERITAGE study dataset, whereas the resting $\dot{V}O_2$ was assumed to be 3.5 $mL \cdot min^{-1} \cdot kg^{-1}$, as suggested by the current ACSM guidelines[5] (all values had been previously expressed in relation to body weight). As regards %HRR, both HR_{rest} and HR_{max} were retrieved from the HERITAGE study dataset.

Once calculated, %$\dot{V}O_2R$, %$\dot{V}O_{2max,}$ and %HRR paired data points were used to perform the individual linear regressions for the %HRR-%$\dot{V}O_2R$ and the %HRR-%$\dot{V}O_{2max}$ relationships. As suggested by Swain et al.,[11, 12] a regression was performed for each participant and the %HRR was set as the dependent variable. Data from individual linear regressions resulting from less than 3 paired data points were excluded because they were assumed to be potentially not accurate in representing the true underlying relationship.

Statistical analysis

The analyses were performed using Excel (Microsoft Office, v.2016), SPSS Statistics (IBM, v.20), and R (R Core Team, v.3.2.3 – "Robust" package, v.0.4/16) software, with a α level of statistical significance of 0.05.

The study dataset was filtered and analyzed twice using a univariate and a univariate-bivariate blended approach. In both approaches data were adjusted for the familial clusters of the original HERITAGE study dataset (see the specific paragraph below for details). A flowchart illustrating the number of cases resulting from the analyses is presented in Figure 1. See Table 1 for details of the characteristics of the participants.

Table 1. Baseline characteristics of the subjects retained after applying the screening and filtering procedures to the original dataset of the HERITAGE Family Study.

		Age (yr)	Height (m)	Weight (kg)	Fat mass (%)	HR_{rest} (bpm)	HR_{max} (bpm)	$\dot{V}O_{2max}$ ($mL \cdot min^{-1} \cdot kg^{-1}$)
Univariate approach (both relationships: n=508; M=227, F=281)								
	Mean	35.01	1.70	76.61	27.41	65.39	184.41	31.63
	SD	13.38	0.09	17.81	10.47	8.86	13.89	8.59
	Minimum	17.00	1.47	39.60	3.00	40.00	136.00	15.17
	Maximum	65.90	1.96	142.40	52.70	105.00	214.00	54.86
Univariate-bivariate approach for %HRR-%$\dot{V}O_2$R (n=451; M=225, F=226)								
	Mean	34.85	1.71	77.74	26.95	65.00	184.95	32.55
	SD	13.19	0.09	17.18	10.34	8.68	13.38	8.65
	Minimum	17.00	1.47	39.60	3.00	40.00	137.00	15.17
	Maximum	65.90	1.96	142.40	52.70	105.00	214.00	54.86
Univariate-bivariate approach for %HRR-%$\dot{V}O_{2max}$ (n=450; M=224, F=226)								
	Mean	34.73	1.71	77.69	26.95	64.98	184.97	32.58
	SD	13.14	0.09	17.16	10.36	8.65	13.36	8.63
	Minimum	17.00	1.47	39.60	3.00	40.00	137.00	15.17
	Maximum	65.90	1.96	142.40	52.70	105.00	214.00	54.86

HR_{rest}, resting heart rate; HR_{max}, maximal heart rate; $\dot{V}O_{2max}$, maximal oxygen uptake; HRR, heart rate reserve; n, number of subjects; M, number of male subjects; F, number of female subjects; SD, standard deviation.

Univariate approach

Data filtering

After excluding the linear regressions whose slopes were lower than zero, the slope of each linear regression was compared to zero using a 2-tailed regression slope t test. The regressions whose slopes were not significantly different from zero were excluded.

Statistics

For each relationship, the mean slope and intercept were compared to the line of identity (i.e., to 1 and 0, respectively) using two 2-tailed 1-sample t tests with degrees of freedom corrected for familial clusters (see specific paragraph below).

Univariate-bivariate approach

Data filtering

For each relationship, paired data-points were filtered using the DFFITS influential statistics and those having an absolute value of DFFITS larger than the size adjusted cut-off (i.e., double the square root of the ratio between the number of the regression's parameters and the number of paired data points, as proposed by Belsley et al.[31]) were excluded. Since the DFFITS procedure requires at least four values to be performed, all the regressions resulting from less than four paired data points were also excluded. Subsequently, the individual linear regressions were run using the remaining paired data points, and those resulting from less than three paired data points and those with a slope both lower than zero and not significantly different from zero (2-tailed regression slope t test) were excluded as well (see Figure 1).

Robust means and the variance-covariance matrix were then calculated using the Huber M-estimator.[32] Thereafter, a bivariate paired data point filtering procedure was performed by adapting the ISO 13528:2015 rule.[33] Briefly, the 99% confidence ellipse was created using the robust means and the variance-covariance matrix and all paired data laying outside the ellipse were assumed to be bivariate outliers, hence excluded (Figure 2).

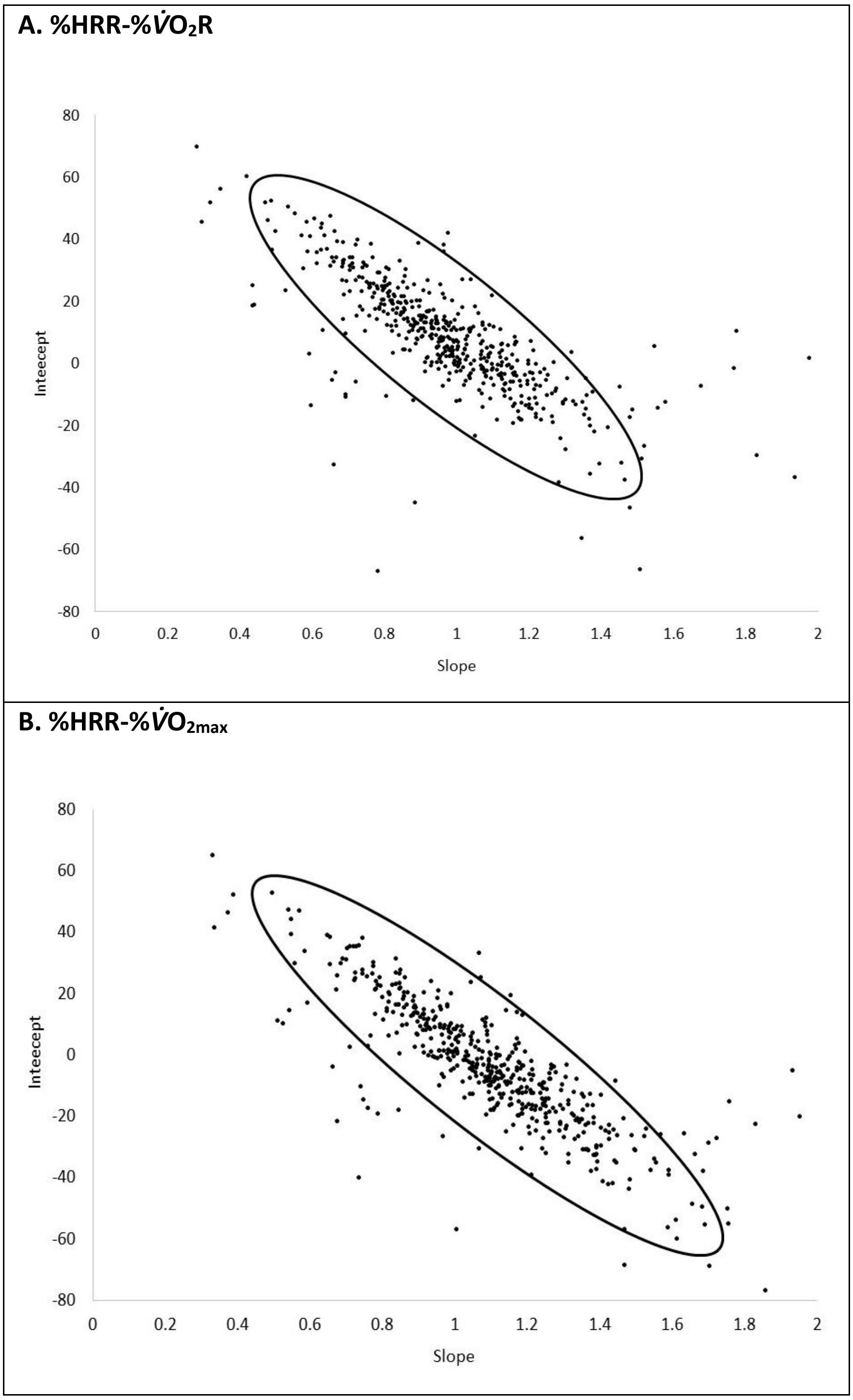

Figure 2. Bivariate 99% confidence ellipses calculated for the %HRR-%$\dot{V}O_2$R (panel A) and the %HRR-%$\dot{V}O_{2max}$ (panel B) relationships. %HRR, percentage of heart rate reserve; %$\dot{V}O_2$R, percentage of oxygen uptake reserve; %$\dot{V}O_{2max}$, percentage of maximal oxygen uptake.

Statistics

A test for Pearson's *r* significance was performed to evaluate the correlation between intercepts and slopes of both the %HRR-%$\dot{V}O_2$R and the %HRR-%$\dot{V}O_{2max}$ relationships.

The slopes and intercepts were used to build a mean vector $\binom{a}{b}$ that was compared to the expected vector $\binom{0}{1}$ using the bivariate Mahalanobis distance and the Wishart distribution. Post-hoc univariate analyses were then performed using two 2-tailed 1-sample t tests to compare the average slopes and intercepts to 1 and 0, respectively. The degrees of freedom used for Mahalanobis distance and post-hoc tests were those obtained from familial cluster adjustment calculations (see below).

The equations of the individual linear regressions retained were also used to calculate, for each subject, the predicted %HRRs over the $\dot{V}O_2R$ and $\dot{V}O_{2max}$ continua (0% to 100%). The mean %HRRs predicted at 30%, 40%, 50%, 60%, 70%, 80%, and 90% of $\dot{V}O_2R$ and $\dot{V}O_{2max}$ were then reported in Table 3 along with the relevant descriptive statistics and the 95% confidence intervals (CI) of the effect size (ES).

Finally, for each relationship the average root mean square error (RMSE) was calculated as follows. For each participant, the difference between the actual %HRR and the $\%\dot{V}O_2R$ or $\%\dot{V}O_{2max}$ of each stage of the T1 was calculated. The sum of the squared differences was then divided by the number of stages completed before calculating the square root of each relationship and their averages. The RMSEs of the two relationships were compared using a two-tailed, paired sample t-test (in order to be as conservative as possible, the number of families was assumed to be the sample size; degrees of freedom: 155).

Familial cluster adjustments

In order to take into account the heritage effect on each regression variable (see Table 2), the following procedure was performed: i) the eta squared (η^2) for univariate ANOVA with random effect (family membership) was calculated (the dependent variables were either slope or intercept); ii) the η^2 was computed in the equation of Shieh[34] and an intraclass correlation coefficient (ICC) was obtained; iii) the variance inflation factor (VIF) was calculated using the ICC and the mean size of the grouped data; iv) the VIF was used to calculate the corrected sample size (n^{corr}) for clustered data,[35] which was used for both analyses (see Table 2 for details).

Results

The results are presented separately for each approach used.

Univariate approach

The intercepts of both %HRR-%$\dot{V}O_2R$ and %HRR-$\dot{V}O_{2max}$ regressions were significantly different from 0, whereas only the slope of the %HRR-%$\dot{V}O_{2max}$ regression was significantly different form 1 (see Table 2 for details).

Table 2. Average values, familial cluster adjustments, and statistics for the univariate and the blended univariate-bivariate approaches.

	Univariate approach				Univariate-bivariate approach			
	%HRR-%$\dot{V}O_2R$		%HRR-%$\dot{V}O_{2max}$		%HRR-$\dot{V}O_2R$		%HRR-$\dot{V}O_{2max}$	
	Slope	Intercept	Slope	Intercept	Slope	Intercept	Slope	Intercept
Mean	0.979	7.578	1.112	-5.706	0.972	8.855	1.096	-3.616
SD	0.214	16.509	0.243	19.547	0.189	16.022	0.216	18.993
CV	0.219	2.179	0.219	3.426	0.195	1.809	0.197	5.252
ICC	0.431	0.411	0.476	0.445	0.418	0.501	0.414	0.440
VIF	1.821	1.782	1.906	1.847	1.762	1.914	1.756	1.803
n^{corr}	279.091	285.051	266.551	275.065	255.329	235.131	256.310	249.594
t	1.662	6.728	7.483	4.841	2.377	8.475	7.085	3.008
p(t)	0.098^{ns}	$< 0.001^{\#}$	< 0.001*	$0.000^{\#}$	0.018*	$< 0.000^{\#}$	< 0.000*	$0.003^{\#}$

%HRR, percentage of heart rate reserve; %$\dot{V}O_2R$, percentage of oxygen uptake reserve; %$\dot{V}O_{2max}$, percentage of maximal oxygen uptake; SD, standard deviation; CV, coefficient of variation; ICC, intraclass correlation coefficient; VIF, variance inflation factor; n^{corr}, corrected number of subjects; t, t-value; *p*(t), level of significance; ^{ns}, non-significantly different from 1; $^{\#}$, significantly different from 0; *, significantly different from 1.

Univariate-bivariate approach

The t-test for the correlation index between the slopes and the intercepts revealed a significant correlation for both the %HRR-%$\dot{V}O_2R$ (r=-0.72; p<0.0001) and the %HRR-%$\dot{V}O_{2max}$ (r=-0.79; p<0.0001) relationships.

The Mahalanobis distance showed a highly significant difference (p<0.0001) between the mean vector $\binom{a}{b}$ and the expected vector $\binom{0}{1}$ for both the %HRR-%$\dot{V}O_2R$ ($\chi^2_{(2)}$=186; p<0.0001) and the %HRR-%$\dot{V}O_{2max}$ ($\chi^2_{(2)}$=98; p<0.0001) relationships. Post-hoc univariate t tests (see Table 2) revealed that, in both relationships, the slopes and the intercepts were significantly different from 1 and 0, respectively (see Figure 3 for a graphical representation of both regressions over the expected identity line).

