Are first ventilatory threshold and 6-minute walk test heart rate interchangeable? A pilot study in healthy elders and cardiac patients

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**A R T I C L E   I N F O**

Article history:
Received 26 March 2014
Accepted 30 July 2014

**A B S T R A C T**

Background: Heart rate (HR) at the ventilatory threshold (VT) is often used to prescribe exercise intensity in cardiac rehabilitation. Some studies have reported no significant difference between HR at VT and HR measured at the end of a 6-min walk test (6-MWT) in cardiac patients. The aim of this work was to assess the potential equivalence between those parameters at the individual level.

Method: Three groups of subjects performed a stress test and a 6-MWT: 22 healthy elders (GES, 77 ± 3.7 years), 10 stable coronary artery disease (CAD) patients (GES, 50.9 ± 4.2 years) and 30 patients with chronic heart failure (GHF, 63.3 ± 10 years). We analyzed the correlation, mean bias, 95% confidence interval (95% CI) of the mean bias and the magnitude of the bias between 6-MWT-THR and VT-HR.

Results: There was a significant difference between 6-MWT and VT-HR in GHF (99.1 ± 8.8 vs 91.6 ± 18.6 bpm, P = 0.016) but not in GES and GM. The correlation between these 2 parameters was high for GMI (r = 0.78, P < 0.05), and moderate for GES and GHF (r = 0.48 and 0.55, respectively, P < 0.05). The 95% CI of bias was large (> 30%) in GES and GHF and acceptable in GMI (8–12%).

Conclusion: 6-MWT-HR and VT-HR do not appear interchangeable at the individual level in healthy elders and CHF patients. In CAD patients, further larger studies and/or the development of other walk tests could help in confirming the interest of a training prescription based on walking performance, after an exhaustive study of their cardiometabolic requirements.

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1. Introduction

Exercise training is one of the core components of cardiac rehabilitation (CR), with secondary prevention program [1,2]. However, the optimal method to personalize training intensity remains controversial, as recommendations vary considerably (ranging from 50 to 100% of the maximal exercise capacity) [1–3].

Cardiopulmonary exercise testing (CPET) is recommended in entering CR, firstly in order to screen for potential myocardial ischemia, for threatening arrhythmia or for effort-induced hypertension. CPET can also be used to help in estimating the prognosis of mortality [4], to evaluate the maximal and submaximal exercise capacity and prescribe tailored program for physical activity,[5] particularly during CR [6]. Training intensity is usually prescribed at a target heart rate (THR) [7], commonly set at the HR corresponding to the first ventilatory threshold (VT) [8–11]. Indeed, one of the main aims of CR is to improve submaximal aerobic capacity. However, no robust prospective studies clearly support the systematic use of the THR at the first VT in CAD patients. Moreover, considering the prevalence of cardiovascular disease, it is difficult to perform a CPET with VO2 measurement for all these patients, as it requires a specialized infrastructure and expensive resources. In addition, a CPET could be contraindicated for debilitated patients because it exposes to musculoskeletal damage and to various cardiac events [12]. Finally, CPET may be perceived as an unpleasant experience, thus leading to a lack of motivation to reach maximal effort that can alter the results significance.

Other easier and faster testing modalities thus appear useful to evaluate patients at various submaximal levels that are more relevant to daily activities [13,14] Even if there are still no recommendations regarding potential alternatives to CPET,
functional evaluations, such as walk tests are thus being more and more used. The 6-min walk test (6-MWT) is now widely proposed to assess functional exercise capacity and prognosis since it is reproducible, well tolerated and corresponds to submaximal moderate exercise. Some studies showed that its relative intensity corresponds approximately to the first VT in elderly and cardiac patients [13,15–18], whereas other authors found that HR or VO₂ recorded during the 6-MWT was higher than that observed at this first VT in elderly [19], and chronic heart failure (CHF) patients [20,21].

In a recent pilot study, Greneaux et al. showed that setting exercise intensity prescription at the HR measured at the end of the 6-MWT allowed to obtain a similar exercise capacity improvement than with a conventional protocol using a training HR derived from maximal HR of the CPET [18]. Another study showed that walking speed at self selected (comfortable) velocity could be used to personalize training intensity in CAD patients [22], with the advantage of being perceived as pleasant, which is a positive point for a really prolonged behavioral change [23].

The aim of this work was to assess the potential equivalence between the 6-MWT-HR and the first VT-HR at the individual level in 3 populations for whom exercise training is recommended in primary or secondary prevention: healthy elderly subjects, coronary artery disease patients, and CHF patients.

