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Exercise Intensities in MS - Comparison between the Physiological Threshold Values of a Cardiopulmonary Exercise Test and the Estimated Values by Training Formulas

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Abstract

Background: Quantification of training intensities via current formulas (e.g. 75% of the estimated maximum heart rate (HR-peak)) is practical and a time saving compromise. However misinterpretations of cardiorespiratory fitness in persons with MS (pwMS) may lead to stagnancy or loss of exercise capacity.

Objectives: Feasibility of different training intensities of established training formulas in pwMS using a method comparison according to Bland-Altman.

Methods: 83 pwMS were included and the thresholds were determined via breathing gas analysis of peak oxygen consumption (VO2) and carbondioxide (CO_2). The sample was divided according to the expandend disability status scale (EDSS) in mildly (EDSS 1.0-4.0) and moderately impaired (EDSS 4.5 - 6.5). The formulas (210 age)*0.65, (210-age)*0.70, (210-age)*0.80, 180-age, 65% of the effective highest heart rate during CPET (HR-Peak), 70%HR-peak, 75% HR-peak and 80% HR-peak were used for the estimation of the training heart rates. Method comparisons were performed using Passing-Bablok regression and Bland-Altman plots. All values are expressed as mean and 95% confidence interval (CI).

Results: Passing-Bablok regression show that for mildly impaired pwMS 70% and 75% HR-peak show an agreement with the threshold values. For severely impaired pwMS 65% HR-peak showed by trend an agreement with the threshold values. Other formula values missed the criteria for agreement.

Conclusion: This study indicates that 70% and 75% HR-peak for moderately impaired PwMS gave adequate training intensities comparable to the threshold values.

Keywords: Multiple sclerosis; Cardiopulmonary exercise test; Exercise; Training intensities

Introduction

MS is a chronic disease of the central nervous system, accompanied by varying inflammatory manifestations, demyelization and axonal loss [1]. With chronic progressive or relapsing-remitting disease onsets persons with MS (PwMS) progressively develop impaired functional capacity and show reduced physical activity compared to healthy controls [2]. Findings show that the degree of impairments are not primarily due to the disease itself but for the most part due to secondary causes like inactivation that further decrease health status of PwMS [3].

Exercise has become an efficient strategy within rehabilitative programs and is part of a goal-orientated multidisciplinary approach to improve disability and participation in PwMS [4-7]. Exercise ranges from passive physiotherapy-based interventions to submaximal endurance training sessions. It has become clear that an eventual worsening of the sensory symptoms – expressed by 40% of PwMS – is temporal and will normalize in within half an hour after the exercise session [8,9].

Current recommendations advise PwMS that exercise should be matched with the individual performance capacities [10]. However only few interventions perform a CPET or graded exercise test in pwMS for quantifying levels cardiorespiratory fitness.

The gold standard for the quantification of cardiorespiratory fitness is an individual determination of the fitness level by direct and continuous measurements (breath by breath) of the maximum oxygen consumption (VO_{2max}) via ergospirometry [11]. VO_{2max} is an important marker for general health and the general exercise performance [12] that is associated with higher physical (walking speed) and cognitive functions [13]. VO_2 measurements are time-consuming and cost intense therefore often not practical for clinical routines. Quantification of the training intensities via current formulas e.g. (210-age) * 0.7 is by contrast practical and a time saving compromise. However misinterpretations of the cardiorespiratory fitness levels in pwMS may lead to physical under- or overload that provokes stagnancy or loss of exercise capacity during standardized rehabilitation [14]. This method comparison analyzes if the obtained training intensities from current formulas are comparable with the physiological threshold values and are adequate for pwMS.

Materials and Methods

Experimental design

This retrospective method comparison analyzed the achieved training intensities between the established training formulas and the physiological threshold values obtained by cardiopulmonary exercise test (CPET) in pwMS.

83 pwMS were advised for cardiopulmonary exercise testing (CPET) and were tested at entry to the Valens clinic.