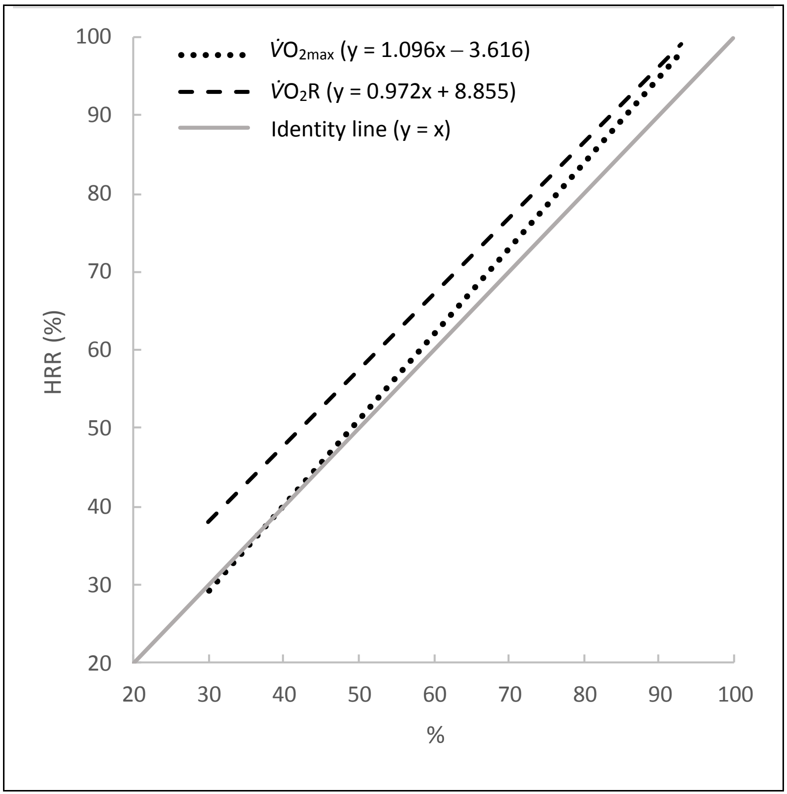

Figure 3. The regression lines of the %HRR-%$\dot{V}O_2R$ and %HRR-%$\dot{V}O_{2max}$ relationships are plotted over the expected identity line (y = x). HRR, heart rate reserve; $\dot{V}O_{2max}$, maximal oxygen uptake; $\dot{V}O_2R$, oxygen uptake reserve.

The predicted %HRRs were significantly different from the identity line (i.e., the expected zero ES did not lie within the 95% CIs of the ES) for all the percentages calculated for the %HRR-$\dot{V}O_2R$ relationship, whereas for the %HRR-$\dot{V}O_{2max}$ relationship, they differed significantly from the identity line above 50% of the $\dot{V}O_{2max}$ (Table 3).

Table 3. %HRRs calculated averaging the predicted %HRR resulting from each individual linear regression, and relevant descriptive statistics, at different %$\dot{V}O_2$R and %$\dot{V}O_{2max}$.

	%HRR	SD	Diff	PE	ES	CI$_{\text{INF}}$	CI$_{\text{SUP}}$
%$\dot{V}O_2$R							
30	38.008	11.287	8.008	-26.693	0.709	**0.574**	**0.843**
40	47.725	9.936	7.725	-19.314	0.777	**0.641**	**0.912**
50	57.443	8.79	7.443	-14.886	0.847	**0.709**	**0.982**
60	67.16	7.939	7.16	-11.934	0.902	**0.764**	**1.038**
70	76.878	7.483	6.878	-9.826	0.919	**0.781**	**1.055**
80	86.596	7.495	6.596	-8.244	0.880	**0.742**	**1.016**
90	96.313	7.973	6.313	-7.015	0.792	**0.655**	**0.926**
%$\dot{V}O_{2max}$							
30	29.257	13.314	-0.743	2.478	-0.056	-0.186	0.075
40	40.214	11.612	0.214	-0.536	0.018	-0.112	0.149
50	51.172	10.089	1.172	-2.344	0.116	-0.015	0.247
60	62.13	8.837	2.130	-3.549	0.241	**0.110**	**0.372**
70	73.087	7.985	3.087	-4.410	0.387	**0.225**	**0.518**
80	84.045	7.668	4.045	-5.056	0.528	**0.393**	**0.659**
90	95.003	7.950	5.003	-5.559	0.629	**0.494**	**0.762**

%HRR, percentage of heart rate reserve (average of the predicted); %$\dot{V}O_2$R, percentage of oxygen uptake reserve; %$\dot{V}O_{2max}$, percentage of maximal oxygen uptake; SD, standard deviation; Diff, difference between the predicted and the expected percentage; PE, percentage error (of the Diff); ES, effect size; CI, inferior (INF) and superior (SUP) 95% confidence intervals of the ES (bold when the zero expected ES does not lay within the interval).

The average RMSE of the %HRR-%$\dot{V}O_{2max}$ relationship (7.78%±4.49%) was significantly lower ($t=5.172$; $p<0.001$) than that of the %HRR-%$\dot{V}O_2$R relationship (9.25%±5.54%).

Discussion

The main finding of the present study is that the regression between %HRR and %$\dot{V}O_2$R does differ from the identity line, which conflicts with the current guidelines on aerobic exercise intensity prescription.

We used two different approaches to analyze the relationships, and both provided results oriented in the same direction.

When straight t tests were performed on the data retained for the univariate approach, only the slope of the %HRR-%$\dot{V}O_2$R relationship was non-significantly different from the expected (having a negligible effect size), whereas all the other comparisons showed significant differences (with small ES).

This widely used approach[12, 15-18, 20-24] was mainly adopted to assess the reproducibility of the results in the literature using a larger and more heterogeneous dataset, whose data quality has already been proven. Indeed, quality assurance and control procedures were implemented within the HERITAGE study showing an overall high quality of the measurements.[36] In particular, the procedures showed good reproducibility of

$\dot{V}O_{2max}$ and HR_{max} measurements,[37] as well as high reliability of resting HR measurements[38] and anthropometrics and body composition parameters,[39] all of which are relevant to the present study.

Conflicting results in the literature may stem from methodological limitations. Firstly, several investigators[16, 25] set the %HRR as the independent rather than the dependent variable of the individual linear regressions as suggested by Swain & Leutholtz.[12] Secondly, in some of the investigations, the linear regressions were performed also including the resting values of the percentages of the reserve,[12, 15, 16, 20-23] which, along with the maximal values, could induce the slope and intercept to tend to 1 and 0, respectively. Thirdly, in several studies[15-18, 21, 22, 24] the resting HR was not properly measured (i.e., as recommended by the ACSM[40]), which could affect the extent of the reserve.

As suggested by Swain et al.,[11] a regression was performed for each participant and the %HRR was set as the dependent variable in order to accurately reflect the variability within the data and not to obscure the individual relationships. This approach is theoretically correct from both the physiological standpoint (HR does not elicit whole body $\dot{V}O_2$, while $\dot{V}O_2$ is clearly the main factor determining the demand for HR) and statistical standpoint (the transposition of a linear regression equation does not yield the same values as those that would be obtained if the regression had initially been performed with the dependent and independent variables reversed).

Resting HR was measured immediately before the exercise test and at the end of a 5-min rest period with the subject sitting quietly in a chair. This procedure is in line with current ASCM recommendations[40], which recommends that resting HR should be measured after at least 5-min of quiet rest, preferably with the subject in a similar position as in the prescribed exercise mode.[40]

We surmised that more stringent data filtering procedures were necessary. Hence, the study dataset was re-analyzed to avoid any potential confounding effects that may have been caused by outliers in the UNIVARIATE approach. Two additional data filtering procedures were applied, deleting both influential paired data points (DFFIT) of the individual linear regressions and the individuals whose outcomes/dependent variables (i.e., the slopes and intercepts deriving from the individual linear regressions) were outliers.

Since the dependent variables showed significant correlations for both the %HRR-%$\dot{V}O_2$R (r=-0.72; p<0.0001) and the %HRR-%$\dot{V}O_{2max}$ (r=-0.79; p<0.0001) relationships, a bivariate filter was applied (Figure 2) and the slope and intercept were analyzed using a multivariate inferential statistic. Both %HRR-%$\dot{V}O_2$R and %HRR-%$\dot{V}O_{2max}$ relationships were found to be significantly different from the identity line, with χ^2 of the Mahalanobis distances vs. the identity line of 186 and 98, respectively.

The post hoc tests showed that both the %HRR-%$\dot{V}O_2$R and %HRR-%$\dot{V}O_{2max}$ relationships were significantly different from the identity line, with all the slopes and intercepts significantly different from 1 and 0, respectively. Regarding the ES of the %HRR-%$\dot{V}O_2$R and %HRR-%$\dot{V}O_{2max}$ relationships vs. the identity line, the slope showed a negligible (-0.15) and small (0.44) ES (in line with the univariate approach), whereas the ES of the intercepts differed from the univariate approach, showing a medium (0.55) and negligible (-0.19) ES, respectively.

When the %HRRs were predicted at different exercise intensities from the individual linear regressions, the predicted %HRRs were always different from the expected values of the identity line in the %HRR-%$\dot{V}O_2R$ relationship, whereas they only differed above 50% in the %HRR-%$\dot{V}O_{2max}$ relationship (see Table 3). Moreover, the difference between the predicted and expected percentages, their percentage error, and ES seem to be higher in the %HRR-%$\dot{V}O_2R$ than in the %HRR-%$\dot{V}O_{2max}$ relationship (see Table 3).

Likewise, the RMSEs were also higher ($t=8.875$; $p<0.001$) for the %HRR-%$\dot{V}O_2R$ relationship (9.25%±5.54%) than they were for the %HRR-%$\dot{V}O_{2max}$ relationship (7.78%±4.49%), with a mean difference of 1.47%±3.55% and an ES of 0.41.

A limitation of the present study is that resting $\dot{V}O_2$ was not measured but assumed to be 3.5 $mL \cdot min^{-1} \cdot kg^{-1}$. However, this value is adopted by the current guidelines as well.

Conclusions

Both relationships are slightly (in terms of mean difference and ES) but significantly different from the identity line. Although the difference is small, the intercepts and slopes are highly variable with a high SD. The same is true for the average RMSE and the predicted HRR at different intensities.

Therefore, even though the intercept and slopes are close – on average – to the identity line, using a single equation to predict the individual equation can cause an important and substantial error when applied to a single individual.

In the present study we chose not to create subject subgroups (age, gender, race, etc.) because the current guidelines adopt a 1:1 relationship between %HRR-%$\dot{V}O_2R$ for all subjects. Therefore, future studies assessing the influence of different variables (age, body composition, $\dot{V}O_{2max}$, gender, HR_{rest}) on the relationship are necessary. In addition, both the type of ergometer used and the incremental protocol adopted should be taken into account as influential variables. Future studies that take all these variables into consideration may help to explain the high variability of intercepts and slopes among different individuals.

Finally, it would also be useful to consider the possibility that the relationship between %HRR and %$\dot{V}O_2R$ might be not perfectly linear, either as a whole or within a specific range of intensity of the incremental exercise test.

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STUDY 2

Population-specific equations do not increase the prediction accuracy of the relationship between oxygen uptake reserve and heart rate reserve during incremental exercise

Introduction

It is well known that cardiorespiratory fitness is positively associated with health status, and structured and individualized aerobic exercise training is the most widely recommended form of exercise prescribed in order to improve it.[1] Structuring an aerobic exercise prescription involves the manipulation of several parameters related to both the overall training regimen (e.g., weekly exercise frequency, volume, progression, etc.) and the single exercise session (e.g., duration, intensity, etc.). Intensity is an important consideration when tailoring aerobic exercise prescription. Indeed, low intensity is considered safe but may not be sufficient to elicit the biological responses that improve cardiorespiratory fitness,[1] whereas vigorous intensity, although effective in improving cardiorespiratory fitness,[1] can increase the risks associated with exercise.[2]

Aerobic exercise intensity is usually prescribed and monitored using parameters calculated on the basis of the objective physiological measures of either oxygen uptake ($\dot{V}O_2$) or heart rate (HR).[2] Over the years, correlations between HR and $\dot{V}O_2$ have been found, and these two parameters have been used interchangeably to prescribe and monitor aerobic exercise.

Initially, a linear relation was found between the percentages of maximal $\dot{V}O_2$ ($\dot{V}O_{2max}$) and maximal HR (HR_{max}).[3-7] However, it was found that this relationship can vary among individuals, depending on, for instance, individual cardiorespiratory fitness level.[8] Therefore, the relation between the percentage reserve values (i.e., the difference between the maximal and resting values) of $\dot{V}O_2$ ($\dot{V}O_2R$) and HR (HRR) was further investigated. Swain et al.[8] proved that %HRR and %$\dot{V}O_2R$ were strongly correlated and their regression line was not distinguishable from the identity line (i.e., the regression line with slope = 1 and intercept = 0), which means that the percentages of the two reserves had a 1:1 relationship. As a result of such findings, since 1998 the American College of Sports Medicine (ACSM) has recommended adopting either %$\dot{V}O_2R$ or %HRR as the primary parameters for establishing aerobic exercise intensity.[9]

Subsequently, several studies confirmed that the percentages of HRR and $\dot{V}O_2R$ are indistinguishable from the identity line.[8, 10-15] However, other investigations yielded conflicting results, showing that the relation between %HRR and %$\dot{V}O_2R$ was different from the identity line.[10, 14, 16-20]

The highly variable conflicting nature of the results present in the available literature was further reinforced by the results obtained in the first study (STUDY 1) of the present work. STUDY 1 showed high standard deviations (SD) for both intercepts and slopes of the individual linear regressions performed with %HRR (dependent variable) and %$\dot{V}O_2R$ (independent variable), highlighting high variability among individuals.

Therefore, using a single equation, which is represented by the mean slope and intercept, as proposed in the current literature,[2] to predict the individual relationships between %HRR and %$\dot{V}O_2R$ can lead to important and substantial error in single individual (see STUDY 1).

The high variability within and between studies, along with the aforementioned conflicting nature of their results, are cause for concern when we consider that the HR-$\dot{V}O_2$ relationships are used to prescribe aerobic exercise intensity.

