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

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Abstract

Background: Heart rate recovery at one minute of rest (HRR_1) 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_1 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_1 recorded at the 6MWT.

Results: HRR_1 and 6MWD were significantly different in the 3 groups. Mean values of HRR_1 and 6MWD were: HRR_1 = 12 ± 14 beat/min G1; 18 ± 16 beat/min G2 and 21 ± 13 beat/min G3; 6MWD = 423 ± 102 m G1; 396 ± 101m G2 and 484 ± 96 m G3 ($p < 0.05$). Results showed a correlation between HRR_1 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_1 response was attenuated in patients using βB and showed correlation with 6MWD, reflecting better exercise tolerance. HRR_1 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 system[1,2] 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 (HRR_1), which has been associated with poor outcomes in HF in several trials using treadmill tests[9-12].

Beta-blockers (βB) are mandatory in HF treatment due to protection against catecholamine deleterious effects on myocardial cells besides mortality decrease[8,9,11-13], although they hamper the HRR_1 in exercise tests and may interfere with its prognostic value[13-17].

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HRR_1 has been studied in cardiopulmonary exercise tests[18], 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 HF[19,20].

Previous studies have validated the 6MWT as predictive and it seems an appropriate method to evaluate exercise tolerance in HF[16,17,20], as well as a better representation of actual exertion in daily living activities[5,16,17,19].

Little is known about the prognostic value of HRR_1 in the 6MWT[21,22]. A previous study observed this correlation in idiopathic pulmonary fibrosis[21,22] 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 testing[22]. Although there have been no studies with the specific purpose of evaluating HRR_1 at the 6MWT, the present study aimed to determine HRR_1 response and identify a correlation between HRR_1 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[23-25], distributed into 2 groups, receiving or not β-blocker (Carvedilol, mean dose 30 ± 29 mg), respectively G1 and G2[11]. 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[17,19,25-29]. 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[25,26,29-30].

Exclusion criteria were based on the exercise test's safety protocols, with individualized evaluation[26,28-30]: chronic obstructive pulmonary disease, atrial fibrillation, unstable angina, acute myocarditis or pericarditis, acute systemic disease or fever, neuromuscular diseases, orthostatic hypotension > 20 mmHg (symptomatic), sinus tachycardia > 120 beat/min (at rest) and resting systolic blood pressure (SBP) ≥ 180 mmHg and diastolic blood pressure (DBP) ≥ 110 mmHg[26,28-30]. Patients with Chagas etiology were also excluded.

Variables were recorded using a systematic protocol[28,29] HR; HRR_1; SBP; DBP; mean arterial pressure (MAP); pulse pressure (PP); peripheral oxygen saturation (SpO_2); respiratory rate (RR); Borg Scale and 6MWD[26,27].

The 6MWT was performed according to AACVPR, after 15 minutes of rest and HR and SpO_2 were recorded throughout the procedure, specifically at the end of the 2nd, 4th and 6th minutes during 6MWT and immediately after the test, at the 1st and 2nd min during the recovery period. HR and SpO_2 were acquired by digital finger oximeters (Nonin Onyx 9500, Onyx manufactory, Massachusetts, USA)[20,24,25]. Limiting symptoms and Borg scale were observed during the entire test[28-30].

Abnormal HRR_1 was established as a decrease of 13-12 beats/min or less[14-16,21,22].

All tests were performed on a level hallway surface, 30 meters long, marked at each 1-m distance, with traffic cones placed at the point of return[26-29].

During the 6 MWT, Borg scale and dyspnea were recorded and time was informed each 2 minutes. Exactly at the 6th minute, patients were instructed to stop at the precise place, sat on a chair and were examined during the recovery period[26,27].

The HRR_1 was measured through a double check measurement, recorded by an oximeter and confirmed with palpable method of radial pulse, always on the left arm, during one minute.

Statistical Analysis

The minimum sample size was determined to be at least 69 subjects, as found in previous publications. All results were expressed as means ± SEM and $p < 0.05$ was considered significant. Statistical analysis was performed by One-way ANOVA for repeated measures to compare variables and groups and Tukey's test when "p" value showed significance. Pearson's correlation coefficient (r) was obtained to assess the association between HRR_1 and 6MWD.