The physiological breakpoints of the thresholds were determined via breathing gas analysis of peak oxygen consumption (VO_2) and carbon dioxide (CO_2). The sample was divided according to the expanded disability status scale (EDSS) in moderately impaired – pwMS holding an EDSS of 1.0 - 4.0 – and severely impaired – pwMS holding an EDSS of 4.5 - 6.5. The formulas (210-age) * 0.65, (210-age) * 0.70, (210-age) * 0.80, 180-age, 65% of the effective maximum rate in CPET (HR-max), 70% HR-max, 75% HR-max and 80% HR-max were used for the estimation of the training intensity.

Sample size calculations were based on a pragmatic approach. For the scope of this study the aim was to recruit at least 60 patients within a period of approximately 2½ years.

Subjects

All participants were inpatients for rehabilitation at the Valens Rehabilitation Center, Switzerland. 170 patients held a definite MS diagnosis [revised Mc Donald criteria [15]] and were screened over a three-year period (12 July 2010 to 10 April 2013) for study inclusion on the day of their clinical admission. 105 MS patients fulfilled the main study criteria of an expanded disability status scale (EDSS) score between 1.0 and 6.5. Patients underwent a general medical screening for study eligibility and were excluded if persistent infections, cardiovascular and pulmonal diseases were existent. Participants were excluded if they had acute relapses or symptom exacerbations the day prior to cardiopulmonary exercise testing.

83 pwMS were eligible for inclusion and performed CPET. Baseline characteristics of the data are given in Table 1.

Cardiopulmonary exercise test (CPET)

All participants performed a progressive CPET on a cycle ergometer (Ergoline 800, Germany) at entry. Individual cardiopulmonary fitness level was monitored by direct and continuous measurements (breath by breath) of maximum oxygen consumption (VO_{2max}) by ergospirometry (PanGas CPX, Germany) [11].

The exercise protocol consisted of (a) first three minutes at rest (no pedaling) on the cycle ergometer; (b) three minutes of unloaded pedaling as warming up; (c) testing phase until the participant reached a symptom limited maximum. Workload was continuously ramp typed increased by 5-10 Watts every minute to ensure 8-12 minutes of testing; (d) final three minutes as unloaded pedaling for cooling down. Heart rate (Polar Electro, Kempele, Finland) and blood pressure (Riva Rocci) were continuously monitored the last ten seconds every two minutes during test. Peak oxygen consumption (VO_{2peak}) was defined as the highest VO_2 value when the following criteria were attained: respiratory equivalent ratio (RER) > 1,10; HR-peak within 10 beats min-1 of age predicted maximum and rating of perceived exertion (RPE > 8,5) via the Borg scale [11,16].

Statistical analyzes

Means and 95% confidence intervals were calculated for the aerobic (lactate) threshold (VO_2), the estimated training intensity through the formulas and the absolute differences between estimated and measured values (HR-estimated – HR-measured). The box-plots of the threshold and formula values display the distribution between estimated and threshold values. Scatterplots including the identity lines of five beats min^{-1} were drawn for all analyzed formulas. Pearson correlations coefficients were calculated to test if the EDSS had an influence on the training intensity. A method comparison was performed to determine the feasibility of the training formulas with a Passing and Bablok regression. The criteria for a method agreement were set through the slope and intercept of the function (slope=1; intercept=0).

Data in the figures and tables are presented using mean and 95% confidence intervals (CI) and the level of significance was set at 0.05. All statistical calculations were conducted with the Statistical Package of Social Sciences version 19.0 for Mac (SPSS Inc, Chicago, USA) and medcal.

Results

83 (25 male / 58 female) subjects with a mean age of 48 years (95%CI 46-51 years; min. 23 years, max. 78) were tested. 34 participants were moderately impaired (EDSS 1.0- 4.0) and 49 were severely impaired (EDSS 4.5-6.5).

Box-plot analysis for EDSS revealed that for the moderately impaired pwMS (210-age) * 0.7 [113.7; -0.1 beats / min^{-1} (CI -5 to 4.8 beats / min^{-1})] and 75% HR-max [113.2; -0.7 beats / min^{-1} (CI -4.3 to 3.0 beats / min^{-1})] show comparable training intensities.

