Heart Rate Recovery in the First Minute at the Six-Minute Walk Test in Patients with Heart Failure

Sabrina Lindemberg1,2, Sergio Chermont1,2, Mônica Quintão1,2, Milena Derossi1, Sergio Guilhon1,3, Sabrina Bernardetz1, Luana Marchese1,2, Wolney Martins1,2, Antônio Claudio L. Nóbrega1, Evandro Tinoco Mesquita1

Programa de Pós-graduação em Ciências Cardiovasculares / Universidade Federal Fluminense1, Niterói, RJ; Clínica de Insuficiência Cardíaca (CLIC) / Centro Universitário Serra dos Órgãos2, Teresópolis, RJ; Instituto de Cardiologia Aloisio de Castro3, Rio de Janeiro, RJ - Brazil

Abstract

Background: Heart rate recovery at one minute of rest (HRR) is a predictor of mortality in heart failure (HF), but its prognosis has not been assessed at six-minute walk test (6MWT) in these patients.

Objective: This study aimed to determine the HRR, at 6MWT in patients with HF and its correlation with six-minute walk distance (6MWD).

Methods: Cross-sectional, controlled protocol with 161 individuals, 126 patients with stable systolic HF, allocated into 2 groups (G1 and G2) receiving or not β-blocker and 35 volunteers in control group (G3) had HRR recorded at the 6MWT.

Results: HRR and 6MWD were significantly different in the 3 groups. Mean values of HRR, and 6MWD were: HRR = 12 ± 14 beat/min G1; 18 ± 16 beat/min G2 and 21 ± 13 beat/min G3; 6MWD = 423 ± 102 m G1; 396 ± 101 m G2 and 484 ± 96 m G3 (p < 0.05). Results showed a correlation between HRR, and 6MWD in G1(r = 0.3; p = 0.04) and in G3(r = 0.4; p= 0.03), but not in G2 (r= 0.12; p= 0.48).

Conclusion: HRR response was attenuated in patients using βB and showed correlation with 6MWD, reflecting better exercise tolerance. HRR, after 6MWT seems to represent an alternative when treadmill tests could not be tolerated. (Arq Bras Cardiol. 2014; 102(3):279-287)

Keywords: Heart rate; Heart failure; Walking; Exercise.

Introduction

Heart rate recovery (HRR) shows the autonomic activity in cardiovascular system1,2 and is predictive of morbidity and mortality in patients with heart failure (HF)3-8 and when calculated by difference of HR at peak exercise to HR measured at the first minute immediately after exercise, it becomes the HRR after one minute of rest (HRR1), which has been associated with poor outcomes in HF in several trials using treadmill tests9,10,11-12.

Beta-blockers (βB) are mandatory in HF treatment due to protection against catecholamine deleterious effects on myocardial cells besides mortality decrease9-11-13, although they hamper the HRR, in exercise tests and may interfere with its prognostic value13-17.

HRR, has been studied in cardiopulmonary exercise tests18, recommended as the gold standard for exercise test in HF. Another alternative to evaluate exercise tolerance in HF is the six-minute walk test (6MWT), applied in clinical practice with a significant association between the six-minute walk distance (6MWD) and mortality in patients with HF19,20.

Previous studies have validated the 6MWT as predictive and it seems an appropriate method to evaluate exercise tolerance in HF16,17,20, as well as a better representation of actual exertion in daily living activities15,16,17,19.

Little is known about the prognostic value of HRR, in the 6MWT21,22. A previous study observed this correlation in idiopathic pulmonary fibrosis21,22 and a recent editorial observed the clinical usefulness of HRR after submaximal exercise in HF and showed sensitivity of 6MWT to differentiate abnormal HRR response. The 6MWT may produce a cardiac response such as that obtained during maximal effort in cardiopulmonary testing22. Although there have been no studies with the specific purpose of evaluating HRR, at the 6MWT, the present study aimed to determine HRR response and identify a correlation between HRR, and 6MWD in HF. In this study the possible influence of βB therapy on HRR was also considered.
Methods

Following a cross-sectional, controlled protocol, of 161 individuals: 126 patients (72 male; age 62 ± 13 years; BMI 27 ± 5 Kg/m²) and 35 volunteer individuals without HF (16 male, age 60 ± 13 years; BMI 27 ± 3 Kg/m²; sedentary) in control group, were assessed according to inclusion and exclusion criteria.