A possible explanation that may have accounted for the high SD found in the regression coefficients (i.e., slopes and intercepts) of the individual linear regressions between %HRR and %$\dot{V}O_2R$ in STUDY 1 was the heterogeneity of the participants (see Table 1).

Subject characteristics have been found to be related to the relationships (i.e., slopes and intercepts) between HR and $\dot{V}O_2$,[15, 19] and the need for population-specific equations for a more accurate exercise prescription based on %HRR, %$\dot{V}O_{2max}$ and %$\dot{V}O_2R$ relationships is highlighted in Cunha's review.[21]

Determining whether individual characteristics affect and account for part of the variance of individual linear regression intercepts and slopes would directly affect and potentially improve the accuracy of aerobic exercise intensity prescription, allowing practitioners and researchers to prescribe aerobic exercise intensity by tailoring the %HRR and %$\dot{V}O_2R$ relationship according to individual characteristics.

Aim

The aim of the present study was to assess the potential confounding effect of several individual characteristics on the relationship (i.e., slopes and intercepts) between the percentages of HRR and $\dot{V}O_2R$, and subsequently to use those variables as predictors to increase the accuracy of the %HRR vs. %$\dot{V}O_2R$ relationship.

Methods

Sample

The sample of the present investigation was composed of 741 members of Caucasian and African American families participating in the pre-training assessments of the HERITAGE Family Study (see Bouchard et al.[22] for details regarding ethical approval, inclusion and exclusion criteria, and study design).

All the subjects enrolled in the HERITAGE study, ranging in age from 17 to 65, were healthy (i.e., with no significant medical conditions or diseases), sedentary (i.e., they had not engaged in regular physical activity in the previous 6 months), and were not taking any medications that could affect the outcome variables of the present investigation.

HERITAGE study assessments

The HERITAGE study included several exercise and non-exercise tests performed before and after an aerobic exercise training intervention. In the present study, only baseline (body weight, body composition and pre-exercise HR) and exercise testing ($\dot{V}O_{2max}$ tests) data of selected pre-training assessments were used (see below).

Body weight, body composition and pre-exercise heart rate

Body mass was measured to the nearest 0.1 kg using a balance beam scale. Body composition was measured by means of underwater weighing performed in the post-absorptive state and body fat percentage (BFP) was calculated. Resting HR (HR_{rest}) was measured both immediately before the exercise test and at the end of a 5-min rest period with the subject sitting quietly in a chair.

Maximum oxygen uptake

Participants' $\dot{V}O_{2max}$ was identified based on the results of two cardiorespiratory fitness tests. First, a continuous, incremental exercise test to exhaustion (T1) was performed on a cycle ergometer (model 800S – Sensor Medics, Yorba Linda, CA, USA) connected to a mixing-chamber metabolic cart (model 2900 – Sensor Medics, Yorba Linda, CA, USA). In the first 3-min stage, participants pedalled at 50 W. The resistance of the ergometer was then increased by 25 W every 2 minutes until volitional exhaustion (in older, smaller, or less fit subjects, starting the test with a lower power output and/or making smaller increases every 2 minutes was permitted). At least 48 hours later, a submaximal, steady-state exercise test was performed, followed by a progressive test to maximum (T2). After the first phase of the test (which is not relevant to the present investigation but involved having the subjects exercise at a steady-state intensity of about 60% of the $\dot{V}O_{2max}$ measured in T1), participants peddled for 3 minutes at the power output corresponding to 80% of the $\dot{V}O_{2max}$ measured in T1. Thereafter, a 2-min stage at the highest power output attained in T1 was performed, and the resistance was then increased, if necessary, by the same increment used in T1, every 2 minutes until volitional exhaustion. Since the cycle ergometer was able to keep the power output constant regardless of the pedalling frequency, each participant was allowed to choose his/her own "comfortable" cadence (usually around 60 rpm), which was noted and used in both T1 and T2.

In both tests, $\dot{V}O_2$ (along with other gas exchange variables that were not used in the present investigation) was determined every 20 seconds and retained for subsequent analysis as the average of the last three 20-s values of each stage, whereas HR was measured continuously by means of ECG (in order to confirm HR, ECG rhythm strips were taken within the last 15 seconds of each stage and at maximum).

The criteria used for the attainment of $\dot{V}O_{2max}$ were: a *plateau* in $\dot{V}O_2$, i.e., a change <100 $mL \cdot min^{-1}$ in the last three consecutive 20-s intervals; a HR within 10 bpm of the age-predicted HR_{max}; a respiratory exchange ratio >1.1. All participants met at least one of these criteria in one of the two tests,[23] but most subjects met two or more.[24] Hence, when the $\dot{V}O_2$ peak of only one test met at least one criterion, it was assumed to be the $\dot{V}O_{2max}$. When both T1 and T2 $\dot{V}O_2$ peaks met the criteria and the values were within 5% of each other, their average was calculated and assumed to be the $\dot{V}O_{2max}$; otherwise, the highest value was assumed to be the $\dot{V}O_{2max}$.[23] HR_{max} was assumed to be the highest value attained during either of the two maximal exercise tests.

Study dataset implementation

Before carrying out the analyses, “dataset preparation and processing” and “data filtering” procedures, which are explained in detail below, were performed on the Heritage study dataset.

Data preparation and processing

Each $\dot{V}O_2$ and HR recorded for each stage of the T1 was computed as a percentage of the reserve values using the following formula: 100 x (recorded value – resting value) / (maximal value – resting value). In the calculation of $\%\dot{V}O_2R$, the $\dot{V}O_{2max}$ was retrieved from the HERITAGE study dataset, whereas the resting $\dot{V}O_2$ was assumed to be 3.5 $mL \cdot min^{-1} \cdot kg^{-1}$, as suggested in the current ACSM guidelines[2] (all values had been previously expressed in relation to body weight). As regards %HRR, both HR_{rest} and HR_{max} were retrieved from the HERITAGE study dataset.

Once calculated, %$\dot{V}O_2R$ and %HRR paired data points were used to perform the individual linear regressions for the %HRR-%$\dot{V}O_2R$ relationships. As suggested by Swain et al.,[7, 8] a regression was performed for each participant, and the %HRR was set as the dependent variable. Data from individual linear regressions resulting from less than 3 paired data points were excluded because they were assumed to be potentially inaccurate in representing the true underlying relationship.

Data filtering

The original dataset of the HERITAGE study was reduced from 741 to 450 subjects, which yielded 450 individual linear regressions between %HRR and %$\dot{V}O_2R$, after applying the filtering and screening procedures described below.

The integrity of the HERITAGE study dataset was first assessed by means of range checks and missing data filtering. Subsequently, the subjects whose linear regressions had less than 4 paired data points were excluded. Each individual linear regression was then screened for potentially influential data points, which were deleted when present. The individual linear regressions whose slopes were lower than 0 or not significantly different from 0 were then excluded and the slopes and intercepts of the remaining individual linear regressions were screened for bivariate outliers[25] (see STUDY 1 for details regarding study dataset implementation).

Finally, the variables assumed to have an effect on the slopes and intercepts of the individual linear regressions (i.e., age, BFP, HR_{rest}, and $\dot{V}O_{2max}$) were screened for outliers by means of range checks and box plots and one subject was excluded from the analyses reported below.

Statistical analysis

The following analyses were performed using Stata Statistical Software (StataCorp, v.13) and SPSS Statistics Software (IBM, v.20).

Due to the presence of two dependent variables (i.e., slope and intercept computed from the individual linear regressions between %HRR and %$\dot{V}O_2R$; see “Data preparation and processing”) a multivariate approach was appropriate. However, the HERITAGE study data violate two assumptions required for using a multivariate approach (i.e., multivariate multiple regression). Firstly, the dependent variables showed a high negative correlation ($r=-0.886$), which violates the assumption requiring that the dependent variables are not multicollinear.[26] Secondly, data of the HERITAGE study are from family clusters; hence, the assumption requiring that subjects’ scores are independent (i.e., each person's score is independent from every other person's score) cannot be met.[26]

Therefore, the influence of different factors on the dependent variables was assessed separately, which implied using a multiple linear regression for each dependent variable,[26] and the presence of clusters was addressed by computing cluster-robust standard errors for the regression coefficients. In order to control for type I error inflation due to multiple testing, the α level of statistical significance was adjusted to 0.025 according to Bonferroni's criterion.

Hence, two multiple linear robust regressions (MLR) with backward elimination were performed, using either the slopes or intercepts as the dependent variable and sex, age, HR_{rest}, $\dot{V}O_{2max}$, and BFP as independent variables. Each independent variable was visually screened versus the dependent variables in order to verify the assumptions of linearity, heteroscedasticity and the presence of multivariate outliers. Additionally, the independent variables were checked for multicollinearity (see Table 2). Since $\dot{V}O_{2max}$ showed a high negative correlation with BFP (r=-0.853), the two variables were assumed to be multicollinear[27] and BFP was excluded.

For each MLR, the model with the highest adjusted R^2 (FINAL model) was assumed to best predict the outcome variable.[28] The residuals of the FINAL models were examined to ensure that the MLR assumptions of linearity, homoscedasticity and normality were met. Graphical analyses of the residuals showed no patterns, outliers or heteroskedasticity and, according to the Kolmogorov-Smirnov tests, the residuals were normally distributed in both MLRs.

Results

Descriptive statistics of subject characteristics (i.e., independent variables) and individual linear regression slopes and intercepts (i.e., dependent variables) are presented in Table 1.

Table 1. Descriptive statistics of dependent and independent variables.

Variable	N	Mean	SD	Minimum	Maximum
Intercept	450	8.872	16.036	-38.478	52.407
Slope	450	0.971	0.190	0.473	1.468
Age (yr)	450	34.9	13.2	17.0	65.9
BFP (%)	424	27.0	10.4	3.0	52.7
HR_{rest} (bpm)	450	64.9	8.5	40.3	86.0
$\dot{V}O_{2max}$ ($mL \cdot min^{-1} \cdot kg^{-1}$)	450	32.5	8.6	15.2	54.9

N, number of subjects; SD, standard deviation; BFP, body fat percentage; HR_{rest}, resting heart rate; $\dot{V}O_{2max}$, maximal oxygen uptake.

Pearson's correlation coefficients between independent variables are presented in Table 2.

Table 2. Pearson's correlation coefficients between independent variables.

	Age (yr)	BFP (%)	HR_{rest} (bpm)	$\dot{V}O_{2max}$ ($mL \cdot min^{-1} \cdot kg^{-1}$)
Age	1.000			
BFP	0.404	1.000		
HR_{rest}	0.085	0.347	1.000	
$\dot{V}O_{2max}$	-0.538	-0.853	-0.387	1.000

BFP, body fat percentage; HR_{rest}, resting heart rate; $\dot{V}O_{2max}$, maximal oxygen uptake.

Table 3 shows the goodness of fit and summary statistics of the initial (i.e., the model with all the predictors entered) and FINAL model (i.e., the model with the highest adjusted R^2) of the two MLRs performed with either intercepts or slopes deriving from the individual linear regressions as the dependent variable.

FINAL models were able to explain 3.8% of the variance in intercept (R^2 = 0.038, adjusted R^2 = 0.031, RMSE = 15.784) and 1.3% of the variance in slope (R^2 = 0.013, adjusted R^2 = 0.006, RMSE = 0.189).

However, the regression equations of the FINAL models were able to significantly predict intercept ($F_{(3,155)}$=6.57, p<0.001) but not slope (F($_{3,155}$)=1.83, p=0.144).

Table 3. Goodness of fit statistics of the initial and final model of the two multiple linear robust regressions.

Dependent variable	Model	F	p	r	R^2	AdjR^2	RMSE
Intercept							
	Initial	4.92	0.001	0.195	0.038	0.029	15.799
	FINAL	6.57	<0.001	0.194	0.038	0.031	15.784
Slope							
	Initial	1.46	0.216	0.113	0.013	0.004	0.190
	FINAL	1.83	0.144	0.112	0.013	0.006	0.189

Intercept and Slope, coefficients of the individual linear regressions; initial, model with all the predictors entered; FINAL, model with the highest adjusted R^2; F, value of F-test for multiple linear regression; p, probability value associated with F; r, coefficient of correlation; R^2, coefficient of determination; AdjR^2, adjusted R^2; RMSE, root mean square error.

The independent variables retained in FINAL models, along with their regression coefficients and related statistics are presented in Table 4.

Table 4. Regression coefficients of the final models of the two multiple linear robust regressions.

DV	IV	B	SE of B	β	t	p	CI_{inf} of B	CI_{sup} of B
Intercept								
	Sex	2.454	1.586	0.077	1.55	0.124	-0.679	5.587
	Age	-0.183	0.056	-0.151	-3.25	0.001	-0.295	-0.072
	HR_{rest}	-0.186	0.096	-0.098	-1.93	0.056	-0.376	0.005
	Constant	23.639	6.191		3.82	0	11.410	35.868
Slope								
	Age	0.001	0.001	0.103	1.72	0.087	0.000	0.003
	HR_{rest}	0.002	0.001	0.078	1.42	0.158	-0.001	0.004
	$\dot{V}O_{2max}$	0.003	0.001	0.130	2.12	0.035	0.000	0.005
	Constant	0.713	0.118		6.05	0	0.480	0.946

Intercept and Slope, coefficients of the individual linear regressions; final model, model with the highest adjusted R^2; DV, dependent variable; IV, independent variable; B, unstandardized beta coefficient; SE, cluster-robust standard error; β, standardized beta coefficient; t, t value of regression coefficient t test; p, probability value associated with t; CI, inferior (INF) and superior (SUP) 95% confidence intervals of B; sex (males = 0 and females = 1); age (years); HR_{rest}, resting heart rate (bpm); $\dot{V}O_{2max}$, maximal oxygen uptake ($mL·min^{-1}·kg^{-1}$).

Discussion

The present study shows that the high interindividual variability in the relationships between the percentages of HRR and $\dot{V}O_2R$, which was found in STUDY 1, is not reduced meaningfully by accounting for several confounding variables.