2. Methods

2.1. Participants

Participants were included if they had completed an exercise training program or a CR program. Patients were not included if they presented: significant cognitive disorders that hampered participation in the tests (Mini Mental State examination < 24); atrial fibrillation; acute or chronic respiratory failure; or any associated disease that limited walking capacity apart from aging or cardiac disease. All data were collected on a personal form, included in the patient’s medical file. This study was approved by the local ethic committee, and informed written consent was obtained for all participants after they had been informed of all of the risks, the discomfort and benefits involved in this study.

2.1.1. Elderly participants (GES group)

They were healthy community-dwelling older volunteers enrolled in a large prospective study investigating the effects of one-year exercise training program in healthy elderly (24). Twenty two participants completed this program combining aerobic and strength training, in line with recommendations [2]. Sessions were performed in the rehabilitation department of Dijon University Hospital twice a week and at home once a week [24].

2.1.2. Cardiac (coronary and CHF) patients (GMI and GHF groups)

Patients were included without distinction of gender, if they were aged between 35 and 80 years; they were at the end of an outpatient program of CR [1,25]; they had been referred for: myocardial infarction, coronary angioplasty ± stenting, coronary artery bypass surgery, stable angina, CHF. CHF was defined as left ventricular ejection fraction < 45% using the echocardiographic Simpson method. Patients were excluded if they presented: renal failure, exercise-induced arrhythmia, or residual myocardial ischaemia; pacemaker; severe obstructive heart disease; moderate to severe aortic stenosis; intracavitary thrombosis; pulmonary hypertension > 70 mmHg; modification of drugs affecting adaptation to effort within the 15 days preceding the tests (diuretics, angiotensin conversion enzyme inhibitor, angiotensin receptor antagonist 2, beta-blockers, anti-aldosterone, ivabradine). On the other hand, the drugs class, even influencing the HR (for example beta-blocker), was not an exclusion criterion. Sessions were performed in the rehabilitation department of Dijon University Hospital twice a week and at home once a week.

2.2. Protocol Design

2.2.1. Measurements

At baseline and after the training period, participants performed a symptom-limited CPET on a cycle ergometer and a 6-MWT. The walk test was performed 2 to 4 days after the CPET. We only analyzed the post-training data, in order to avoid the influence of potential medical treatment modifications, especially in the GMI and GHF groups.

2.2.2. Symptom-limited CPET

Each participant performed one symptom-limited incremental CPET on a cycloergometer (Lode, Groningen, Netherlands). After a 1-min warm-up period pedaling at 20 W, the work rate was increased by 10 W every minute. A 12-lead electrocardiogram (Cardiosystem Marquette Hellige, Milwaukue, Wisconsin, USA) was continuously monitored. Left arm blood pressure was measured every 2 min using a standard cuff mercury sphygmonanometer. Gas exchange was measured breath-by-breath by a computerized system (CPX, Medical Graphics, St. Paul, MN). The exercise was stopped when the subject was unable to maintain the imposed pedaling rhythm of 60 revolutions per minute, and the reason for stopping (dyspnea, exhaustion, leg fatigue) was noted. Before each test, the system was calibrated with a 3-L Rudolph syringe and a standard gas of known concentration. The inspiratory airflow and the fraction of expired oxygen and carbon dioxide were measured every second. Averages were then established every ten seconds for ventilation, oxygen uptake, carbon dioxide production, respiratory ratio and breathing frequency. Peak VO₂ and peak HR were defined as the mean oxygen uptake and heart rate values during the last 30 s of exercise. The first VT was determined by two blinded and independent investigators, using Wasserman’s method [26]. HR value corresponding to the first VT was noted.

2.2.3. Walk tests

The 6-MWT walk test was administered by a therapist blinded to the CPET result. It was performed on a 50-m unobstructed path. The patients were instructed to walk at a self-selected pace from one end of the path to the other and back, in order to cover as much distance as they could during the allotted time. The test was monitored and the time was called out every 2 min. Standard encouragement at 30-s intervals was provided. Slowing down and stopping to rest were permitted. At the end of 6 min, the total distance walked in meters (m) was measured. These technical aspects are in line with the American Thoracic Society recommendations for the 6-MWTc (32). At first, the patients performed a familiarization test in order to avoid learning effects.