All patients were selected from the Heart Failure Clinic of Universidade Federal Fluminense, with stable systolic HF (LVEF < 50%, Simpson), as Framingham and Boston criteria, NYHA II-III, distributed into 2 groups, receiving or not β-blocker (Carvedilol, mean dose 30 ± 29 mg), respectively G1 and G2. The group without β-blocker consisted of patients at their first visit, so they were not yet receiving β-blocker and were submitted to 6MWT. Healthy individuals were allotted in a third group (G3). Both patients and healthy individuals were submitted to 6MWT following the American Association of Cardiovascular and Pulmonary Rehabilitation (AACVPR) guidelines. The study was approved by the institution research ethics committee and all patients signed the free and informed consent form.

Inclusion criteria consisted of individuals with a diagnosis of systolic HF, ischemic or non-ischemic, without history of pulmonary or peripheral vascular disease, age > 21 years, of both sexes, in sinus rhythm, undergoing standardized pharmacological treatment, all receiving beta-blockers, stable in last 3 months.

Exclusion criteria were based on the exercise test's safety protocols, with individualized evaluation: chronic obstructive pulmonary disease, atrial fibrillation, unstable angina, acute myocarditis or pericarditis, acute systemic disease or fever, neuromuscular diseases, orthostatic hypotension > 20 mmHg, resting systolic blood pressure (SBP) ≥ 180 mmHg and diastolic blood pressure (DBP) ≥ 110 mmHg.

Variables measured during and after 6MWT are shown in Table 1.

Results

All 161 subjects were submitted to the protocol. A hundred fifty-four individuals completed all steps of the study. Seven patients (5 women) interrupted the test referring dyspnea and fatigue. Baseline characteristics are shown in Table 1.

HRR, at 6MWT was analyzed for each group and in comparison between groups. The possible influence of beta-blocker therapy in HRR, was considered and standard pharmacological treatment was described in Table 2.

Variables measured during and after 6MWT are shown in Table 3, for all sample and groups.

Responses of HRR, at 6MWT were different in all groups (p = 0.0002), as shown in Figure 1. In G1, G2 and G3 there was a significant difference for results related to HRR. Mean values of HRR, were: HRR = 12 ± 14 beat/min for G1; HRR = 18 ± 16 beat/min for G2 and HRR = 21 ± 13 beat/min for G3. There was no difference for HRR response when comparing genders in all groups.

Results showed HRR, and 6MWD had a significant correlation between G1 (r = 0.3; p = 0.04) and G3 (r = 0.4; p = 0.03), confirmed by Pearson test, as observed in Figures 2 and 3, respectively. However, this correlation between HRR, and 6MWD was not shown in G2 patients (r = 0.12; p = 0.48).

The 3 groups were different when 6MWD was compared, as observed in figure 4. (p = 0.0038) Mean values of 6MWD were: 423 ± 102 m for G1; 396 ± 101 m for G2 and 484 ± 96 m for G3.

Discussion

In this present study we investigated the applicability of HRR, to the 6MWT. The HRR, is a strong prognostic marker in HF and the 6MWT allows the assessment of exercise tolerance of HF patients, especially for patients that do not tolerate the treadmill test.

This fact is in agreement with a previous study, of which purposes were to define cut-off values for abnormal HRR and to determine whether an abnormal HRR carries prognostic value after a 6MWT in patients with idiopathic pulmonary fibrosis (IPF), which supports the rationale of this present study with HF patients.
Table 1 – Baseline characteristics for patients with HF allocated in the groups (n = 154)