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_1 at 6MWT was analyzed for each group and in comparison between groups. The possible influence of beta-blocker therapy in HRR_1 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_1 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_1. Mean values of HRR_1 were: $HRR_1 = 12 \pm 14$ beat/min for G1; $HRR_1 = 18 \pm 16$ beat/min for G2 and $HRR_1 = 21 \pm 13$ beat/min for G3. There was no difference for HRR_1 response when comparing genders in all groups.

Results showed HRR_1 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_1 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_1 to the 6MWT. The HRR_1 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[4,19,21,22].

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[21].

Table 1 – Baseline characteristics for patients with HF allocated in the groups (n = 154)

Variables	G1 (n = 84)	G2 (n = 35)	G3 (n = 35)	* p value
Male	55(65.4%)	15(42.8%)	16(45.7%)	0.030*
Female	29(34.6%)	20(57.2%)	19(54.3%)	
Age (years)	61 ± 12	64 ± 14	60 ± 13	0,254
Height (cm)	165 ± 1	160 ± 10	161 ± 28	0.026*
Weight (kg)	73 ± 16	71 ± 19	74 ± 12	0.525
BMI (kg/m2)	27 ± 5	27 ± 5	27 ± 3	0.629
LVEF (%) (Simpson)	42 ± 6	41 ± 7	-----	0.283
NYHA II (n)	58 (69%)	23 (66%)	-----	0.763
NYHA III (n)	26 (31%)	12 (34%)	-----	
Resting SBP (mmHg)	132± 15	125 ± 18	124 ± 15	0.021*
Resting DBP (mmHg)	81 ± 11	78 ± 12	79 ± 7	0.142
Resting HR (beats/min)	71 ± 14	82 ± 10	76 ± 9	0.0001*
Borg (0-10)	0 ± 1	1 ± 1	0 ± 0	0.449
Dyspnea scale(0-5)	0 ± 1	0 ± 1	0 ± 1	0.032*

*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 HR: heart rate. p< 0,05 * (variables with statistical significance).*

Table 2 – Standard pharmacological treatment

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

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

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

Variables	G3 (n = 84)	G2 (n = 35)	G3 (n = 35)	* p < 0,05
Resting HR (beats/min)	71 ± 14	82 ± 10	76 ± 9	0.0001*
2º min. HR (beats/min) (during 6MWT)	100 ± 17	107 ± 18	108 ± 19	0.009*
4º min. HR (beats/min) (during 6MWT)	105 ± 20	109 ± 15	104 ± 18	0.253
6º min. HR (beats/min) (during 6MWT)	99 ± 20	107 ± 16	106 ± 17	0.012*
Predicted HR (beats/min)	159 ± 12	156 ± 14	160 ± 14	0.254
Chronotropic Reserve (predicted HR – Resting HR)	40 ± 16	36 ± 15	41 ± 15	0.0001*
Chronotropic Deficit	31 ± 12	31 ± 12	27 ± 10	0.022*
HRR_1 (beat/min)	12 ± 14	18 ± 16	21 ± 13	0.0002*
SBP (mmHg)	132± 15	125 ± 18	124 ± 15	0.006*
DBP (mmHg)	81 ± 11	78 ± 12	79 ± 7	0.267
Borg (0-10)	2 ± 2	3 ± 2	1 ± 1	0.009*
Dyspnea scale (0-5)	1 ± 1	1 ± 2	0 ± 1	0.004*
6MWD (meters)	423 ± 102	396 ± 101	484 ± 96	0.003*

*G1: group 1 (patients underwent beta-blocker); G2: group 2 (patients without beta-blocker); G3: group 3 (individuals without heart failure); HR: heart rate; HRR1: 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).*