HR was monitored throughout the walk-test with a telemetric device (Teleguard, GE Medical Systems, Denmark) and the highest value was noted during the last 30 s of the test. These values allowed assessment of relative cardiac intensity of the 6-MWT with respect to the CPX maximal HR. Blood pressure was measured before and immediately after each test at the left arm using a standard cuff mercury sphygmonanometer. Any clinical symptoms such as angina were recorded.

2.3. Statistical analysis

Standard statistical methods were used for the calculation of means and standard deviations.

Normal Gaussian distribution of the data was verified by the Shapiro-Wilk test and homoscedasticity by a modified Levenne
Table 1
Patient’s clinical and anthropometric data.

<table>
<thead>
<tr>
<th>Population</th>
<th>Eiders (n = 24)</th>
<th>CAD (n = 10)</th>
<th>CHF (n = 30)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>77.2 ± 3.6</td>
<td>50 ± 8.5</td>
<td>61.7 ± 10.7</td>
</tr>
<tr>
<td>Sex (M/F)</td>
<td>12/12</td>
<td>10/0</td>
<td>22/8</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>162.8 ± 6.3</td>
<td>178 ± 6</td>
<td>170 ± 7.3</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>67.4 ± 11.6</td>
<td>81.7 ± 15</td>
<td>73.2 ± 14.5</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>25.3 ± 3</td>
<td>25.8 ± 4.1</td>
<td>25.2 ± 4.1</td>
</tr>
<tr>
<td>Medications (n)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>β-blockers</td>
<td>10</td>
<td>30</td>
<td></td>
</tr>
<tr>
<td>ACE inhibitors</td>
<td>10</td>
<td>25</td>
<td></td>
</tr>
<tr>
<td>ARB</td>
<td>0</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Diuretics</td>
<td>0</td>
<td>19</td>
<td></td>
</tr>
</tbody>
</table>

M: male; F: female; BMI: body mass index; CAD: coronary artery disease; CHF: chronic heart failure; ACE: angiotensin-converting enzyme; ARB: angiotensin receptor blockers.

Table 2
Maximal exercise test and walk tests results in the 3 groups.

<table>
<thead>
<tr>
<th>Population</th>
<th>GES (n=22)</th>
<th>GMI (n=10)</th>
<th>CHF (n=30)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peak VO₂ (mL/min/kg)</td>
<td>21.6 ± 4.2</td>
<td>27.4 ± 6.6</td>
<td>19.6 ± 5.8</td>
</tr>
<tr>
<td>VT VO₂ (mL/min/kg)</td>
<td>14.4 ± 2.4</td>
<td>19.2 ± 7.8</td>
<td>11.9 ± 4.2</td>
</tr>
<tr>
<td>ET peak HR (bpm)</td>
<td>134.8 ± 16.2</td>
<td>126.2 ± 11.6</td>
<td>116.9 ± 24</td>
</tr>
<tr>
<td>VT HR (bpm)</td>
<td>104.2 ± 14.3</td>
<td>94.2 ± 4.8</td>
<td>91.6 ± 18.6</td>
</tr>
<tr>
<td>VT relative intensity (% maxHR)</td>
<td>77.20%</td>
<td>74.60%</td>
<td>78.30%</td>
</tr>
<tr>
<td>6-MWT HR (bpm)</td>
<td>104.04 ± 16.8</td>
<td>92.1 ± 6.8</td>
<td>99.1 ± 18.8</td>
</tr>
<tr>
<td>VT relative intensity (% maxHR)</td>
<td>77.20%</td>
<td>73%</td>
<td>84.70%</td>
</tr>
<tr>
<td>6-MWT distance (m)</td>
<td>464.9 ± 60.1</td>
<td>559.7 ± 54.8</td>
<td>485.9 ± 92.3</td>
</tr>
</tbody>
</table>

ml: milliliters; min: minute; kg: kilograms; CPET: cardio-pulmonary exercise test; HR: heart rate; VT: ventilatory threshold; 6-MWT: 6-min walk test.

test. Mean bias, which represents the mean difference between repeated measurements, was assessed with a non-parametric Wilcoxon matched pairs test. The magnitude of difference was assessed by the Hedges’s g (g), calculated as follows [27]: g = J × d; where J is a correction factor calculated according to Eq. 1 and d is Cohen’s d, calculated according to Eq. 2.

Eq. 1:

\[ f = \frac{3}{4d f - 1} \]

where df represents the degrees of freedom (df = n–1 in the case of dependent groups);

Eq. 2:

\[ d = \frac{M_1 - M_2}{S_{within}} \]

where M1 and M2 are the mean of the first and the second trials and Swithin is the standard deviation within groups, calculated as follows:

\[ S_{within} = \frac{S_{diff} f}{\sqrt{f}} \]

where Sdiff is the standard deviation of differences between pairs and r is the correlation between pairs).