<table>
<thead>
<tr>
<th>Variables</th>
<th>G1 (n = 84)</th>
<th>G2 (n = 35)</th>
<th>G3 (n = 35)</th>
<th>* p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>55 (65.4%)</td>
<td>15 (42.8%)</td>
<td>16 (45.7%)</td>
<td>0.030*</td>
</tr>
<tr>
<td>Female</td>
<td>29 (34.6%)</td>
<td>20 (57.2%)</td>
<td>19 (54.3%)</td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>61 ± 12</td>
<td>64 ± 14</td>
<td>60 ± 13</td>
<td>0.254</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>165 ± 1</td>
<td>160 ± 10</td>
<td>161 ± 28</td>
<td>0.026*</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>73 ± 16</td>
<td>71 ± 19</td>
<td>74 ± 12</td>
<td>0.525</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>27 ± 5</td>
<td>27 ± 5</td>
<td>27 ± 3</td>
<td>0.629</td>
</tr>
<tr>
<td>LVF (%) (Simpson)</td>
<td>42 ± 6</td>
<td>41 ± 7</td>
<td>----</td>
<td>0.283</td>
</tr>
<tr>
<td>NYHA II (n)</td>
<td>58 (69%)</td>
<td>23 (66%)</td>
<td>----</td>
<td>0.763</td>
</tr>
<tr>
<td>NYHA III (n)</td>
<td>26 (31%)</td>
<td>12 (34%)</td>
<td>----</td>
<td></td>
</tr>
<tr>
<td>Resting SBP (mmHg)</td>
<td>132 ± 15</td>
<td>125 ± 18</td>
<td>124 ± 15</td>
<td>0.021*</td>
</tr>
<tr>
<td>Resting DBP (mmHg)</td>
<td>81 ± 11</td>
<td>78 ± 12</td>
<td>79 ± 7</td>
<td>0.142</td>
</tr>
<tr>
<td>Resting HR (beats/min)</td>
<td>71 ± 14</td>
<td>82 ± 10</td>
<td>76 ± 9</td>
<td>0.0001*</td>
</tr>
<tr>
<td>Borg (0-10)</td>
<td>0 ± 1</td>
<td>1 ± 1</td>
<td>0 ± 0</td>
<td>0.449</td>
</tr>
<tr>
<td>Dyspnea scale (0-5)</td>
<td>0 ± 1</td>
<td>0 ± 1</td>
<td>0 ± 1</td>
<td>0.032*</td>
</tr>
</tbody>
</table>

G1: group 1 (patients underwent beta-blocker); G2: group 2 (patients without beta-blocker); G3: group 3 (individuals without heart failure); BMI: body mass index; LVEF: left ventricular ejection fraction; NYHA: New York Heart Association; SBP: systolic blood pressure; DBP: diastolic blood pressure. *p < 0.05 (variables with statistical significance).

Table 2 – Standard pharmacological treatment

<table>
<thead>
<tr>
<th>Drugs</th>
<th>G1 (%)</th>
<th>G2 (%)</th>
<th>G3 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>βB dose (mg) / (nº of patients in use; %)</td>
<td>30 ± 29 (100%)</td>
<td>----</td>
<td>----</td>
</tr>
<tr>
<td>ACEI (nº of patients in use; %)</td>
<td>66 (78.6%)</td>
<td>35 (100%)</td>
<td>----</td>
</tr>
<tr>
<td>Digoxin (nº of patients in use; %)</td>
<td>56 (66.7%)</td>
<td>11 (31.4%)</td>
<td>----</td>
</tr>
<tr>
<td>Diuretic (nº of patients in use; %)</td>
<td>70 (83.3%)</td>
<td>31 (88.6%)</td>
<td>----</td>
</tr>
</tbody>
</table>

βB: beta-blocker; ACEI: Angiotensin converting enzyme inhibitors.