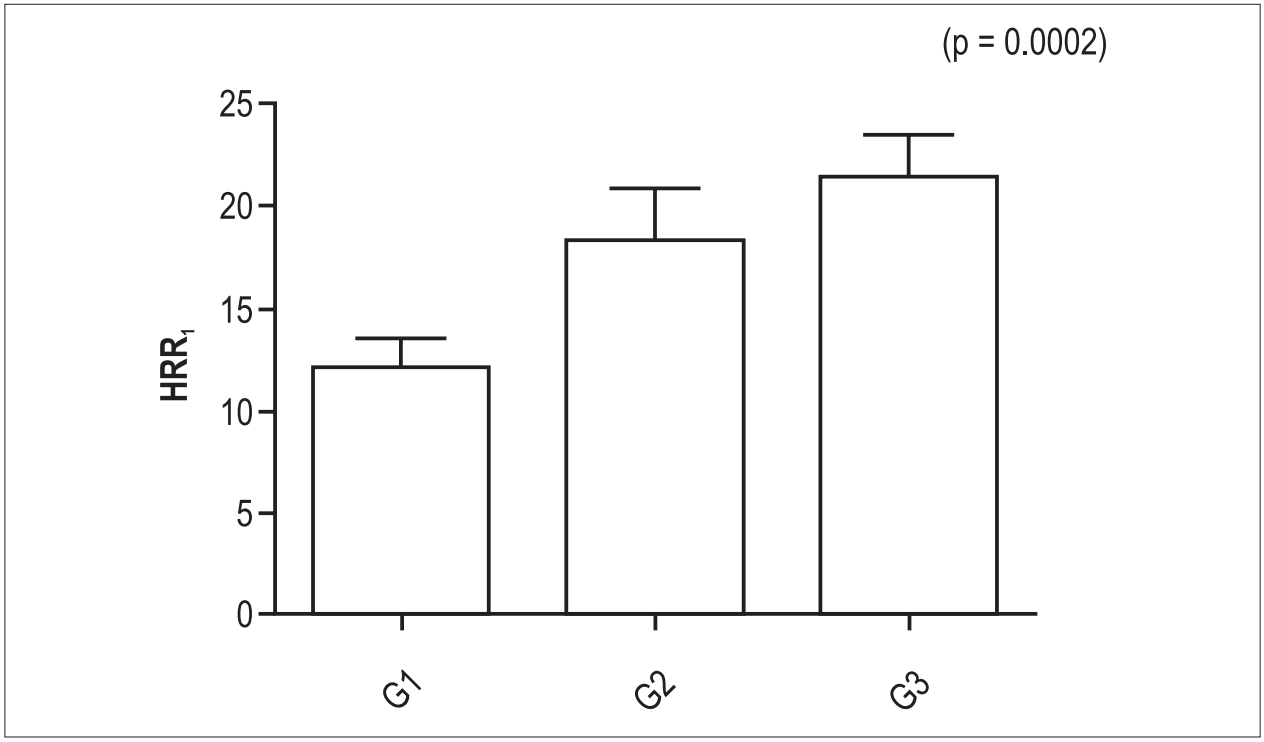

Figure 1 – *HRR_1 after 6MWT in 3 groups. HRR_1: heart rate recovery in first minute; 6MWT: six-minute walk test.*

