Predictors of abnormal heart rate recovery in patients with heart failure reduced and preserved ejection fraction

Lawrence P Cahalin, Ross Arena, Valentina Labate, Francesco Bandera and Marco Guazzi

European Journal of Preventive Cardiology published online 18 January 2013
DOI: 10.1177/2047487313475892

The online version of this article can be found at:
http://cpr.sagepub.com/content/early/2013/03/11/2047487313475892

Published by:
SAGE
http://www.sagepublications.com

On behalf of:
European Society of Cardiology
EACPR

Additional services and information for European Journal of Preventive Cardiology can be found at:

Email Alerts: http://cpr.sagepub.com/cgi/alerts
Subscriptions: http://cpr.sagepub.com/subscriptions
Reprints: http://www.sagepub.com/journalsReprints.nav
Permissions: http://www.sagepub.com/journalsPermissions.nav

>> OnlineFirst Version of Record - Mar 11, 2013
OnlineFirst Version of Record - Jan 18, 2013

What is This?
Predictors of abnormal heart rate recovery in patients with heart failure reduced and preserved ejection fraction

Lawrence P Cahalin¹, Ross Arena², Valentina Labate³, Francesco Bandera³ and Marco Guazzi³

Abstract

Background: Heart rate recovery (HRR) is becoming an important prognostic marker in heart failure (HF), but very little is known about the underlying mechanisms responsible for its clinical efficacy. Therefore, we examined echocardiographic and exercise (submaximal and maximal) characteristics to gain a better appreciation of HRR and factors responsible for the development of abnormal HRR in patients with both heart failure reduced ejection fraction (HFrEF) and heart failure preserved ejection fraction (HFpEF).

Methods: Cardiopulmonary exercise testing (CPX), a 6-minute walk test (6MWT), and resting 2D echocardiography were randomly performed in 240 HF patients (200 HFrEF, 40 HFpEF) after which HRR was measured. HRR was defined as the difference between heart rate at peak exercise and 1 minute following test termination.

Results: Bivariate correlation analyses found significant relationships among most CPX and 6MWT measurements with the highest correlations between 6MWT HRR and 6MWT peak HR (r = 0.65; p < 0.001) and CPX HRR and CPX HRreserve (r = 0.63; p < 0.001). The relationship between 6MWT HRR and CPX HRR was very good (r = 0.91; p < 0.001). Multivariate logistic regression of submaximal and maximal exercise found 6MWT peak HR and exercise oscillatory ventilation (EOV), respectively, were the strongest predictors (p < 0.001) of abnormal HRR. The E/E₀ was a significant predictor (p < 0.001) of abnormal HRR, but EOV was the strongest predictor of abnormal HRR (OR = 6.5).

Conclusions: HRR after both CPX and the 6MWT is significantly related to many exercise and echocardiographic measures with the most significant predictors of abnormal HRR being related to indices of cardiorespiratory performance in patients with HFrEF and HFpEF.

Keywords
Cardiopulmonary exercise testing, heart failure, heart rate recovery, 6-minute walk test, prediction

Received 15 July 2012; accepted 7 January 2013

Introduction

The decline in heart rate (HR) after exercise has been found to be an important prognostic variable in apparently healthy individuals referred for aerobic exercise testing and in a variety of patient populations.¹–⁸ In fact, a lower heart rate recovery (HRR) has consistently been observed to be prognostic of survival in patients with heart failure (HF)⁵–⁸ and more recently has been observed to be prognostic of survival in patients with idiopathic pulmonary fibrosis.⁹ The inability of the HR to decrease after exercise appears to be related to poorer fitness and the impact of various disease states on autonomic function since HRR reflects parasympathetic reactivation.¹⁰–¹⁵ Some degree of consensus exists for the threshold of an abnormal HRR to be ≤12 beats at 1-minute post exercise.¹,2,14,15

To our knowledge, only one previous study has examined predictors of abnormal HRR in patients with HF.¹⁶ In this study, HRR at minutes 1 and 2

¹University of Miami, Miami, FL, USA
²University of New Mexico School of Medicine, Albuquerque, NM, USA
³University of Milano, I.R.C.C.S. Policlinico San Donato, San Donato Milanese, Italy