Although the FINAL models showed that combinations of the predictors were able to significantly predict the intercept (but not the slope) of the participants, the significance of the MLR performed with the intercept as the dependent variable should be interpreted cautiously. This result, in fact, is due to the relatively large sample size rather than to the accuracy of the model. Indeed, the MLR was able to explain only 3.8% of the variance in the intercept (R^2=0.038), and its prediction presented a high error (RMSE=15.784) (see Table 3). The MLR performed with the slope as the dependent variable showed a lower prediction ability and was able to explain approximately 1% of the variance in the slope (R^2=0.013), which explains why the model was not able to significantly predict the slope in spite of the relatively large sample size.

The coefficients of the MLR performed with the intercept as the dependent variable were significant as combinations; however, the only coefficient that was significantly different from 0 was the subjects' age, highlighting the low predictive ability of the independent variables (see Table 4). In fact, the contribution of each independent variable to the prediction of the dependent variables was relatively small, as shown by the low standardized beta coefficients, which is in line with the low predictive ability of the two MLRs (see Table 4). The age of the subjects in the MLR performed with the intercept as the dependent variable presented, again, the highest absolute standardized beta coefficient with a negative sign, which implies that the older the subject was the lower the intercept (see Table 4).

The results of the present study support those of STUDY 1, i.e., that using a single equation does not appear to be suitable for predicting an individual relationship due to the high variability (i.e., high SD) of the slopes and intercepts of the individual linear regressions. Moreover, the high variability in the slopes and intercepts of the individual linear regressions, which could have been caused by the heterogeneity of the HERITAGE study dataset, was not accounted for by the differences in several subject characteristics. Indeed, in the present study the variance of the two dependent variables of the MLRs remained largely unexplained (see Table 3).

The results of the present study are in line with the results of Cunha,[16] who showed a high variability among the subjects' intercepts and slopes even though the sample of their study was relatively homogenous and composed of healthy young adult subjects who were involved in aerobic activities.

The prediction error of the MLRs found in the present study were high even though the MLRs were created with no validation procedure, which implies that if used in other populations, the error would probably be higher.

Conclusions

Several subject characteristics influenced the relationship between %HRR and %$\dot{V}O_2R$; however, these characteristics did not explain most of the variance of the slopes and intercepts. Indeed, the prediction models showed low precision and high error.

The relationship between %HRR and %$\dot{V}O_2R$ showed a high variability among individuals and was not 1:1 as indicated by the current guidelines. Therefore, using a single equation for the whole population does not appear to be suitable for representing an individual equation and has low predictive ability even when several confounding factors are included in the regression equation. Hence, the use of the individual relationships between the %HRR and %$\dot{V}O_2R$ should be preferred when prescribing the intensity of aerobic exercise in order to avoid the potentially high error associated with using a standardized relationship for the whole population.

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STUDY 3

Can incremental exercise tests accurately predict steady-state aerobic exercise intensity? Exploring a possible methodological flaw in the current guidelines for exercise prescription

Introduction

Aerobic exercise is universally known to be an effective method for improving health.[1] Indeed, an inverse relationship exists between physical activity level and all-cause mortality.[2]

The beneficial effects of aerobic exercise on health status depends on the modulation of the parameters contained in the FITT-VP principle,[2] which is the acronym for Frequency, Intensity, Time, Type, Volume, Pattern and Progression. Among these parameters, intensity is considered the most important to modulate in order to obtain the health benefits deriving from exercise while reducing the risks associated with aerobic exercise: if the intensity is too low – under a certain threshold – the stimulus will not be sufficient to obtain the positive effects of the exercise, such as the increase of the maximal oxygen uptake,[1] whereas if the intensity is excessively high – above a certain threshold – the risks associated with the exercise increase.[2] Therefore, aerobic exercise intensity and its accurate prescription and monitoring are essential to increase the benefits/risks ratio of an exercise program.

Aerobic exercise intensity is typically prescribed and monitored by using two parameters: oxygen uptake ($\dot{V}O_2$) and heart rate (HR). There are two methods to prescribe and tailor exercise intensity to individual needs using these two parameters. The first method, the simpler of the two, is based on the use of a percentage of the maximum values of HR (HR_{max}) and $\dot{V}O_2$ ($\dot{V}O_{2max}$), whereas the second method, which is more accurate from a theoretical point of view, uses the reserve values of HR and $\dot{V}O_2$ (i.e., the difference between maximal and resting values; see ACSM's resource manual for Guidelines for exercise testing and prescription.[3] In the first case, a maximal exercise test is performed and the desired percentages are applied to the maximal values obtained in the test. In the second case, the desired percentages are applied to the reserves calculated using the maximal values derived from the maximal test and the resting values.

Over the years, HR and $\dot{V}O_2$ have been found to be correlated. The original correlation that was investigated was between the percentages of the maximum values ($\dot{V}O_{2max}$ and HR_{max}) and it was found to be strong.[4-8] More recent studies[9-15] have shown that the percentages of the two reserves (HRR and $\dot{V}O_2R$) are also strongly correlated and that their relationship is 1:1, namely slope = 1 and intercept = 0). Indeed, since 1998,[16] the American College of Sports Medicine (ACSM) recommends adopting the same percentage of either %$\dot{V}O_2R$ or %HRR as the most accurate parameter to prescribe aerobic exercise intensity.[2]

However, the actual association between %$\dot{V}O_2R$ and %HRR has always been questionable. Indeed, several studies[9, 13, 17-21] have failed to find a 1:1 relationship between %$\dot{V}O_2R$ and %HRR. Moreover, the relationships between HR and $\dot{V}O_2$ on which the current literature is based are derived from graded exercise tests (GXT) but are commonly used (as recommended in the latest ACSM guidelines[2]) to prescribe aerobic exercise intensity during steady-state exercises (SSE) having a prolonged duration, which is a possible methodological bias.[22] Therefore, these relationships lack external validity because during prolonged SSE, several acute physiological adaptations occur, namely cardiovascular drift[23] and $\dot{V}O_2$ slow component.[24, 25] Indeed, during prolonged aerobic exercise, cardiovascular drift and $\dot{V}O_2$ slow component lead to an increase in HR and $\dot{V}O_2$ respectively over time, and this could modify the relationships between HR and $\dot{V}O_2$ derived from a GXT. In fact, Cunha et al.[26] showed that during prolonged aerobic exercise the slope of the increase over time was higher in %HRR than in %$\dot{V}O_2R$, which results in a dissociation – or nonlinear relationship – between %HRR and %$\dot{V}O_2R$. Hence, it may be inappropriate to prescribe the aerobic exercise intensity of a SSE following the recommendations of the current guidelines, i.e., using relationships derived from GXT.

The transferability of the relationships between HR and $\dot{V}O_2$ from GXT to SSE is a much discussed and controversial topic that still needs further investigation. Cunha et al.[26] has shown that the HR-$\dot{V}O_2$ relationships are not preserved during prolonged aerobic exercise. However, Wingo et al.[27, 28] indirectly criticized the approach adopted by Cunha et al.,[26] because it did not take into account the modifications of the maximal values of HR and $\dot{V}O_2$ after a prolonged aerobic exercise. On the other hand, neither Cunha nor Wingo[26-28] directly assessed how effective individual linear regressions derived from a GXT are in predicting the SSE intensity.

Aims

In the present study, the SSE tests of the Heritage Family Study,[29] performed at a fixed power output (50 W) and at a fixed relative exercise intensity (60% $\dot{V}O_{2max}$), were used to assess if: (I) during SSE, the %HRR-%$\dot{V}O_2R$ relationship was 1:1 (the reliability of the 1:1 relationship was also assessed); (II) the relationships obtained during an incremental exercise (i.e., individual linear regressions) can be used to predict exercise intensity during a steady-state exercise; (III) using the individual linear regression over the general 1:1 equation would improve the accuracy of the relationship between %HRR and %$\dot{V}O_2R$.

Methods

Sample

The sample of the present investigation was composed of 741 members of Caucasian and African American families participating in the pre-training assessments of the HERITAGE study (see Bouchard et al.[29] for details regarding ethical approval, inclusion and exclusion criteria, and study design).

All the subjects enrolled in the HERITAGE study, ranging in age from 17 to 65, were healthy (i.e., with no significant medical conditions or diseases), sedentary (i.e., they had not engaged in regular physical activity in the previous 6 months), and were not taking any medications that could affect resting and/or exercise HR.

HERITAGE study assessments

The HERITAGE study included several exercise and non-exercise tests performed before and after an aerobic exercise training intervention. In the present study, only the results of selected pre-training assessments were used (see below).

Body weight and pre-exercise heart rate

Body mass was measured to the nearest 0.1 kg using a balance beam scale. Resting HR (HR_{rest}) was measured both immediately before the exercise test and at the end of a 5-min rest period with the subject sitting quietly in a chair.

Maximal, submaximal and submaximal to maximal test

HERITAGE study participants underwent three experimental sessions on separate occasions. All tests were performed on a cycle ergometer (model 800S – Sensor Medics, Yorba Linda, CA, USA) connected to a mixing-chamber metabolic cart (model 2900 – Sensor Medics, Yorba Linda, CA, USA). At the first visit to the lab a continuous, graded exercise test to exhaustion (GXT_1) was performed: in the first 3-min stage participants pedalled at 50 W, then the resistance of the ergometer was increased by 25 W every 2 minutes until volitional exhaustion (in older, smaller, or less fit subjects, starting the test with a lower power output and/or making smaller increases every 2 minutes was permitted). At their second visit participants performed two submaximal SSE bouts (SSE_1) – divided by 4 min of seated rest – at 50 W and at 60% of the $\dot{V}O_{2max}$ recorded during the GXT_1. The power output (PO), corresponding to 60% of the $\dot{V}O_{2max}$, was determined for each participant as follows: firstly, $\dot{V}O_2$ and PO data deriving from the GXT_1 were plotted on a scatter diagram; the

PO, corresponding to 60% of the maximal $\dot{V}O_2$ achieved during GXT_1, was then determined. To avoid an overshooting of the $\dot{V}O_2$, the SSE at 60% of the $\dot{V}O_{2max}$ started at a PO 10 to 15 W lower than the previously determined PO. The $\dot{V}O_2$ was constantly monitored throughout the SSE and adjusted accordingly in order to maintain the intensity always within the range of 55-65% of the $\dot{V}O_{2max}$. At their last visit participants performed two submaximal SSE bouts (same resting period and intensities as visit 2) followed by a GXT (SSE_2+GXT_2). The GXT_2 protocol started immediately after the end of the second SSE bout with 3 minutes at the power output corresponding to 80% of the $\dot{V}O_{2max}$ measured in the GXT_1; thereafter, a 2-min stage at the highest power output attained in the GXT_1 was performed, and the resistance was then increased, if necessary, by the same increment used in the GXT_1, every 2 minutes until volitional exhaustion.

Since the cycle ergometer was able to keep the power output constant regardless of the pedalling frequency, each participant was allowed to choose his/her own "comfortable" cadence (usually around 60 rpm), which was noted and used in all tests of the same subject. In each test, $\dot{V}O_2$ (along with other gas exchange variables that were not used in the present investigation) was determined every 20 seconds and retained for subsequent analysis as the average of the last three 20-s values of each stage. HR was measured continuously by means of ECG and, in order to confirm HR, ECG rhythm strips were taken within the last 15 seconds of each stage during the GXT_1, at maximum during the GXT_1 and GXT_2, and after the achievement of the steady-state during SSE_1 and SSE_2.

The criteria used for the attainment of $\dot{V}O_{2max}$ were: a plateau in $\dot{V}O_2$, i.e., a change <100 $mL \cdot min^{-1}$ in the last three consecutive 20-s intervals; a HR within 10 bpm of the age-predicted HR_{max}; a respiratory exchange ratio >1.1. All participants met at least one of these criteria in either GXT_1 or GXT_2[30] but most subjects met two or more.[31] Hence, when the $\dot{V}O_2$ peak of only one test met at least one criterion, it was assumed to be the $\dot{V}O_{2max}$. When both GXT_1 and GXT_2 $\dot{V}O_2$ peaks met the criteria and the values were within 5% of each other, their average was calculated and assumed to be the $\dot{V}O_{2max}$; otherwise, the highest value was assumed to be the $\dot{V}O_{2max}$.[30] HR_{max} was assumed to be the highest value attained during either GXT_1 or GXT_2.

Achievement of the steady-state was individually assessed during SSE_1 and SSE_2, and the participants exercised for approximately 12 to 15 min at each power output.[32]

HR and $\dot{V}O_2$ values, representing the SSEs at 50 W (SSE_{50}) and at 60% of the $\dot{V}O_{2max}$ (SSE_{60}), were computed as the mean HR and $\dot{V}O_2$ of the SSE_1 and SSE_2.[32]

Study dataset implementation

Before carrying out the analyses, “dataset preparation and processing” and “data filtering” procedures, which are explained in detail below, were performed on the Heritage study dataset.

Data preparation and processing

Each $\dot{V}O_2$ and HR recorded for each stage of the GXT_1 and during the SSEs (at 50 W and at 60% of maximum $\dot{V}O_2$) was computed as a percentage of the reserve values using the following formula: 100 x (recorded value – resting value) / (maximal value – resting value). In the calculation of $\%\dot{V}O_2R$, the $\dot{V}O_{2max}$ was retrieved from the HERITAGE study dataset, whereas the resting $\dot{V}O_2$ was assumed to be 3.5 $mL \cdot min^{-1} \cdot kg^{-1}$, as suggested in the current ACSM guidelines[2] (all values had been previously expressed in relation to body weight). As regards %HRR, both HR_{rest} and HR_{max} were retrieved from the HERITAGE study dataset.

Once calculated, $\%\dot{V}O_2R$ and %HRR paired data points recorded during the GXT_1 were used to perform the individual linear regressions for the %HRR-$\%\dot{V}O_2R$ relationships. As suggested by Swain et al.,[8, 15] a regression was performed for each participant, and the %HRR was set as the dependent variable. Data from individual linear regressions resulting from less than 3 paired data points were excluded because they were assumed to be potentially inaccurate in representing the true underlying relationship. For each participant, the slope and the intercept of the individual linear regression equation derived from the GXT_1 were then used to compute his/her own predicted %HRRs at both SSE_{50} ($GXT_{50}HRR$) and SSE_{60} ($GXT_{60}HRR$) using the following formulas: slope x SSE_{50} actual $\%\dot{V}O_2R$ + intercept; slope x SSE_{60} actual $\%\dot{V}O_2R$ + intercept.