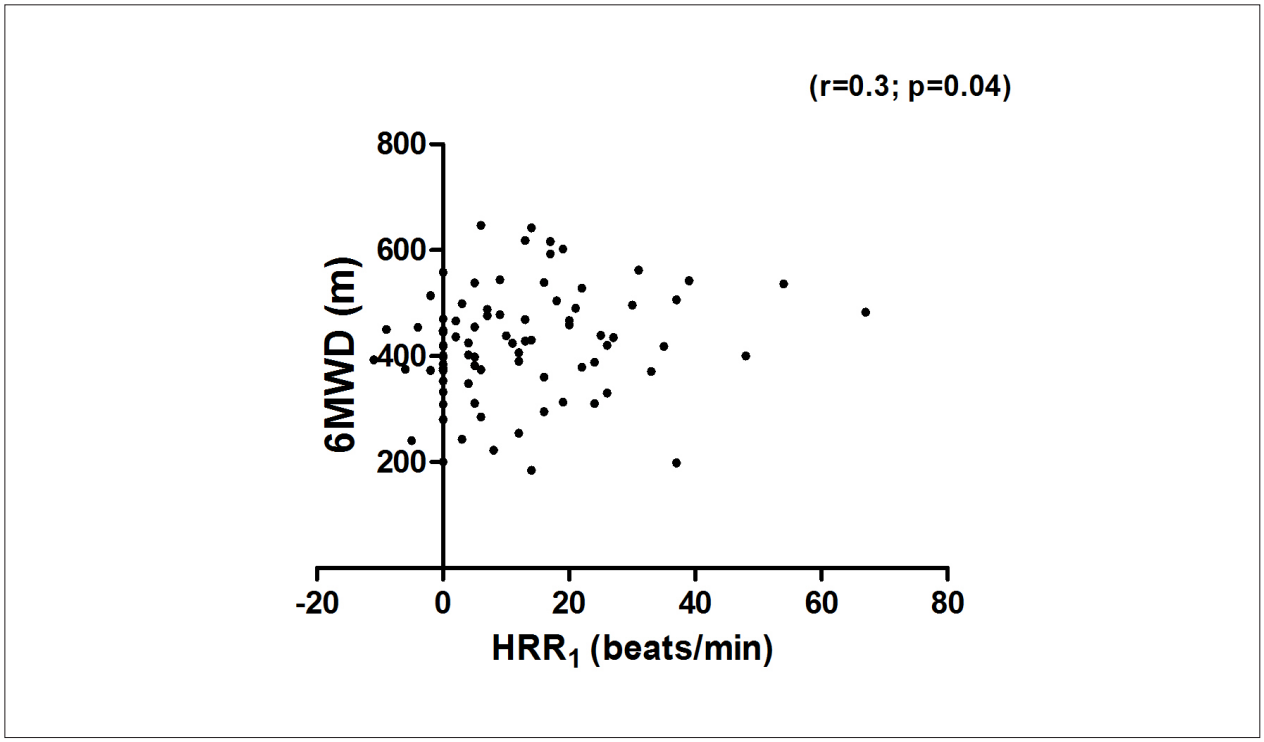

Figure 2 – *HRR_1 and 6MWD correlation in G1. HRR_1: heart rate recovery in first minute; 6MWD: six-minute walk distance.*

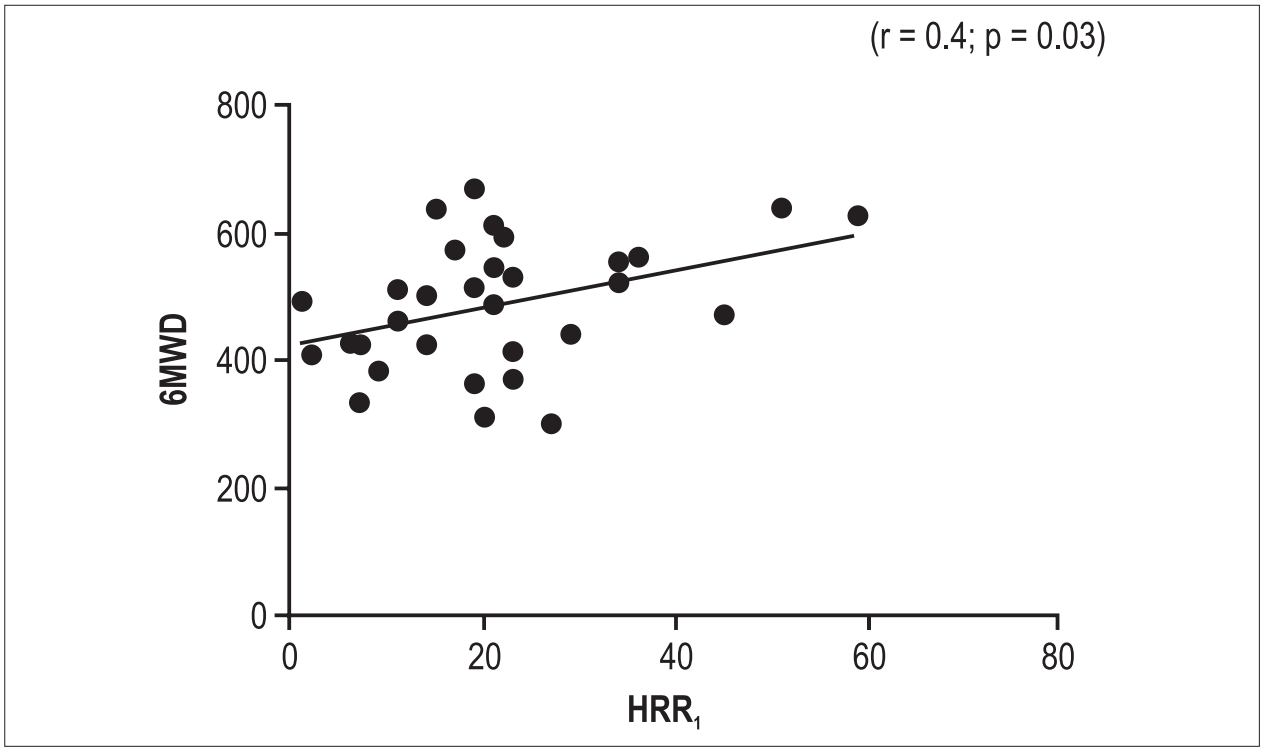

Figure 3 – *HRR1 and 6MWD correlation in G3. HRR_1: heart rate recovery in first minute; 6MWD: six-minute walk distance.*