Table 3 – Variables measured and calculated during and after 6MWT

<table>
<thead>
<tr>
<th>Variables</th>
<th>G3 (n = 84)</th>
<th>G2 (n = 35)</th>
<th>G3 (n = 35)</th>
<th>* p &lt; 0.05</th>
</tr>
</thead>
<tbody>
<tr>
<td>Resting HR (beats/min)</td>
<td>71 ± 14</td>
<td>82 ± 10</td>
<td>76 ± 9</td>
<td>0.0001*</td>
</tr>
<tr>
<td>2º min. HR (beats/min)</td>
<td>100 ± 17</td>
<td>107 ± 18</td>
<td>108 ± 19</td>
<td>0.009*</td>
</tr>
<tr>
<td>4º min. HR (beats/min)</td>
<td>105 ± 20</td>
<td>109 ± 15</td>
<td>104 ± 18</td>
<td>0.253</td>
</tr>
<tr>
<td>6º min. HR (beats/min)</td>
<td>99 ± 20</td>
<td>107 ± 16</td>
<td>106 ± 17</td>
<td>0.012*</td>
</tr>
<tr>
<td>Predicted HR (beats/min)</td>
<td>159 ± 12</td>
<td>156 ± 14</td>
<td>160 ± 14</td>
<td>0.254</td>
</tr>
<tr>
<td>Chronotrophic Reserve (predicted HR – Resting HR)</td>
<td>40 ± 16</td>
<td>36 ± 15</td>
<td>41 ± 15</td>
<td>0.0001*</td>
</tr>
<tr>
<td>Chronotrophic Deficit</td>
<td>31 ± 12</td>
<td>31 ± 12</td>
<td>27 ± 10</td>
<td>0.022*</td>
</tr>
<tr>
<td>HRR (beats/min)</td>
<td>12 ± 14</td>
<td>18 ± 16</td>
<td>21 ± 13</td>
<td>0.0002*</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>132 ± 15</td>
<td>125 ± 18</td>
<td>124 ± 15</td>
<td>0.006*</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>81 ± 11</td>
<td>78 ± 12</td>
<td>79 ± 7</td>
<td>0.267</td>
</tr>
<tr>
<td>Borg (0-10)</td>
<td>2 ± 2</td>
<td>3 ± 2</td>
<td>1 ± 1</td>
<td>0.009*</td>
</tr>
<tr>
<td>Dyspnea scale (0-5)</td>
<td>1 ± 1</td>
<td>1 ± 2</td>
<td>0 ± 1</td>
<td>0.004*</td>
</tr>
<tr>
<td>6MWD (meters)</td>
<td>423 ± 102</td>
<td>396 ± 101</td>
<td>484 ± 96</td>
<td>0.003*</td>
</tr>
</tbody>
</table>

G1: group 1 (patients underwent beta-blocker); G2: group 2 (patients without beta-blocker); G3: group 3 (individuals without heart failure); HR: heart rate; HRR: heart rate recovery in first minute; SBP: systolic blood pressure; DBP: diastolic blood pressure; 6MWD: six-minute walk distance. *p < 0.05 (variables with statistical significance).
Figure 1 – HRR after 6MWT in 3 groups. HRR, heart rate recovery in first minute; 6MWT: six-minute walk test.

Figure 2 – HRR and 6MWD correlation in G1. HRR, heart rate recovery in first minute; 6MWD: six-minute walk distance.
Figure 3 – HRR1 and 6MWD correlation in G3. HRR1: heart rate recovery in first minute; 6MWD: six-minute walk distance.

Figure 4 – Comparison of 6MWD in 3 groups. 6MWD: six-minute walk distance
HRR, has been shown to be a predictor of adverse events in HF after treadmill tests. However, HRR, after 6MWT was not assessed in HF patients yet, but only in patients with IPF. The results observed in this present study showed a pattern of HRR, response that was studied and compared among the 3 groups of this sample with a significant difference between HRR, performance in the 3 groups (p = 0.0002).

The abnormal value of HRR, was determined as a reduction ≤ 12 beat/min in 6MWT. Previous studies using treadmill tests with this cut-off point showed a mortality of 19% in the group with a HRR, ≤ 12 beat/min. Thus, in present study, a HRR, value validated for HF patients was used in treadmill tests.

HRR, reflects chronotropic response and appears to be attenuated in HF patients; however there are divergences regarding βB interference. In agreement with literature, in this present study we observed an attenuated pattern of response of HRR, in patients receiving βB when compared with non-βB patients and healthy volunteers.

This response could be attributed to a lower basal HR and not achieving the peak HR in the test is possibly due to βB effects, according to Cole et al. and Sheppard et al., which determined a peak HR of 116 ± 21 beat/min, in parallel with the results of the present study.

The possible mechanism that explains this attenuated response of HRR1 in HF is poorly elucidated. In normal conditions, β-1 and β-2 receptors have an important role in mediating the sympathetic stimulation. This response is characterized by a dominance of β-1 receptors over β-2 receptors and the parasympathetic reactivation it is not suppressed by the sympathetic system after exercise.

Ushijima et al. described that sympathetic hyperactivity with norepinephrine release, as well as "down regulation" of β-adrenergic receptors are involved in this attenuated response of HRR. The sympathetic stimulation during exercise inhibits the parasympathetic reactivation that occurs after exercise, and consequently, when this sympathetic activity remains exacerbated, it could limit HR response to exercise and these results of attenuated HRR.