Data filtering

The original dataset of the HERITAGE study was reduced from 741 to 440 subjects after the following filtering and screening procedures.

The integrity of the HERITAGE study dataset was first assessed by means of range checks and missing data filtering. Data deriving from the GXT_1 were then filtered (see STUDY 1 for details regarding study dataset implementation), and subjects whose linear regressions had less than 4 paired data points were excluded. Hence, each individual linear regression was screened for potentially influential data points, which were deleted when present. The individual linear regressions whose slopes were lower than 0 or not significantly different from 0 were subsequently excluded and the slopes and intercepts of the remaining individual linear regressions were screened for bivariate outliers.[33]

Finally, SSEs data were filtered and the actual %HRR and $\%\dot{V}O_2R$ of both the SSE_{50} and SSE_{60} were screened for univariate outliers by means of range checks. The percentages of HRR ($SSE_{50}HRR$; $SSE_{60}HRR$) and $\dot{V}O_2R$ ($SSE_{50}\dot{V}O_2R$; $SSE_{60}\dot{V}O_2R$) of the SSEs were then screened, separately, for multivariate outliers, and subjects having a Mahalanobis distance with a $p<0.001$ were considered outliers and excluded.[34]

Statistical analysis

To assess if the 1:1 relationship between %HRR-%$\dot{V}O_2R$ was reliable during either SSE_{50} or SSE_{60}, paired sample t tests, intraclass correlation coefficients (ICC) and Bland-Altman plots were used to compare, separately, $SSE_{50}HRR$ to $SSE_{50}\dot{V}O_2R$ and $SSE_{60}HRR$ to $SSE_{60}\dot{V}O_2R$.

To assess if the individual relationships between %HRR and %$\dot{V}O_2R$ derived from the data of a prior GXT were reliable during either SSE_{50} or SSE_{60} the same analyses described above were used to compare, separately, $SSE_{50}HRR$ to $GXT_{50}HRR$ and $SSE_{60}HRR$ to $GXT_{60}HRR$.

The differences (Δ) used to perform the paired sample t tests and the Bland-Altman plots were computed subtracting from $SSE_{50}HRR$ either $SSE_{50}\dot{V}O_2R$ or $GXT_{50}HRR$ and from $SSE_{60}HRR$ either $SSE_{60}\dot{V}O_2R$ or $GXT_{60}HRR$

The t tests were always adjusted for the familial clusters of the original HERITAGE study dataset as follows: the Δs of each t test were separately used to compute the cluster robust standard error,[35] which was then used to compute both the variance inflation factor (VIF) and the corrected sample size (n^{corr}) for clustered data (see Table 3 for details). The mean square error (MSE) and the root MSE (RMSE) were also calculated for each prediction modality (i.e., based upon either the 1:1 relationship or the GXT-derived relationship). MSEs were computed as the sum of the squared Δ of each participant divided by the number of participants, while RMSEs were computed as the square root of MSE.

The analyses were performed using Stata (StataCorp, v.13) and SPSS Statistics (IBM, v.20) software. Alpha was set at 0.01 in order to control for type I error inflation due to multiple testing.

Results

Participant characteristics are presented in Table 1.

Table 1. Characteristics of the participants.

Variable	Mean	SD	Minimum	Maximum
Age (yr)	34.7	13.1	17.0	65.9
Height (cm)	170.8	9.3	147.1	195.6
Weight (kg)	77.6	16.7	48.6	140.2
BFP (%)	26.7	10.2	3.0	52.7
HR_{rest} (bpm)	64.8	8.6	40.3	105.3
HR_{max} (bpm)	185.1	13.3	137.0	213.0
$\dot{V}O_{2max}$ (mL·min^{-1}·kg^{-1})	32.7	8.6	15.6	54.9

SD, standard deviation; BFP, body fat percentage; HR_{rest}, resting heart rate; HR_{max}, maximal heart rate; $\dot{V}O_{2max}$, maximal oxygen uptake.

The descriptive statistics of the actual SSE %HRR, %$\dot{V}O_2R$, and the predicted %HRR according to the relationships between %HRR and %$\dot{V}O_2R$ during the GXT are reported in Table 2.

Table 2. Descriptive statistics of the exercise prescription modalities for each exercise intensity.

	Mean	SD	Minimum	Maximum
$SSE_{50}HRR$	42.55	11.55	18.44	76.51
$SSE_{50}\dot{V}O_2R$	36.94	10.67	18.28	72.54
$GXT_{50}HRR$	44.86	13.67	15.39	85.00
$SSE_{60}HRR$	62.16	8.96	34.70	86.21
$SSE_{60}\dot{V}O_2R$	56.04	4.60	40.37	71.47
$GXT_{60}HRR$	63.34	9.49	22.78	90.48

SD, standard deviation; GXT, graded exercise test; $SSE_{50}HRR$, actual percentage of heart rate reserve (HRR) of steady-state exercise at 50 W (SSE_{50}); $SSE_{50}\dot{V}O_2R$, actual percentage of oxygen uptake reserve ($\dot{V}O_2R$) of SSE_{50}; $GXT_{50}HRR$, GXT predicted %HRR at SSE_{50}; $SSE_{60}HRR$, actual %HRR of steady-state exercise at 60% of the $\dot{V}O_{2max}$ (SSE_{60}); $SSE_{60}\dot{V}O_2R$, actual %$\dot{V}O_2R$ of SSE_{60}; $GXT_{60}HRR$, GXT predicted %HRR at SSE_{60}.

The mean Δs of the exercise prescription modalities at the two SSE intensities, along with the relative descriptive statistics are shown in Table 3.

For both SSE intensities (see Table 3), the actual SSE %HRRs were significantly different from both the actual %$\dot{V}O_2R$ during SSE and the %HRR predicted using the individual linear regression performed with the GXT data, and hence showed systematic biases.

Table 3. Average differences, familial cluster adjustments, and statistics for the t tests and Bland-Altman plots.

	Steady-state exercise at 50 W		**Steady-state exercise at 60% of the $\dot{V}O_{2max}$**	
	Difference in %HRR (actual – 1:1 predicted)	Difference in %HRR (actual – GXT predicted)	Difference in %HRR (actual – 1:1 predicted)	Difference in %HRR (actual – GXT predicted)
Mean	5.61	-2.32	6.13	-1.18
SD	7.07	8.02	7.76	7.70
Minimum	-16.65	-32.39	-17.44	-27.39
Maximum	28.26	32.70	27.51	31.79
LoA_{SUP}	19.46	13.40	21.33	13.91
LoA_{INF}	-8.25	-18.03	-9.08	-16.27
VIF	1.45	1.21	1.64	1.38
N	440	440	440	440
n^{corr}	302.69	364.84	268.10	318.73
t	13.80	-5.52	12.93	-2.73
ES	0.79	-0.29	0.79	-0.15
p(t)	<0.001 *	<0.001 *	<0.001 *	0.007 *

%$\dot{V}O_{2max}$, percentage of maximum oxygen uptake; %HRR, percentage of heart rate reserve; %$\dot{V}O_2R$, percentage of oxygen uptake reserve; difference in %HRR, difference between the actual %HRRs recorded during the steady-state-exercises and the %HRRs predicted according to the assumed 1:1 relationship (actual – 1:1 predicted) and the relationship computed during graded exercise tests (actual – GXT predicted) between %HRR and %$\dot{V}O_2R$; SD, standard deviation; LoA, inferior (INF) and superior (SUP) 95% limits of agreement of the Bland-Altman plots, which correspond to 95% confidence interval of the differences; VIF, variance inflation factor; N, uncorrected number of subjects; n^{corr}, corrected number of subjects; t, t-value; ES, effect size; *p*(t), level of significance; *, significantly different from 0.

The distributions of the Δs are graphically displayed using Bland-Altman plots (see Figure 1).

A high linear correlation (r=0.638) was found between the Δs and the mean values of $SSE_{60}HRR$ and $SSE_{60}\dot{V}O_2R$, showing a proportional bias,[36] which was not present when $SSE_{60}HRR$ were compared to $GXT_{60}HRR$ (r=-0.076). The proportional biases at SSE_{50} showed a correlation coefficient of r=0.131 and r=-0.279 when $SSE_{50}HRR$ were compared to $SSE_{50}\dot{V}O_2R$ and $GXT_{50}HRR$, respectively.

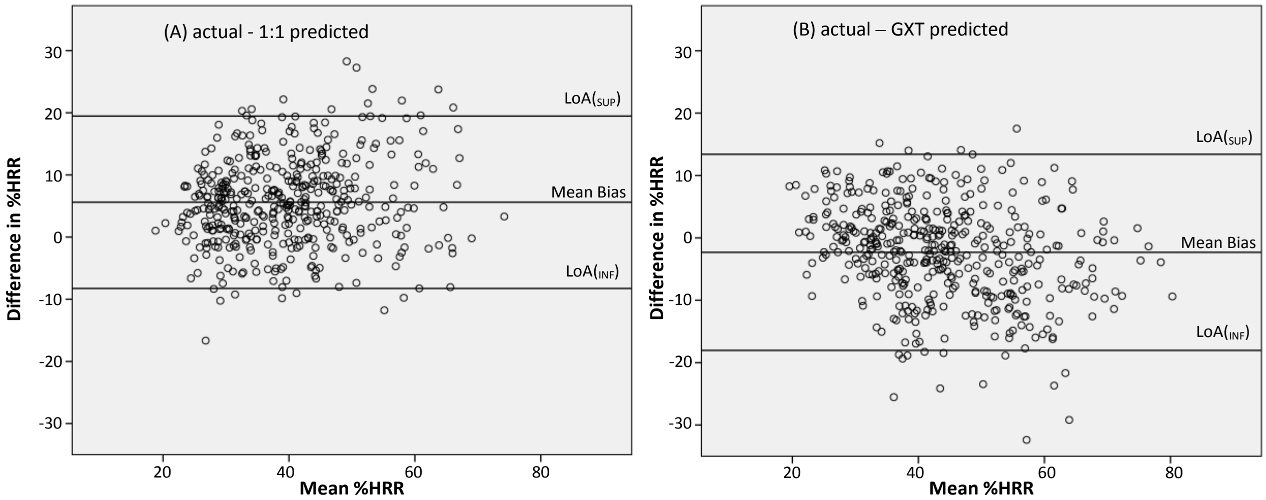
The ICCs for the exercise prescription modalities and the relevant errors, are presented in Table 4.

Table 4. ICC, MSE and RMSE of the actual %HRR during steady-state exercises at 50 W and at 60% of the $\dot{V}O_{2max}$ vs. predicted %HRR from either its 1:1 or GXT's individual relationships with the %$\dot{V}O_2R$.

	ICC	ICC (CI_{INF})	ICC (CI_{SUP})	MSE	RMSE
%HRR during steady-state exercise at 50 W					
Actual vs. 1:1 predicted	0.829	0.483	0.919	81.27	9.02
Actual vs. GXT predicted	0.880	0.844	0.907	69.52	8.34
%HRR during steady-state exercise at 60% of the $\dot{V}O_{2max}$					
Actual vs. 1:1 predicted	0.458	0.068	0.659	97.59	9.88
Actual vs. GXT predicted	0.786	0.741	0.823	60.51	7.78

ICC, intraclass correlation coefficients; ICC, inferior (CI_{INF}) and superior (CI_{SUP}) 95% confidence intervals of the ICC; MSE, mean square error; RMSE, root mean square error; %HRR, percentage of heart rate reserve; $\dot{V}O_{2max}$, percentage of maximum oxygen uptake %$\dot{V}O_2R$, percentage of oxygen uptake reserve; GXT, graded exercise test; comparison between the actual %HRRs recorded during the steady-state exercises and the predicted %HRRs according to the assumed 1:1 (actual vs. 1:1 predicted) and computed during graded exercise tests (actual vs. GXT predicted) relationship between %HRR and %$\dot{V}O_2R$.

Steady-state exercise at 50 W



Steady-state exercise at 60% of the $\dot{V}O_{2max}$

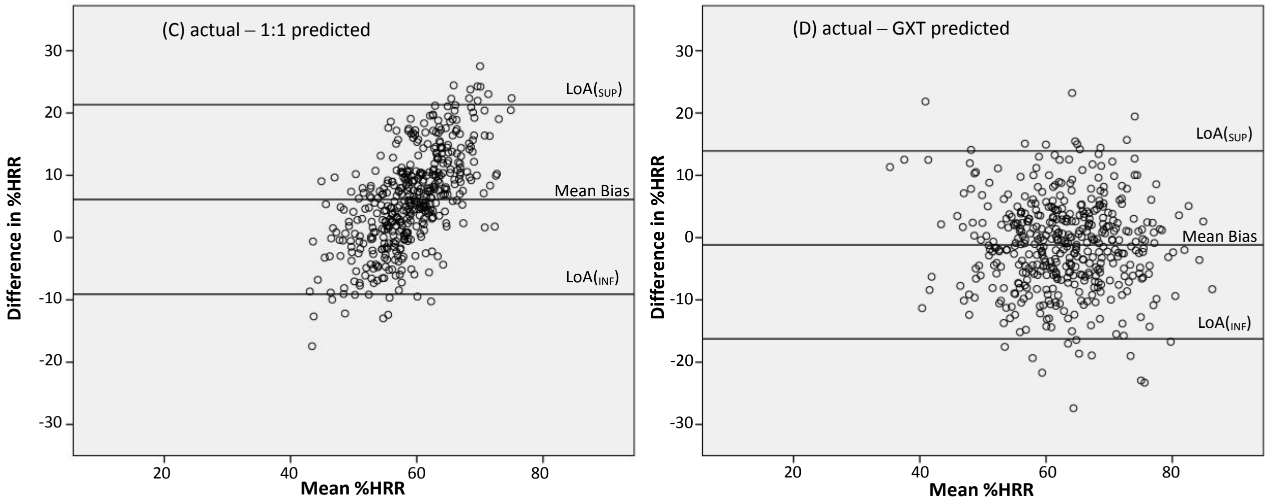


Figure 1. Bland-Altman plots showing the individual differences vs. means (see below) between the actual and predicted %HRR during steady-state exercises performed on a cycle ergometer at the constant intensities of 50 Watts or 60% of the individual's maximal oxygen consumption.