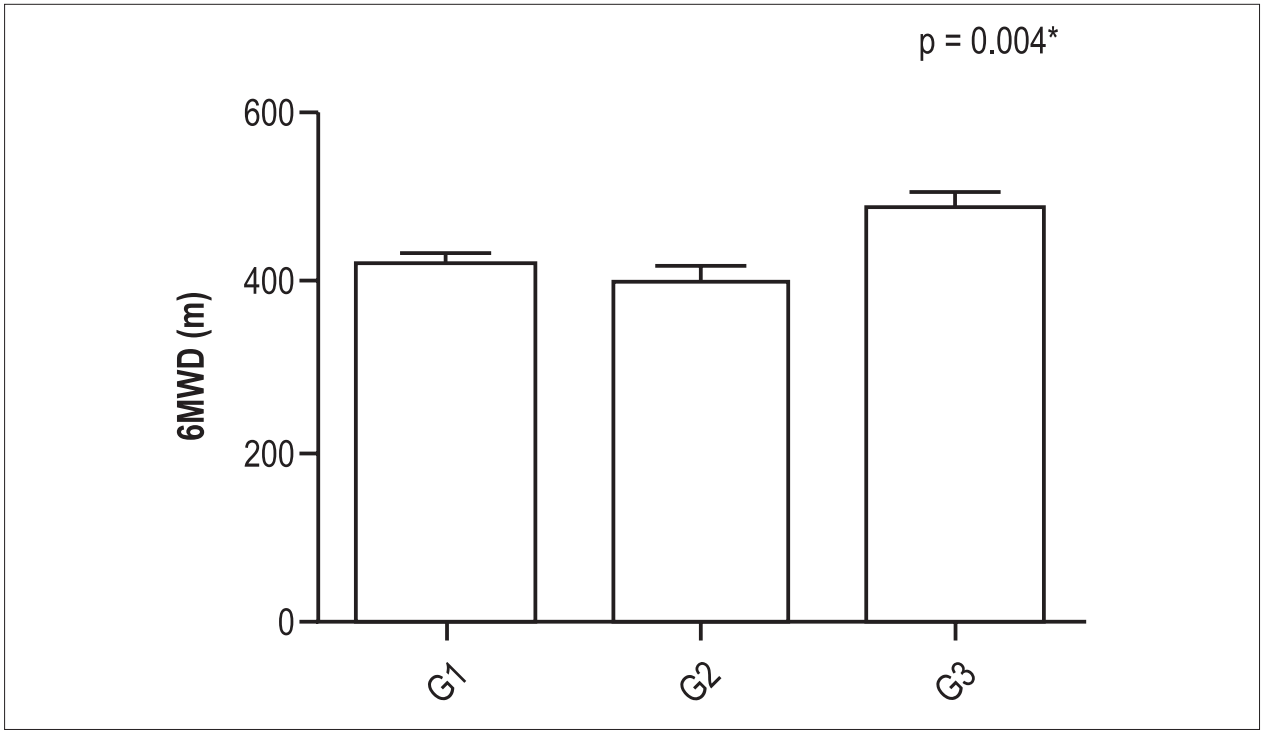

Figure 4 – *Comparison of 6MWD in 3 groups. 6MWD: six-minute walk distance*

HRR_1 has been shown to be a predictor of adverse events in HF after treadmill tests[31-35]. However, HRR_1 after 6MWT was not assessed in HF patients yet, but only in patients with IPF[21].

The results observed in this present study showed a pattern of HRR_1 response that was studied and compared among the 3 groups of this sample with a significant difference between HRR_1 performance in the 3 groups ($p = 0.0002$).

The abnormal value of HRR_1 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_1 ≤ 12 beat/min[21,33]. Thus, in present study, a HRR_1 value validated for HF patients was used in treadmill tests[22].

HRR_1 reflects chronotropic response and appears to be attenuated in HF patients; however there are divergences regarding βB interference[21,36]. In agreement with literature, in this present study we observed an attenuated pattern of response of HRR_1 in patients receiving βB when compared with non-βB patients and healthy volunteers[6,21].