For severely impaired pwMS (210-age) * 0.65 [104.7; 1.1 beats / min^{-1} (CI -2.5 to 4.8 beats / min-1)], 75% HR-max [100.5; -3.0 beats / Min (CI -7.0 to 1.0 beats / min^{-1})] and 80% HR-max [107.2; 3.7 beats / min^{-1} (CI -0.5 to 7.9 beats / min^{-1})] show comparable training intensities.

Data show associations between the differences of the estimated values, the threshold values and the EDSS.

Passing-Bablok regression for moderately impaired pwMS show that 70% (slope=0.99; 95% CI: 0.67-1.26; intercept=-9.30; 95% CI: 42.00-32.00) and 75% (slope=1.64; 95% CI: 0.71-1.36; intercept=-10.51; 95% CI: -46.63-31.86) of HR-peak show an agreement with the threshold values. Data show no significant deviations from linearity ($p > 0.1$).

For severely impaired pwMS only 65% HR-max showed by trend an agreement with the threshold values (slope=1.26; 95% CI: 0.99-1.60; intercept=-44.35; 95%CI: -79.95- -14.95). Other formula values missed the criteria for agreement.

Box-plots of the differences of estimated – threshold values of HR-aerob for the EDSS subdivisions are shown in Figure 1, Bland-Altman plots of 65%, 70% and 75% of HR-max are shown in Figures 2 and 3.

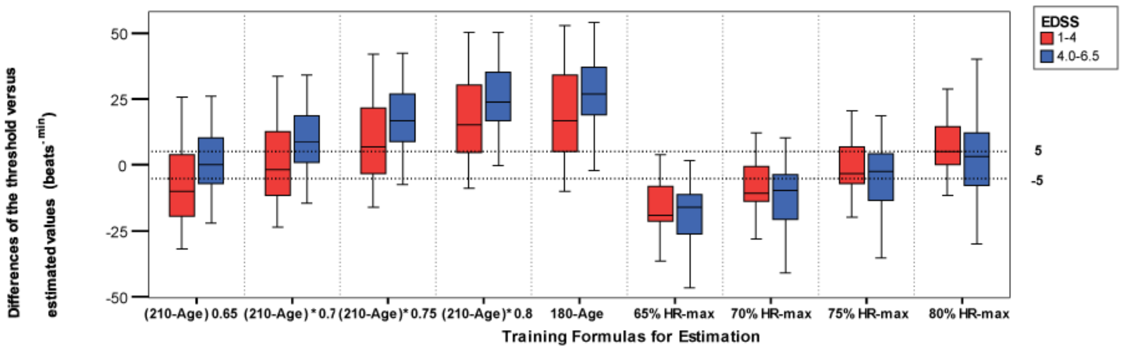

Figure 1: Differences of heart rates at the lactate threshold of the estimated formula and threshold values. Abbreviations: EDSS=Expanded Disability Status Scale; HRaerob: Heart rate at the lactate threshold; HR-max: Effective maximum heart rate during CPET; min: minutes.

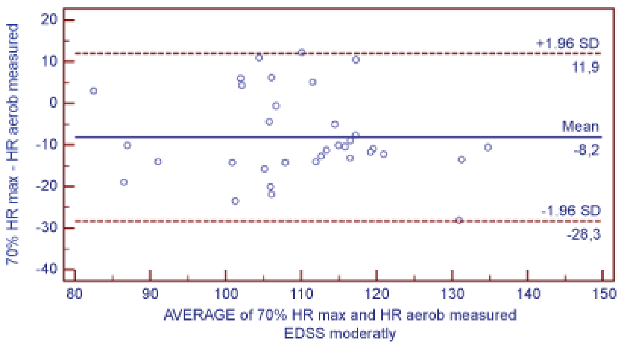

Figure 2: Bland-Altman plot of the comparisons between 70% and 75% of the effective maximum heart rate and the physiological threshold values.

Discussion

Data of this study indicate that the training intensities quantified via current formulas are not suitable for pwMS as the formulas mainly overestimated the target range specified through the threshold values obtained by CPET.

Only 70% and 75% HR-max for moderately impaired pwMS gave an adequate training intensity comparable to the threshold values.

Studies define VO_{2max} as the major function of the cardiovascular and ventilatory system through gas exchanges between the cells [11].