%$\dot{V}O_{2max}$, percentage of maximum oxygen uptake; %HRR, percentage of heart rate reserve; %$\dot{V}O_2R$, percentage of oxygen uptake reserve; Difference in %HRR, difference between the actual %HRRs recorded during the steady-state exercises and the %HRRs predicted according to both the assumed 1:1 relationship between %HRR and %$\dot{V}O_2R$ (panels A and C; actual – 1:1 predicted) and the individual linear regressions between %HRR and %$\dot{V}O_2R$ obtained from prior graded exercise tests (panels B and D; actual – GXT predicted); Mean %HRR, mean between the actual %HRRs recorded during the steady state-exercises and the %HRRs predicted according to both the assumed 1:1 relationship between %HRR and %$\dot{V}O_2R$ (panels A and C; actual – 1:1 predicted) and the individual linear regressions between %HRR and %$\dot{V}O_2R$ obtained from prior graded exercise tests (panels B and D; actual – GXT predicted); LoA, inferior (INF) and superior (SUP) 95% limits of agreement of the Bland-Altman plots; Mean bias, mean of the Difference in %HRR.

Discussion

The main finding of the present study is that both the 1:1 and GXT derived relationship between %HRR and %$\dot{V}O_2$R show relatively high error in predicting SSE intensity.

As shown by the t test results, the actual %HRR were different from the %HRR predicted using either the 1:1 or the GXT derived relationship between %HRR and %$\dot{V}O_2$R. Hence, both the 1:1 and GXT derived relationship between %HRR and %$\dot{V}O_2$R showed a systematic bias (see Table 3). However, the effect size (ES) of the Δs computed assuming a 1:1 relationship was large at both intensities of the SSEs, whereas it was small at SSE_{50} and negligible at SSE_{60} when computed using the individual linear relationship found during the GXT. This is due to the relatively smaller mean Δs when the %HRR at SSE_{50} and SSE_{60} were predicted by the GXTs' relationships rather than by the 1:1 relationship.

Importantly, HRR percentages were overestimated during SSE when predicted according to the 1:1 relationship between %HRR and %$\dot{V}O_2$R and underestimated when predicted using the relationships derived from GXTs. The underestimation of the GXT predicted %HRR during SSEs is consistent with the effect of cardiovascular drift during prolonged aerobic exercises found by Cunha and colleagues[26]. Indeed, Cunha and colleagues[26] reported a dissociation between %HRR and %$\dot{V}O_2$R, due to the higher slope of increase over time in %HRR compared to %$\dot{V}O_2$R, showing the possible inappropriateness of using a GXT to predict SSE intensities.

In line with the aforementioned results, the ICCs showed the lower reliability of the 1:1 relationship in predicting the actual %HRR during SSE compared to the relationships derived from prior GXTs, which is revealed by both the mean ICCs and their 95% confidence intervals. Indeed, the ICCs 95% confidence intervals were broader when %HRRs were predicted according to the 1:1 relationship between %HRR and %$\dot{V}O_2$R (see Table 4).

The results of the ICCs, along with the ESs and mean differences between the actual SSE and predicted %HRRs seem to contradict the 1:1 relationship between %HRR and %$\dot{V}O_2$R and support the use of a prior GXT to predict the actual relationship between %HRR and %$\dot{V}O_2$R during SSE, regardless of the lack external validity due to the different physiological adjustments occurring during an incremental or a steady-state prolonged exercise.[22] However, from a practical standpoint, the error (i.e., MSE and RMSE) of the GXT predictions, though lower than the error made using the 1:1 relationship, is still relatively high (see Table 4). Indeed, RMSEs of around 8 percentage points are relatively large considering, for instance, that aerobic exercise of moderate intensity ranges from 40% to 59% of either HRR or $\dot{V}O_2$R.[2] Hence, the prediction error should be taken into account when prescribing aerobic exercise intensity.

The Bland-Altman plots (see Figure 1 and Table 3) graphically reinforce and support the results obtained with the t tests and the ESs. Indeed, the plots show that the systematic bias is more pronounced, and hence, on average, shows a greater divergence from the actual relationship when the relationships between %HRR and %$\dot{V}O_2R$ are considered 1:1 instead of being individually predicted from GXTs. Also, the broad error ranges of the 95% limits of agreement of the Bland-Altman plots are in line with the results obtained with the RMSE showing a high prediction error.

Predicting the actual %HRRs during SSE_{60} using the individual relation with the %$\dot{V}O_2R$ deriving from a prior GXT instead of using the proposed 1:1 %HRR-%$\dot{V}O_2R$ relationship also seems to protect from proportional bias. Indeed, an upward trend is clearly visible solely in panel C of Figure 1, and this observation is supported by the high correlation coefficient between the Δs and the mean values of $SSE_{60}HRR$ and $SSE_{60}\dot{V}O_2R$.

The relatively high accuracy of GXTs in predicting the relationships between %HRR and %$\dot{V}O_2R$ during SSEs found in the present study seems to support the transferability of the relationships deriving from GXTs to SSEs. These results are in conflict with other studies in the literature,[26, 27] which show that the relationship between %HRR and %$\dot{V}O_2R$ changes during SSEs. This led the authors of these studies to assume, without a direct assessment, that the relationships found during GXTs are not applicable to SSEs.

However, the discrepancy between the results of the present study and those found in the literature is probably due to the different kind of analysis performed and the differences among the SSEs employed in the present study compared to those previously adopted. Indeed, one of the parameters that affect the HR-$\dot{V}O_2$ relationship is exercise duration.[26] Since the SSEs of the HERITAGE study had a shorter duration (maximum 15 minutes) compared to 45 minutes of the aforementioned studies they could have been less affected by the acute cardiorespiratory adjustments to steady-state exercise. Therefore, the results of the present study should be carefully extrapolated to every SSE, especially those having a duration longer than 15 minutes. Hence, additional studies examining how the HR-$\dot{V}O_2$ relationships are affected by steady-state exercise characteristics (e.g. duration, intensities, modalities, etc.) are warranted to improve the accuracy of aerobic exercise intensity prescription.

Conclusions

The 1:1 relationship between the percentages of HRR and $\dot{V}O_2R$ does not appear to be suitable for predicting the intensity of SSEs. Predicting the %HRR using its individual relationship with %$\dot{V}O_2R$ derived from prior GXTs increases prescription accuracy compared to the straight application of the 1:1 relationship in relatively short SSEs performed at both 50 W and 60% of $\dot{V}O_{2max}$.

Although the individual relationships derived from prior GXTs allowed us to predict rather accurately the SSE relationships between %HRR and %$\dot{V}O_2R$ in the whole study sample, the prediction errors were high for all prediction modalities. Therefore, the prediction error for the average individual is relatively high, especially when considering the different ranges of aerobic exercise intensity.

In conclusion, to prescribe the intensity of SSEs of relatively short duration, the 1:1 %HRR-%$\dot{V}O_2$R relationship does not appear to be suitable, and the individual relationship derived from a prior GXT should be preferred. However, even when the individual relationship derived from a prior GXT is used, the prediction error remains relatively high and should be taken into account, particularly when exercise intensity is an important consideration from a safety standpoint.

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STUDY 4

Validity of the HRR-$\dot{V}O_2R$ relationship derived from incremental exercise protocols in predicting the intensity of steady-state aerobic training: preliminary results

Introduction

Aerobic exercise is universally known to be an effective method for improving health.[1] However, the beneficial effects of aerobic exercise programs vary according to how several of its parameters (such as weekly frequency, modality, volume, progression, duration and intensity) are manipulated.[2] Aerobic exercise intensity is an important consideration in tailoring exercise programs. Indeed, selecting the proper intensity yields positive results, such as improvements in cardiorespiratory fitness,[1] while reducing the risks associated with exercise.[2]

Aerobic exercise intensity is usually prescribed and monitored using parameters based on oxygen uptake ($\dot{V}O_2$) or heart rate (HR).[2] HR and $\dot{V}O_2$, either expressed as straight percentages of their maximal values[3-7] (HR_{max} and $\dot{V}O_{2max}$, respectively) or as percentages of their reserve values[8-18] (HRR and $\dot{V}O_2R$, respectively), have been found to be linearly related. From a theoretical point of view, prescribing the intensity of aerobic exercise using percentages of the reserve values, which are calculated as the difference between maximal and resting values, is the most accurate method. This is because it allows us to correct for nonzero resting values[19] and to avoid under- and over-estimation errors that may occur if the target intensity derives from a straight percentage of the maximal values.[2] Moreover, the percentages of the two reserves have been found to be highly correlated, with a 1:1 relationship,[19] which makes it possible to apply the same percentage of either HRR or $\dot{V}O_2R$ to obtain the target aerobic exercise intensity. This is particularly useful for fitness professionals, who usually prescribe a target HR in order to obtain the desired $\dot{V}O_2$ of an aerobic exercise.

However, the 1:1 %HRR-%$\dot{V}O_2R$ relationship on which the current American College of Sports Medicine (ACSM) guidelines[2] are based is the result of studies that only investigated this relationship using data sampled during graded exercise tests (GXT). On the contrary, that relationship is to be used during aerobic exercise having constant intensity and prolonged duration according to ACSM's guidelines.[2]

Using the %HRR-%$\dot{V}O_2R$ relationship deriving from GXTs for prolonged exercise lacks external validity, as highlighted by Cunha and colleagues.[20] In addition, during prolonged aerobic exercise several acute time-dependent physiological adaptations occur, namely cardiovascular drift[21] and $\dot{V}O_2$ slow component,[22, 23] which could modify the relationships between HR and $\dot{V}O_2$ found during GXT. In fact, Cunha et al.[24] assessed the validity of the %HRR-%$\dot{V}O_2R$ relationship during prolonged aerobic exercise at three aerobic exercise intensities, and reported that the slope of the increase over time was higher in %HRR than in %$\dot{V}O_2R$, resulting in a dissociation, or nonlinear relationship, between %HRR and %$\dot{V}O_2R$. Moreover, Cunha et al.[24] showed that %HRR was significantly higher than %$\dot{V}O_2R$, which indicates that the relationship between the percentages of the two reserves was not 1:1.

On the other hand, Wingo and colleagues[25, 26] stated in their reviews that during prolonged aerobic exercises the dissociation between %HRR and %$\dot{V}O_2R$ is partially mitigated by a decrease in $\dot{V}O_{2max}$, which induces higher %$\dot{V}O_2R$. However, Wingo and colleagues did not directly assess if the %HRR and %$\dot{V}O_2R$ were equal and therefore had a 1:1 relation; they analyzed data deriving from previous studies they authored[27-30] and reported a positive relation between the changes in the percentages of $\dot{V}O_2R$ and HRR over time.

Aims

The aims of this study were to assess, during steady-state aerobic exercises (SSE), I) if the percentages of HRR and $\dot{V}O_2R$ show a 1:1 relationship, and II) the effect of exercise intensity and duration, and their interaction on the %HRR-%$\dot{V}O_2R$ relationship.

Methods

Participants

Six healthy physically active male subjects, with at least 3 years of treadmill experience volunteered to participate in this study (mean ± SD age 21.8 ± 1.0 years; height 182.9 ± 7.8 cm; body mass 73.5 ± 9.9 kg; body mass index 21.9 ± 1.4 kg/m^2; body fat percentage 14.8 ± 4.0).

All participants had obtained medical clearance to perform maximal exercise, and were involved in aerobic exercise training for at least 4 hours per week (from 3 to 5 sessions per week) during the previous year.

Exclusion criteria were: use of medications that have been shown to have effect on the cardiorespiratory system (participants did not use any medication during the study); smoking or use of ergogenic substances; recent orthopedic or musculoskeletal injuries that could have limited or affected exercise performance.

The study was approved by the local Ethics Committee. All subjects were informed of potential risks and discomforts associated with the testing procedures and gave written informed consent before being enrolled in the study.

Experimental design

The participants were tested under all conditions by using a repeated measures experimental design. On the first testing day, pre-exercise and maximal HR and $\dot{V}O_2$ were measured. Four experimental trials were then performed (in random order) to assess HR and $\dot{V}O_2$ responses under 4 different experimental exercise conditions: 15 minutes at 60% and 80% of HRR and 45 minutes at 60% and 80% or HRR. The experimental trials were separated by at least 3 days and were performed at the same time of day to minimize the possible effect of circadian rhythm on HR and $\dot{V}O_2$ values. During the experimental trials the subjects were not allowed to drink and fan airflow was not used.

Between the first visit and experimental trials, 2 practice sessions were scheduled in order to determine the appropriate power output to elicit the desired percentages of HRR.

Participants were instructed to avoid changes in their training and dietary habits, to avoid performing vigorous physical activity or assuming alcohol or caffeine the day before tests and on testing days. The subjects were also told to drink plenty of fluids the day before testing and on the day of testing, to drink 0.5 L of water one hour before the scheduled testing sessions, and to arrive at the laboratory following a 3 hour fasting period. On each testing day compliance to the instructions described above was assessed by means of a questionnaire, which was specifically designed for the present study.

Procedures and data processing

All the exercise tests of the present study were performed on the Matrix T7xe treadmill (Johnson Health Tech Italia Spa, Ascoli Piceno, Italy) set at 0% grade. Holding onto either the side or front bars of the treadmill was not permitted in any exercise test of the present study.

In each testing session participants' $\dot{V}O_2$ and HR were continuously sampled. Breath-by-breath $\dot{V}O_2$, carbon dioxide production, and pulmonary ventilation were measured using the COSMED K5 portable gas analysis system (Cosmed, Rome, Italy). The system was calibrated using room air (21% O_2, 0.03% CO_2) and a certified gas mixture (16% O_2, 5% CO_2; Scott Medical Products™, Plumsteadville, USA) prior to each test. The turbine flowmeter was also calibrated using a 3-L syringe according to the instructions of the manufacturer. HR was recorded in beat-to-beat intervals using the Polar V800 HR monitor (Polar Electro Oy, Kempele, Finland).