This mechanism explained by Ushijima et al. may elucidate this attenuated pattern of HRR, shown in the present study, even in those receiving βB therapy, although we did not quantify markers of parasympathetic activity to confirm this HR performance.

At first, this attenuated response could be characteristic of a worse prognosis, but these patients showed a better 6MWD than patients without βB, similar to results observed in healthy volunteers, which could be due to benefits of βB therapy in improving peripheral muscles.

However, the present study found an important association between HRR, and walked distance as shown by the 6MWT, which also has predictive value.

This finding is consistent with previous investigations demonstrating the capacity of HRR, to predict adverse events in populations other than those with HF. Therefore, the value for abnormal HRR after sub-maximal exercise was defined as a change of 42 beats/min acquired from peak HR subtracted to that measured at 2 minutes into recovery, for healthy subjects. All patients in the present study showed a lower HRR, value than healthy subjects, probably due to poor parasympathetic activity usual in patients with HF.

The six-minute walk test represents an inexpensive method to evaluate exercise tolerance and provides important prognostic information in HF patients using or not βB. Recently, parameters registered by oximeter have been appreciated in determination of prognosis, so that HRR may be considered an easily obtained clinical variable, seldom studied in patients assessed in relation to 6MWD.

The positive correlation between HRR, and 6MWD showed to be an important information in these patients regarding either of the parameters, as HRR, and 6MWD have been shown to predict adverse cardiac outcomes. This current study was the first to show a correlation between 6MWD and HRR, in patients with HF.

There is no agreement about βB influence on HRR response, sympathetic tone and hemodynamic responses at the 6MWT. Thus, it is relevant to determine the pattern of HRR, response, as a predictive parameter in HF patients receiving βB therapy.

Olsson et al., in a systematic review on 6MWT and outcomes in HF patients, analyzed 63 randomized controlled studies, published between 1988 and 2004, in which only 10 studies included patients receiving carvedilol. The mean dose used in the majority of studies was 25 mg/day, which is similar to this present study.

Previous studies with HF patients receiving βB demonstrated an attenuated HRR. Nevertheless, the predictive value of HRR, was not altered and showed correlation with other prognostic parameters, such as maximal oxygen uptake, further adverse outcomes and hospitalizations.

In our study there was a linear correlation between HRR, and 6MWD, both in G1 and G3, but there was no correlation in G2.
increased further until 4 min into recovery, after which time parasympathetic effects on HR remained relatively constant. 

Although mechanisms of impaired HRR, in HF are not totally explained, it may indicate disorder in autonomic balance leading to delayed reactivation of parasympathetic tone, while the association between HRR, and 6MWD appears to be a novel and important finding.

The correlation between HRR, and 6MWD in HF patients consists an original finding and may contribute with relevant clinical information in HF patients. 

This present study may contribute additional evidence that abnormal HRR, could determine an adverse prognosis. This variable obtained at the 6MWT may provide simple clinical information with reference to exercise tolerance.

Conclusion

The present study determined the pattern response of HRR, at 6MWT in patients with HF receiving or not B and in individuals without HF.

Patients with HF receiving B showed better exercise tolerance, even though they had an attenuated HRR, when compared to patients that were not using B. There was a significant correlation between HRR, and 6MWD in patients underwent B and in healthy individuals, but there was no correlation between HRR, and 6MWD in patients not receiving B.

Finally, HRR, may be an important parameter to evaluate the results of 6MWT in HF, although further studies are necessary to explain the magnitude of this variable in this test and its applicability as an outcome marker.

Author contributions

Conception and design of the research: Lindemberg S, Chermont S, Mesquita ET; Acquisition of data: Lindemberg S, Chermont S, Quintão M, Derossi M, Guilhon S, Bernardes S, Marchese L; Analysis and interpretation of the data: Lindemberg S, Chermont S, Quintão M, Derossi M, Guilhon S, Bernardes S, Marchese L, Martins W, Nóbrega ACL, Mesquita ET; Statistical analysis: Lindemberg S, Chermont S, Quintão M, Nóbrega ACL, Mesquita ET; Writing of the manuscript: Chermont S, Marchese L; Critical revision of the manuscript for intellectual content: Lindemberg S, Chermont S, Quintão M, Bernardes S, Martins W, Nóbrega ACL, Mesquita ET.