The scale proposed by Cohen was used for interpretation [28]. The magnitude was considered either very small (g < 0.2), or small (0.2 < g < 0.5), or moderate (0.5 < g < 0.8), or large (g > 0.8).

Table 3
Heart rate during the 6-min walk test and at the ventilatory threshold during the symptom-limited cardiopulmonary exercise test: correlation, bias, 95% confidence interval for the bias and magnitude of the bias. Data are reported as mean ± standard deviation, by the exception of Hedges g (mean ± standard error).

<table>
<thead>
<tr>
<th>Population</th>
<th>Heart rate (bpm)</th>
<th>Correlation</th>
<th>Bias (bpm)</th>
<th>95% CI for the bias</th>
<th>Hedges g</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>6 WT</td>
<td>VT</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GES (n=22)</td>
<td>104.4 ± 16.8</td>
<td>104.2 ± 14.3</td>
<td>0.48*</td>
<td>0.2 ± 15.9</td>
<td>-33.5 &lt; μ₁ - μ₂ &lt; 33.9</td>
</tr>
<tr>
<td>GMI (n=10)</td>
<td>92.1 ± 6.8</td>
<td>94.2 ± 4.8</td>
<td>0.78*</td>
<td>-2.1 ± 4.3</td>
<td>-12.3 &lt; μ₁ - μ₂ &lt; 8.1</td>
</tr>
<tr>
<td>CHF (n=30)</td>
<td>99.1 ± 18.8</td>
<td>91.6 ± 18.6</td>
<td>0.55*</td>
<td>7.5 ± 17.8</td>
<td>-28.9 &lt; μ₁ - μ₂ &lt; 43.9</td>
</tr>
</tbody>
</table>

*P < 0.05; VT: ventilatory threshold; 6-MWT: 6-min walk test; bpm: beat per minute; CI: confidence interval.
To our knowledge, difference between the 6-MWT HR and the first VT-HR has never been investigated at the individual level in those populations.

The potential differences regarding relative intensity of the 6-MWT in elderlies when compared to the study of Kervio et al. might be partially explained by the patients’ characteristics [18]. Indeed, our subjects were older (77.2 ± 3.6 vs 64.7 ± 1.4), had a lower BMI (25.3 ± 3 vs 26.4 ± 0.7). Moreover, they just completed a one-year training program that improved their exercise capacity and might have increased the first VT level. Finally, there are still controversies regarding walking speed instructions during the 6-MWT, that can, at least partially, explain the difference evidenced in those studies. Indeed, the 6-MWT has been first developed for the functional evaluation of CHF patients [30], but has been largely developed and used in chronic respiratory diseases, where it is supposed to measure “the distance that a patient can quickly walk” [31]. The ATS recommendations thus state that “the object of this test is to walk as far as possible for 6 min. You will walk back and forth in this hallway. Six minutes is a long time to walk, so you will be exerting yourself. You will probably get out of breath or become exhausted”. These recommendations may participate to lead patients to perform the walk test at an intensity close to that of peak VO₂ [32]. However, in the initial description of the test by Guyatt, CHF patients (NYHA class 3) are not encouraged to achieve an exhausting effort, but rather to “cover as much ground as they could during the allotted time”, without instruction regarding walking speed or effort intensity [30]. Recommending a self-selected speed (“self-paced” or comfortable speed) appears fundamental, as it corresponds to the greatest energetic efficiency for a given subject (i.e. the lowest energy expenditure per meter) [33].

Concerning GHF, we evidenced a significant difference between the 6-MWT HR and the first VT-HR, in line with other studies conducted by Kervio et al. among CHF patients [20,21]. However, the difference in relative intensity of first VT and 6-MWT, expressed as a percentage of max HR, was less marked in our study (78.3% vs 84.7%, respectively, and 75% vs 90% in the study by Kervio et al). This might be explained by the lowest severity of the disease in ours sample. Indeed, Jahn et al. reported that this could significantly influence the 6-MWT relative intensity [34]. This has led certain authors to propose an adjustment of the instructions by using the Borg scale [35]. Thus, patients are asked to limit their efforts’ intensity during the 6-MWT at a level placed between 11 and 13 on the 6–20 Borg scale in order to avoid an early exhaustion and to make sure of a submaximal test. This method appeared reproducible but was only studied during a treadmill test. Nevertheless, the idea to use the Borg’s scale is interesting because the “Rate of Perceived Exhaustion” (RPE) appears to be correlated with certain physiological parameters. Thus, in the meta-analysis by Chen et al. among healthy subjects [36], RPE was found to be significantly correlated with several physiological parameters usually considered in the determination of the first VT such as VO₂ (r = 0.63), ventilation (r = 0.61) and blood lactate levels (r = 0.57). A more recent review performed by Coquart et al. [37] concluded that the individual relationship between RPE and VO₂ (RPE/VO₂) can be used to predict VO₂ max (or VO₂ peak) from data measured during submaximal exercise tests.