Control tests

Pre-exercise values

On the first testing day the participants underwent the following anthropometric measurements: body weight (barefoot while wearing shorts, to nearest 0.5 kg), height (barefoot and head in the Frankfurt plane, to nearest 0.01 m), body composition (bioimpedance analysis). Thereafter, participants sat quietly in a chair during the equipment set up. HR and $\dot{V}O_2$ were then continuously recorded for 20 min with the subject standing on the treadmill belt. The environment was kept quiet and participants were asked to relax, to avoid talking, and not to hold onto the side or front bars of the treadmill.

Both HR and $\dot{V}O_2$ recordings were divided into four 5-min intervals, and the average of each interval was computed. For each variable, the average of the first 5-min interval was discarded (as suggested in the ACSM guidelines[2]), and the lowest average value of the 3 remaining intervals was assumed as the pre-exercise value of HR and $\dot{V}O_2$.

Maximal exercise tests

Control GXT (GXT_{con}) and verification trial (VT). After pre-exercise value assessments, participants warmed-up for 3 min at 40% of the estimated maximal treadmill speed (see below for details), then performed a GXT using a personalized ramp protocol designed according to indications proposed by da Silva and colleagues.[31] Briefly, $\dot{V}O_{2max}$ was estimated by means of a non-exercise model Matthew et al.[32] that has been cross-validated[33, 34] and proved to be accurate in estimating $\dot{V}O_{2max}$.[31] The speed yielding the estimated $\dot{V}O_{2max}$ (i.e., the final speed) was then calculated from the estimated $\dot{V}O_{2max}$ according to the ACSM's running equation,[2] and the initial speed of the ramp protocol was set at 50% of the final speed. The speed increment of each 1-min stage was calculated as the difference between the final and initial speed divided by 10 min, multiplied by the number of min elapsed from the beginning of the test (warm-up excluded) to the beginning of that given stage. Using this approach should allow attainment of the final speed – and therefore the estimated $\dot{V}O_{2max}$ – approximately at the 10th min of the test.[31]

Following Nolan's protocol,[35] after the end of the GXT_{con}, participants sat quietly for 20 min and then performed a VT. The VT started with a 2-min stage followed by a 1-min stage, respectively at 50% and 70% of the maximal speed achieved during GXT_{con}. The speed was then increased to 105% of the maximal speed achieved during GXT_{con} and maintained until subjects could no longer continue to run. VT has been proved to be effective to confirm the achievement of true $\dot{V}O_{2max}$.[36-40] During both GXT_{con} and VT the participants were verbally encouraged to make their maximum effort.

The $\dot{V}O_2$ and HR raw data were smoothed as 15-breath moving average[41] and 5-second stationary time average,[42] respectively. The highest values of $\dot{V}O_2$ and HR, recorded during either GXT_{con} or VT, were considered maximal values if a $\dot{V}O_2$ plateau (during either GXT_{con} or VT) was present or if the highest HR recoded during the GXT_{con} and VT were within 4 bpm.[42] Briefly, as proposed by Midgley et al.,[42] the $\dot{V}O_2$ achieved a plateau if the difference between modelled and actual $\dot{V}O_{2max}$ (of either the GXT_{con} or VT) was higher than 50% of the regression slope of the individual linear regressions performed between the oxygen uptake (dependent variable) and work rate (independent variable) recorded during the linear portion of the GXT_{con}. Plateau assessments and related analyses (i.e., individual linear regressions) were performed using the $\dot{V}O_2$ expressed as 30-second stationary time average.[42] If the subject did not meet at least one of these criteria, the tests were repeated.

Practice trials

After at least 3 days from the control tests, two practice sessions were performed on two separate days to determine the speeds that elicited 60% and 80% of HRR. The HR and $\dot{V}O_2$ corresponding to the desired percentages of the reserve values (i.e., %HRR and %$\dot{V}O_2$R) were calculated using the following formula: (maximal value – pre-exercise value) x desired percentage.

The practice trials started with 3 min of warm-up at the speed corresponding to 40% of $\dot{V}O_2$R. The speed was then increased to the speed corresponding to either 60% or 80% of $\dot{V}O_2$R (random order). The speeds corresponding to the desired %$\dot{V}O_2$R were calculated using the ACSM’s running equation.[2] After 3 min at those speeds (which were supposed to elicit the desired 60% and 80% of HRR given the 1:1 relationship between %HRR and %$\dot{V}O_2$R), the speed was adjusted every 30 seconds in order to reach the desired target HR using the algorithm proposed by Hunt and Fankhauser.[43] The speeds at the 9th min of the practice trials (warm-up excluded) were used as starting speeds for the experimental trials.

Experimental trials

Steady-state exercise (SSE)

SSEs started with 5 min of warm up at the speed corresponding to 40% of $\dot{V}O_2$R (calculated using the ACSM's running equation[2]), followed by either 15 or 45 min of running at either 60% or 80% of the HRR (random order). After the warm up, the speed was linearly increased every 30 seconds in order to reach the starting speed found during the practice trial in 2.5 min. In order to maintain the target HR, after 3 min running at the starting speed, treadmill belt velocity was adjusted throughout the trial according to the HR response to exercise. The Hunt's algorithm[43] was used to this purpose: 30 seconds stationary time-averaged HRs were inputted into the algorithm that outputted the speed change to apply.

The HR and $\dot{V}O_2$ averages of the last 5 min of each SSE were assumed as representative of the specific experimental condition and converted in percentages of HRR and $\dot{V}O_2R$ by using the pre-exercise values and either the peak values of the GXT_{post} (see below) or the values resulting from the control maximal exercise tests. The following formula was used for this purpose: 100 x (SSE value – pre-exercise value) / (maximal or peak value – pre-exercise value).

Post steady-state exercise GXT (GXTpost)

Immediately after the SSEs (no cessation of exercise), participants underwent the same GXT_{con} performed in DAY1 (warm-up excluded) and HR (HR_{peak}) and $\dot{V}O_2$ ($\dot{V}O_{2peak}$) peaks were measured for each experimental trial.

The $\dot{V}O_2$ and HR raw data were smoothed as 15-breath moving average[41] and 5-second stationary time average,[42] respectively. The highest values of $\dot{V}O_2$ and HR were considered peak values if a $\dot{V}O_2$ plateau was present during GXT_{post}, or if the highest HR, expressed as 5-second stationary time average, recorded during GXT_{post}, was within 4 bpm from the HR_{max} of the control maximal exercise tests. If the test did not meet at least one of these criteria it was repeated.

Statistical analysis

Data collection for the present study is ongoing. Since the number of participants who have already completed all the study sessions is too small to allow for inferential statistical and hypotheses testing analyses, descriptive statistics were employed. SPSS Statistics (IBM, v.20) software was used for all analyses.

SSE intensity compliance

Subjects' compliance to each planned SSE intensity (i.e., target HRs corresponding to either 60% or 80% of HRR) was evaluated by calculating the root mean square error (RMSE). The difference between the actual (expressed as 5-second stationary time average) and the target HR of each 5-second interval was calculated, and the sum of the squared differences was then divided by the number of intervals before calculating the square root. If the RMSE of a trial was higher than 5 bpm, the data of the whole experimental trial session were discarded, and the session was scheduled to be repeated.

Effect of SSE intensity and duration on the %HRR-%$\dot{V}O_2$R relationship

For each of the four experimental conditions, the effect size (ES) between %HRR and %$\dot{V}O_2$R was calculated by dividing the mean of the differences between %HRR and %$\dot{V}O_2$R by the SD of the differences between %HRR and %$\dot{V}O_2$R.

Results

Pre-exercise and maximal HR and $\dot{V}O_2$ values recorded during the control tests are presented in Table 1.

Table 1. Subjects pre-exercise and maximal HR and $\dot{V}O_2$ values recorded during control tests.

	Mean ± SD	Minimum – Maximum
Pre-exercise HR (bpm)	84.5 ± 11.1	76 – 100
Maximal HR (bpm)	200.3 ± 11.1	187 – 214
Pre-exercise $\dot{V}O_2$ (mL·min^{-1}·kg^{-1})	4.8 ± 0.3	4.4 – 5.0
Maximal $\dot{V}O_2$ (mL·min^{-1}·kg^{-1})	55.2 ± 3.6	52.0 – 60.3

SD, standard deviation; HR, heart rate; $\dot{V}O_2$, oxygen uptake.

The RMSE between actual and target HR during the SSEs was lower than the pre-imposed cut-off in each SSE (RMSE: mean = 2.4, SD = 0.7, range = 1.7 to 3.7).

HR and $\dot{V}O_2$ responses to SSEs, expressed as absolute values and percentages of the reserve values, and calculated using both maximal values recorded during the “control maximal exercise tests” (Maximal) and peak values recorded during each GXT$_{post}$ (Peak), are presented in Table 2.

Table 2. HR and $\dot{V}O_2$ responses to 15 and 45 min of SSE with HR held constant at 60% and 80% of HRR (Mean ± SD).

	15 min		**45 min**	
	SSE at 60% of HRR	SSE at 80% of HRR	SSE at 60% of HRR	SSE at 80% of HRR
HR (bpm)	154.3 ± 9.7	177.2 ± 10.5	152.5 ± 8.4	175.2 ± 8.3
$\dot{V}O_2$ (mL·min^{-1}·kg^{-1})	36.1 ± 3.4	50.9 ± 5.9	33.9 ± 7.5	43.1 ± 5.1
HR_{peak} (bpm)	202.2 ± 12.1	197.4 ± 12.0	196.0 ± 13.3	198.5 ± 12.5
$\dot{V}O_{2peak}$ (mL·min^{-1}·kg^{-1})	56.8 ± 4.9	60.7 ± 8.9	55.8 ± 8.3	56.4 ± 3.6
HRR_{max} (%)	60.5 ± 0.9	80.3 ± 0.9	59.0 ± 2.1	78.7 ± 2.2
$\dot{V}O_2R_{max}$ (%)	62.5 ± 10.1	92.4 ± 16.3	58.2 ± 16.5	76.5 ± 12.8
HRR_{peak} (%)	59.4 ± 1.7	82.2 ± 1.6	61.3 ± 3.2	79.8 ± 2.9
$\dot{V}O_2R_{peak}$ (%)	60.1 ± 4.6	82.9 ± 3.3	56.5 ± 8.0	74.0 ± 5.1

HR, heart rate; $\dot{V}O_2$, oxygen uptake; SSE, steady-state exercise; HRR, heart rate reserve; $\dot{V}O_2R$, oxygen uptake reserve; SD, standard deviation; HR_{peak}, peak HR recorded during incremental exercises following each SSE; $\dot{V}O_{2peak}$, peak $\dot{V}O_2$ recorded during incremental exercises following each SSE; HRR and $\dot{V}O_2R$ computed using maximal values obtained during the control exercise tests (max) and peak values recorded during incremental exercise following each SSE (peak).

When expressed relatively to the GXT_{post} peaks, the ESs between %HRR and %$\dot{V}O_2R$ were negligible for both 15 min SSEs, whereas the ESs were large for the 45 min SSEs. The differences between %HRR and %$\dot{V}O_2R$ during SSEs, calculated using Maximal and Peak values, along with the corresponding ESs are presented in Table 3.

Table 3. Mean, SD and ES of the differences between %HRR and %$\dot{V}O_2R$ during SSEs, calculated using Maximal and Peak values.

		15 min		**45 min**	
		Maximal	Peak	Maximal	Peak
SSE at 60% of HRR					
	Mean	-2.05	-0.75	0.78	4.83
	SD	9.76	4.87	14.77	4.93
	ES	-0.21	-0.15	0.05	0.98
SSE at 80% of HRR					
	Mean	-12.10	-0.70	2.18	5.85
	SD	16.29	4.85	11.15	2.44
	ES	-0.74	-0.14	0.20	2.40

SD, standard deviation; ES, effect size; HRR, heart rate reserve; $\dot{V}O_2R$, oxygen uptake reserve; SSE, steady-state exercise; Maximal, maximal values recorded during the control exercise tests; Peak, peak values recorded during incremental exercise following each SSE.

Effect Size of the differences between the percentages of HRR and $\dot{V}O_2R$ during the 4 SSEs, calculated using peak values recorded during the graded exercise tests performed after SSE are graphically displayed in Figure 1.

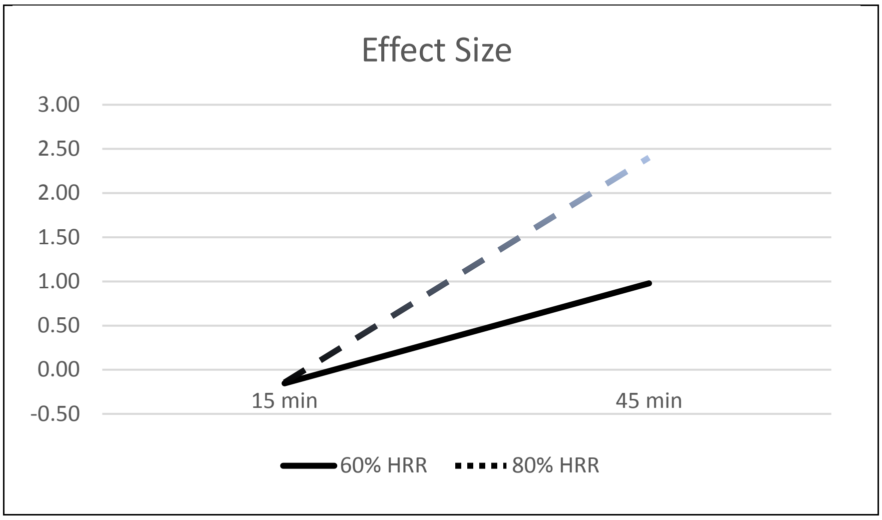

Figure 1. Effect Size of the differences between %HRR and %V̇O₂R during steady-state exercises (SSE), calculated using peak values recorded during the graded exercise tests performed after SSE.
15 min, SSE of 15 minutes; 45 min, SSE of 45 minutes; 60% HRR, SSE at 60% of heart rate reserve (HRR); 0% HRR, SSE at 80% HRR.