As impairments in cardiorespiratory functioning are most apparent during exercise cell respiration stimulation and gas transport immediately impact the cardiovascular system. Both cardiac output and heart rate increase linearly with VO_2 during increasing work rate exercise however exceptions occur when the heart rate response to exercise may inappropriately low. These include patients taking beta-adrenergic blocking drugs, patients with cardiomyopathy and patients with heart block [11,17,18].

Studies question if during step- or ramp wise incremental exercise, the attained values are maximal values and not the highest values achieved in the test (peak values) [18]. In pwMS clinical symptomology affects mainly the lower limbs and reduced motor efficiency due to accompanying spasticities and motor incoordination limiting the maximum effort of the participants to a subjective felt maximum [19]. With disease onset and progressive loss of muscular functions, exercise performance and compliance to the CPET procedures on cycle ergometers becomes more difficult and impossible for pwMS with an EDSS 7.0 [20,21].

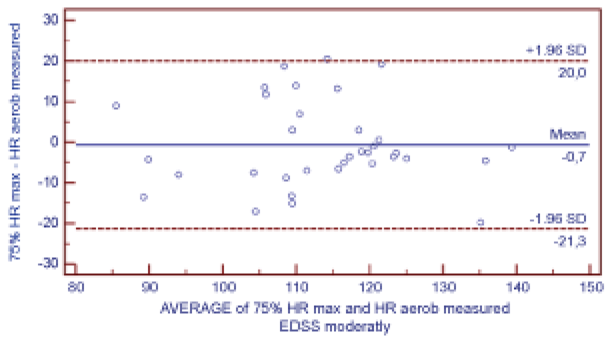

Figure 3: Data of Passing and Bablok regression show the predictability of training heart rates via the formula for moderately impaired pwMS. Data show mean and confidence interval. Abbreviations: EDSS: Expanded Disability Status Scale; HRaerob: Heart rate at the lactate threshold; HR-max: Effective maximum heart rate during CPET; min: minutes; pwMS: Persons with multiple sclerosis.

Also, pwMS show reduced motor efficiency due to accompanying spasticities and motor incoordination letting patients stop at the subjected felt maximum.

In this study the attained CPET values have to be seen peak values of a test performed to the subjective felt (symptom limiting) maximum of the person and the attained effects have to be seen as learning and conditioning effects towards the test procedures over the intervention. This may explain the differences and variations between HR-peak and the age-corrected formula values.

Studies show that the accuracy of a forecasted training intensity of formulas is in general low and the values allow scattering ranges of the training heart rates of 10-15 beats [22].

The method comparison between the physiological values and formula values also show high differences and error rates of 70% of the analyzed formula values. Here, results show that only the acquaintances of the HR-max allowed a high accuracy and consistency for obtaining adequate exercise intensities. This indicates the relevance for a precise quantification of exercise capacity in pwMS through CPET or a graded exercise test.

Data resembles results of intervention studies that show that the attained adaptations through exercise are intensity (mild or strenuous), type (eccentric or concentric) and duration (short- or long-termed) dependent effects [23,24].

There is cumulating evidence that the achieved adaptations are associated with the intensity dependent lactate increases during exercise [25]. This dose-response relationship between the mode and the exercise intensity implicates the relevance of the exercise protocol as higher exercise intensities seem to facilitate greater benefits, also in pwMS [20,23,25-27].

In pwMS however only few interventions perform a CPET or graded exercise test for quantification of cardiorespiratory fitness in pwMS and the performed exercise intensities are not adequately described. Studies that perform CPET in pwMS indicate that the beneficial effects of endurance training are attained and tolerated although participants being fatigued and severely impaired (EDSS 4.5-6.5) [26-33]. Accurate assessment of cardiorespiratory fitness is crucial for optimizing the effects of exercise to a rehabilitative intervention.

Conclusion

This study indicates that training intensities quantified via formulas are not suitable for pwMS. A specific method comparison showed that only 70% and 75% of the maximum heart rate for moderately impaired pwMS gave an adequate training intensity comparable to the threshold values. Rehabilitation programs with pwMS should consider a precise quantification of exercise capacity early in disease progression and accompany with adequate training to build up functional reserves and prevent deconditioning of pwMS. This becomes of more relevance the more disabled the persons are.

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