We did not evidence significant difference between the 6-MWT HR and the first VT-HR in GES and GHF, and found a significant correlation between these parameters. However, our complementary analysis suggest that it remains questionable to consider that these two HR can be considered as interchangeable for training purpose, especially in the GES (mean bias (± 95% IC) = 0.2 ± 15.9 bpm). The correlation between the 6-MWT HR and the first VT HR was the highest in the GMI (r = 0.78, P < 0.05), with a small mean bias (~2.1 bpm), but a standard deviation representing twice this mean bias (~4.3 bpm). This probably explains why the 95% CI remains quite high as the difference might rise up to 12 bpm. However, this appears much more acceptable in clinical practice than that evidenced in GES and GM (> 30%). Moreover, the clinical implications might be negligible as the magnitude of the bias in GMI group appears limited with a small effect size (Hedges g = 0.3 ± 0.41).

In CR, training intensity is usually prescribed using a THR deriving from max HR observed at the end of baseline CPET. However, the recommended intensity is not precisely defined [1,2], and choosing THR as a fraction of max HR probably leads to bias in estimating the optimal training intensity. Indeed, the relationship between exercise relative intensity and HR is disturbed by medications, especially beta-blocker therapy [38], or by the heart disease itself. Moreover, the nature of the initial CPET with workload increments is very different from exercise training sessions usually performed in CR. In athletes, field tests are widely used to build training strategy, as laboratory testing is hard to perform for all athletes. Since the famous 12-min running test described by Cooper [39], large numbers of similar tests have been developed and studied, especially in endurance sports. Few of them have been extensively studied and validated, even though they are widely used to plan training sessions [40].

In this context, with regards to our results in the GMI, the 6-MWT HR could be considered as a valuable alternative in training intensity prescription and assessment of improvement of sub-maximal aerobic capacity, especially in CAD patients. Indeed, given its self-paced nature, one can consider that it leads patient to spontaneously adopt the most efficient walking speed from a bioenergetics point of view, that could help in improve patients adherence to exercise training as we previously reported [18]. This may warrant the possibility of sustaining such efforts long enough to induce significant improvements in exercise capacity.
Our study suffers a few limitations that lead to consider our results with caution. First, the number of patients was quite limited, especially in the GMI. This probably limits the statistical power of our results. We also included selected patients (stable patients, with an intermediate risk profile, without ischemia and other co-morbidities), without women in the GMI group. Second, the assumption made on the intensity of exercise as a fraction of maximal HR could be a source of bias due to the different nature of the exercises. Despite the well-known differences between walk tests and ergocycle incremental tests with regard to the amount of exercising muscle mass and ergonomics [41], we used the ergocycle since it has been recommended as a standard for the assessment of exercise tolerance in healthy subjects [42]. However, to date, most of the studies exploring the relative intensity of the 6-MWT in patients with cardiorespiratory diseases have also performed their symptom-limited exercise test on ergocycle [15,32,43].

Finally, in the GES, the subjects were volunteers recruited by information documents posted in associations for the elderly, and were thus probably more healthy and motivated than old people who do not take part in such activities. However, observed walking speeds were quite close to reference values for this age group [44].

In conclusion, the results of this pilot study show that 6-MWT-HR risk VT-HR do not appear interchangeable at the individual level in healthy elderly and CHF patients. In CAD patients, further studies on a larger sample could help in confirming or infirming, the clinically negligible difference between those parameters in stable CAD patients under optimal medical treatment. In case of negative results, the development of other walk tests could help in confirming the interest of a training prescription based on walking performance, after an exhaustive study of their cardiac-metabolic requirements.

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

Acknowledgements

We would like to thank the whole rehabilitation team for their help during this study, especially Armelle Hannequin and Cyrielle Krawcow.

References