Discussion

The main findings of the present study are that the relationship between %HRR and %V̇O₂R seems to be affected by both the intensity and duration of SSE, and that the 1:1 relationship between the percentages of the two reserves appears not to be valid for SSE of long duration.

When the percentages of the reserve values were calculated using the peak values obtained during GXT_{post}, the differences between %HRR and %V̇O₂R showed negligible negative ESs for both the 60%- and 80%-HRR 15-min SSE. On the contrary, 45-min SSEs yielded large and positive ESs. The positive sign implies a higher %HRR than %V̇O₂R, hence suggesting an effect of the SSE duration on the %HRR-%V̇O₂R relationship (see Table 3).

The ES of the differences between %HRR and %V̇O₂R in the 80%-HRR 45-min SSE was more than twice the ES of the 60%-HRR 45-min SSE; however, the ESs are similar between the two intensities in the SSEs of 15 min, which suggests that SSE intensity has an effect solely when it interacts with SSE duration (see Figure 1).

The difference between the ESs of the two intensities during 45-min SSEs is due in part to the mean difference, which is in line with the ES results, and in part to the lower SD that was recorded during the SSE at 80% HRR (see Table 3), which may have amplified the magnitude of the ES in the SSE of 45 min at 80% HRR, hence the interaction effect of SSE intensity and duration.

Therefore, the aforementioned results suggest that the 1:1 relationship between %HRR and %$\dot{V}O_2R$ is valid during SSEs of 15 min, whereas in SSEs of longer duration, the percentages of the reserve values start to dissociate, and the magnitude of the dissociation is larger at higher exercise intensities (see Figure 1).

To the best of our knowledge, only one study[29] performed the aerobic exercises by maintaining a constant HR; however, subjects' compliance to the target steady-state exercise intensity was not assessed. In the present study, HR was held constant in order to compensate for increased physiological demands that occur during prolonged aerobic exercises when a constant power output is used. Indeed, during prolonged aerobic exercises at constant power outputs physiological adjustments occur, namely cardiovascular drift and $\dot{V}O_2$ slow component, increasing the relative exercise intensity.[24]

HR was chosen as the parameter to be held constant because during prolonged aerobic exercises the maximal HR recorded during the control maximal exercise test or GXT_{post} has been shown not to change in several studies.[27-29, 44, 45] Moreover, even though it was found to change in one study,[30] HR was preferred to $\dot{V}O_2$ because of the well document changes in $\dot{V}O_{2max}$ after prolonged aerobic exercise (see Wingo et al.[26] for a review). Indeed, holding a constant $\dot{V}O_2$ would have resulted in different relative intensities over time throughout the exercise sessions. Moreover, maintaining a constant HR is one of the most common methods used to prescribe aerobic exercise intensity. This is due to the fact that HR monitors are more readily available than metabolic carts, which are not commonly employed in aerobic exercise prescription due to their high cost and the expertise required to use them.

The results of the present study are in line with and reinforce the results obtained in the studies of Wingo and colleagues.[26] Furthermore, these results suggest that calculating the percentages of the reserves using the maximal values recorded during the control maximal exercise tests, which is the approach adopted by Cunha et al.[24], could yield a biased representation of the relationship between %HRR and %$\dot{V}O_2R$ during SSEs. Future studies that investigate the %HRR-%$\dot{V}O_2R$ relationship should therefore assess the peak values after every experimental condition.

The results of the present study cannot be easily compared with the available literature due to the differences among exercise protocols and aims of the studies. Indeed, the investigation of Cunha et al.[24] aimed to assess if the %HRR-%$\dot{V}O_2R$ relationship was 1:1; however, they did not measure the Peak HR and $\dot{V}O_2$ after prolonged aerobic exercises; hence, the %HRR-%$\dot{V}O_2R$ relationship could be biased due to the changes in maximal HR and $\dot{V}O_2$ induced by aerobic exercise.

On the contrary, Wingo et al. in their reviews[25, 26] measured the maximal HR and $\dot{V}O_2$ after prolonged aerobic exercise, but they did not assess if the %HRR and %$\dot{V}O_2R$ have a 1:1 relation. Instead, they analyzed published[29, 30] and unpublished[27, 28] data from several of their studies and reported that the changes over time ($\Delta_{45\text{-}15}$), calculated as the difference between the percentage of a given reserve at 45 minutes and at 15 minutes, were found to be related (unadjusted r = 0.68 and adjusted r = 0.82, the correlation was adjusted for repeated measures) and described by the following equation: $\%\Delta_{45\text{-}15}\dot{V}O_2R = 0.83 \times \%\Delta_{45\text{-}15}HRR + 1.98$. However, the equation was not compared to the identy line (i.e., slope = 1 and intercept = 0); hence, the preservation of the relationship between %HRR and $\%\dot{V}O_2R$ cannot be assumed.

Moreover, only two[29, 30] of the four studies examined in Wingo's reviews[25, 26] reported the actual %HRR and $\%\dot{V}O_2R$ after prolonged aerobic exercise. However, even though a direct interpretation cannot be made because the researchers did not assess if the %HRR and $\%\dot{V}O_2R$ have a 1:1 relationship, the %HRR was higher than $\%\dot{V}O_2R$ in every condition and study, with mean differences between %HRR and $\%\dot{V}O_2R$ of: 8.5% after 15 min and 4.9% after 45 min of aerobic exercise;[30] 9.5% after 15 min and 9.9% after 45 min at a constant power output;[29] and of 6.7% after 15 min and 16.9% after 45 min at a constant HR.[29] These findings seem to disprove the 1:1 relationship between the percentages of the reserve values.

Therefore, a 1:1 relationship, hence equality, between the percentages of HRR and $\dot{V}O_2R$, and the preservation of the relationship during prolonged aerobic exercise should not be inferred from the results presented in Wingo's reviews[25, 26] or articles[29, 30]. Indeed, the current literature along with the results of the present study highlight the inadequacy and pitfalls of the current guidelines, and point to the need for additional studies examining how SSE intensity and duration affect the HR-$\dot{V}O_2$ relationships.

Conclusions

During SSEs the 1:1 relationship between %HRR and $\%\dot{V}O_2R$ seems to be preserved in SSEs of relatively short duration (i.e., 15 min), but does not appear to be preserved in SSEs of longer duration (i.e., 45 min), suggesting an effect of SSE duration on the %HRR-$\%\dot{V}O_2R$ relationship.

The effect of SSE duration on the %HRR-$\%\dot{V}O_2R$ relationship appears to be affected by SSE intensity. Indeed, during SSEs of 45 min, the higher the intensity was (i.e., 80% of HRR) the higher the difference between %HRR and $\%\dot{V}O_2R$, pointing to a possible interaction effect of SSE intensity and duration.

Moreover, the changes over time of %HRR were relatively greater than those of $\%\dot{V}O_2R$, during both SSEs at 60% and at 80% of HRR, suggesting a dissociation between the percentages of the two reserves over time, which induced higher %HRR than $\%\dot{V}O_2R$ after 45 min of SSE.

SSE duration, *per se*, seems to affect the association between %HRR and $\%\dot{V}O_2R$ since its 1:1 relationship was not preserved when relatively long SSEs were employed, while SSE intensity appears to interact with the effect of SSE duration. Indeed, the higher the intensity was the higher the difference between %HRR and

%$\dot{V}O_2R$ at the end of the 45-min SSE only. The changes over time in %HRR seem to be greater than those of %$\dot{V}O_2R$, regardless the SSE intensity.

Therefore, the aforementioned results suggest that the 1:1 relationship between %HRR and %$\dot{V}O_2R$ is valid during relatively short SSEs at 60% and 80% of HRR, whereas in SSEs of longer duration, the percentages of the reserve values start to dissociate and the magnitude of the dissociation grows larger at higher exercise intensities.

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Overall conclusions

The aim of the present work was to delve deeply into the research topic of aerobic exercise intensity prescription by investigating several of its known potential pitfalls and unaddressed issues.

To this end, four different studies were carried out. The first two studies focused on incremental exercise: STUDY 1 investigated the actual relationships between HR and $\dot{V}O_2$, while the influence of individual characteristics on the HRR-$\dot{V}O_2$R relationship was examined in STUDY 2. In the following two studies the issue of the transferability of the HRR-$\dot{V}O_2$R relationship derived from the incremental exercise test to constant intensity exercise was investigated in both steady-state exercise of moderate intensity and short duration (STUDY 3) and steady-state exercise with different intensities and durations (STUDY 4).

STUDY 1 showed that both the %HRR-%$\dot{V}O_2$R and %HRR-%$\dot{V}O_{2max}$ relationships were different from the identity line (i.e., y = x), which is in contrast with the literature on which the current ACSM exercise prescription guidelines are based. In addition, the intercepts and slopes of the regressions of the two relationships showed high standard deviations, which highlights high variability among individuals and can cause a substantial error when the relationship is used to predict HR and/or $\dot{V}O_2$ values for a single person. STUDY 2 showed that although several subject characteristics influenced the relationship between %HRR and %$\dot{V}O_2$R, these characteristics did not explain most of the variance of the slopes and intercepts. Indeed, the prediction models of this study showed low precision and high error. Therefore, STUDY 1 and STUDY 2 show that the relationship between %HRR and %$\dot{V}O_2$R is not 1:1 as indicated by the current ACSM guidelines, and that using a single equation for the whole population does not appear to be suitable for representing the equation of a given subject and has low predictive ability, even when several confounding factors are accounted for. Hence, individual relationships between the %HRR and %$\dot{V}O_2$R are preferable when prescribing the intensity of aerobic exercise in order to avoid the potentially high error associated with using a standardized relationship for the whole population.

STUDY 3 demonstrated the lack of external validity associated with using the %HRR-%$\dot{V}O_2$R relationship derived from incremental exercise for SSE. Indeed, during SSEs of relatively short duration the 1:1 %HRR-%$\dot{V}O_2$R relationship did not appear to be suitable for predicting the intensity of SSEs; hence, the individual relationship derived from a prior GXT is preferable. Nonetheless, the prediction error of both the GXT and 1:1 relationship during SSEs was relatively high and should be taken into account, particularly when exercise intensity is an important consideration from a safety standpoint. STUDY 4 showed that during SSEs the 1:1 relationship between %HRR and %$\dot{V}O_2$R seems to be preserved when exercise duration is relatively short, which is in line with the results of STUDY 3. On the contrary, the 1:1 relationship between %HRR and %$\dot{V}O_2$R did not appear to be preserved in SSEs of longer duration, suggesting an effect of SSE duration on the

%HRR-%$\dot{V}O_2R$ relationship. The effect of SSE duration on the %HRR-%$\dot{V}O_2R$ relationship appeared to be influenced by SSE intensity. Indeed, during SSEs of 45 min, the higher the intensity was (i.e., 80% of HRR) the higher the difference between %HRR and %$\dot{V}O_2R$, pointing to a possible interaction effect of SSE intensity and duration. Therefore, STUDY 3 and STUDY 4 suggest that the 1:1 relationship between %HRR and %$\dot{V}O_2R$ is valid during relatively short cycling and running SSEs at different intensities, whereas during SSEs of long duration the percentages of the reserve values start to dissociate, and the magnitude of the dissociation grows larger at higher exercise intensities.

The present work reveals how the current literature regarding the nature of the association between HR and $\dot{V}O_2$ during incremental exercise and its transferability to steady-state exercise is still inadequate and based on certain assumptions that have not yet been fully investigated. Additionally, the present work reveals that the current methods used to prescribe aerobic exercise intensity yield a relatively high error and might be inappropriate in certain circumstances. Hence, additional studies investigating the HR-$\dot{V}O_2$ relationships during SSEs are warranted to improve the accuracy of aerobic exercise intensity prescription. In particular, the current literature is lacking studies that allow us to predict how the relationships between HR and $\dot{V}O_2$ are affected during SSEs by aerobic exercise modality, intensity, duration, subject characteristics and the interaction of all these variables. The results of the present work, along with future studies addressing the above-mentioned issues, will increase the accuracy of aerobic exercise intensity prescription, which will have direct implications on aerobic exercise efficacy, allowing us to increase the benefits/risks ratio of aerobic exercise programs.

Appendix

List of abbreviations

List of the abbreviations and acronyms used in the text

Abbreviation	Description
ACSM	American College of Sports Medicine
BFP	Body Fat Percentage
CI	Confidence Intervals
ES	Effect Size
FINAL model	model with the highest adjusted R^2
GXT	Graded Exercise Test
$GXT_{50}HRR$	GXT predicted %HRR at SSE_{50}
$GXT_{60}HRR$	GXT predicted %HRR at SSE_{60}
HR	Heart Rate
HR_{max}	maximal Heart Rate
HR_{peak}	peak Heart Rate recorded during GXT post steady-state exercise
HRR	Heart Rate Reserve
HR_{rest}	resting Heart Rate
ICC	Intraclass Correlation Coefficients
Maximal	maximal values recorded during the control maximal exercise test
MLR	Multiple Linear robust Regressions
MSE	Mean Square Error
n^{corr}	corrected sample size for clustered data
Peak	Peak values recorded during GXT post steady-state exercise
PO	Power Output
RMSE	Root Mean Square Error
SD	Standard Deviation
SSE	Steady-State Exercise
SSE_{50}	Steady-State Exercise at 50 W
$SSE_{50}HRR$	actual %HRR of SSE_{50}
$SSE_{50}\dot{V}O_2R$	actual %$\dot{V}O_2R$ of SSE_{50}
SSE_{60}	Steady-State Exercise at 60% of the $\dot{V}O_{2max}$
$SSE_{60}HRR$	actual %HRR of SSE_{60}
$SSE_{60}\dot{V}O_2R$	actual %$\dot{V}O_2R$ of SSE_{60}
T1	incremental exercise test to exhaustion
T2	steady-state exercise test followed by a progressive test to maximum
VIF	Variance Inflation Factor
$\dot{V}O_2$	oxygen uptake
$\dot{V}O_{2max}$	maximal oxygen uptake
$\dot{V}O_{2peak}$	peak oxygen uptake recorded during GXT post steady-state exercise
$\dot{V}O_2R$	oxygen uptake Reserve
VT	Verification Trial
Δ	difference
Δ_{45-15}	changes over time
η^2	eta squared