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[15,16] and Sheppard et al[4], which determined a peak HR of 116 ± 21 beat/min, in parallel with the results of the present study[4,15,16].

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[6,23]. 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[35].

Ushijima et al[32], described that sympathetic hyperactivity with norepinephrine release, as well as *"down regulation"* of β-adrenergic receptors are involved in this attenuated response of HRR_1. 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_1[32].

This mechanism explained by Ushijima et al[32] may elucidate this attenuated pattern of HRR_1 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[35,36].

However, the present study found an important association between HRR_1 and walked distance[29,33,37,38] as shown by the 6MWT, which also has predictive value[17,19,28,29].

This finding is consistent with previous investigations demonstrating the capacity of HRR_1 to predict adverse events in populations other than those with HF[2,4,10,15].

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[16,28,31]. All patients in the present study showed a lower HRR_1 value than healthy subjects, probably due to poor parasympathetic activity usual in patients with HF[30,36,37].

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[22,25,34,35]. 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[21].

The positive correlation between HRR_1 and 6MWD showed to be an important information in these patients regarding either of the parameters, as HRR_1 and 6MWD have been shown to predict adverse cardiac outcomes[30,31,33,36,37]. This current study was the first to show a correlation between 6MWD and HRR_1 in patients with HF.

There is no agreement about βB influence on HRR response, sympathetic tone and hemodynamic responses[28] at the 6MWT. Thus, it is relevant to determine the pattern of HRR_1 response, as a predictive parameter in HF patients receiving βB therapy[2-4,13,39,40].

Olsson et al[19], 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[19].

Previous studies with HF patients receiving βB demonstrated an attenuated HRR. Nevertheless, the predictive value of HRR_1 was not altered and showed correlation with other prognostic parameters, such as maximal oxygen uptake, further adverse outcomes and hospitalizations[17,40].

In our study there was a linear correlation between HRR_1 and 6MWD, both in G1 and G3, but there was no correlation in G2.

Abnormal HRR may suggest abnormalities in cardiovascular capacity of the system responsible for reverse vagal withdrawal during exercise in several patients[5,7,10,12,13,16,31]. A strong correlation between 6MWD and mortality in HF was demonstrated by consistent studies such as SOLVD and a study by Rubim et al[28], which demonstrated a high mortality index, of which mean values for 6MWD were significantly lesser when compared with non-death group ($p < 0.0001$).

In the present study, a short walked distance may be indicative of abnormal autonomic balance favoring sympathetic system in HF[19,26,31,33], in agreement with other studies, but mechanisms that induce a poor course in 6MWT have not been explored.

Possible mechanisms that cause variations in HRR and HRR_1 suggest that the rate at which the parasympathetic tone increases after the cessation of exercise appears to heavily influence the time course of HRR_1[7,9,11,13,15,31,33,36]. Upon interruption of exercise, increase of parasympathetic effects on HR occurred rapidly within the first minute. The intensity of parasympathetic reactivation steadily

increased further until 4 min into recovery, after which time parasympathetic effects on HR remained relatively constant[36,37].

Although mechanisms of impaired HRR_1 in HF are not totally explained, it may indicate disorder in autonomic balance leading to delayed reactivation of parasympathetic tone[5,7,9,11,15,36,37], while the association between HRR_1 and 6MWD appears to be a novel and important finding.

The correlation between HRR_1 and 6MWD in HF patients consists an original finding and may contribute with relevant clinical information in HF patients[22].

This present study may contribute additional evidence that abnormal HRR_1 could determine an adverse prognosis. This variable obtained at the 6MWT may provide simple clinical information with reference to exercise tolerance[2].

Conclusion

The present study determined the pattern response of HRR_1 at 6MWT in patients with HF receiving or not βB and in individuals without HF.

Patients with HF receiving βB showed better exercise tolerance, even though they had an attenuated HRR_1 when compared to patients that were not using βB. There was a significant correlation between HRR_1 and 6MWD in patients underwent βB and in healthy individuals, but there was no correlation between HRR_1 and 6MWD in patients not receiving βB.

Finally, HRR_1 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, Bernardez S, Marchese L; Analysis and interpretation of the data: Lindemberg S, Chermont S, Quintão M, Derossi M, Guilhon S, Bernardez 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, Bernardez S, Martins W, Nóbrega ACL, Mesquita ET.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Study Association

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