Corresponding author:
Marco Guazzi, Cardiology, I.R.C.C.S. Policlinico San Donato, University of Milano, San Donato Milanese, Milan, Italy.
Email: marco.guazzi@unimi.it
after maximal cardiopulmonary exercise testing (CPX) were examined in 30 patients with HF reduced ejection fraction (HFrEF) and 20 patients with HF preserved ejection fraction (HFpEF). Significant univariate predictors of HRR in patients with HF included left ventricular end-diastolic diameter (LVEDD), left ventricular ejection fraction (LVEF), N-terminal pro-brain natriuretic peptide (NT-pro-BNP), peak HR, and peak oxygen consumption (VO2) with peak VO2 being the only predictor of HRR in a multivariate model. This study also identified an optimal HRR cut-off value to discriminate HFrEF from HFpEF to be 12.5 and 24.5 beats at minutes 1 and 2 of recovery, respectively. Using a larger prospective database of patients with both HFrEF and HFpEF, we further examined predictors of abnormal HRR after both submaximal and maximal exercise.

Methods

This was a prospective study of patients with HF referred for functional assessment at San Paolo Hospital, Milan, Italy. The study included 240 patients diagnosed with HF who underwent a 6-minute walk test (6MWT) and CPX between June 1999 and December 2008. Patients who were not in sinus rhythm and who were unable to perform either exercise assessment were not included in the study. All patients were in New York Heart Association (NYHA) functional class II or III. Patients with both HFrEF and HFpEF were enrolled. HFrEF was defined using the following criteria: (1) signs and symptoms as well as a clinical diagnosis of HF and (2) presence of reduced left ventricular (LV) systolic function (LV ejection fraction, LVEF, ≤50%) as assessed by 2D echocardiography. HFpEF was defined using the following criteria: (1) signs and symptoms as well as a clinical diagnosis of HF; (2) presence of preserved LV systolic function LVEF ≥50% as assessed by 2D echocardiography; and (3) documentation of mitral inflow early (E) velocity to mitral annulus early velocity (E') ≥15. Patient treatment was optimal and patients were stable for 3 months prior to enrollment into the study. Approval by the institutional review board was obtained before the study was initiated and all patients provided written informed consent to participate in the study.

6-minute walk test procedures

The 6MWT was performed on a level surface by a physician who was unaware of echocardiographic, CPX, and clinical results. The procedures used to administer the 6MWT in this cohort have been previously described. The distance ambulated was measured by a body-borne pedometer with which the total number of steps taken during the 6MWT were used to calculate the 6MWT distance using the equation reported by Roul et al. \(d = y \times 10 \times x/220 - \text{age}\), where \(d\) is distance ambulated in metres, \(y\) is total number of steps during 6MWT, and \(x\) is number of steps for each subject to cover 10 metres. The distance ambulated in 6 minutes was also dichotomized using the commonly accepted threshold (6MWT distance ≤ and >300 metres). The heart rate was obtained in standing via telemetry electrocardiography at rest before the 6MWT, at the end of the 6MWT, and 1-minute after the 6MWT. The 6MWT HRres was calculated as the difference between the HR at the end of the 6MWT and the resting HR. The 6MWT HRR was defined as the difference between the HR at the end of the 6MWT and 1-minute after the 6MWT. The recovery period following the 6MWT was passive.

Cardiopulmonary exercise testing

Symptom-limited CPX was performed on a bicycle ergometer for all subjects. Pharmacological therapy was maintained during CPX. Individualized ramp protocols were designed to obtain a duration between 8 and 10 minutes. Ventilatory expired gas analysis was performed using a metabolic cart (Vmax; Sensormedics, Yorba Linda, CA, USA). Before each test, the equipment was calibrated according to the manufacturer’s specifications using reference gases.

Standard 12-lead electrocardiograms were obtained at rest, each minute during exercise, and for at least 5 minutes during the recovery phase; blood pressure was measured using a standard cuff sphygmomanometer. Heart rate was determined at rest, peak exercise, and at 1 minute recovery. The percentage predicted maximal HR achieved was determined by the following equation: peak HR = (220 – age) × 100. The CPX HRres was calculated as the difference between the peak HR and resting HR. The CPX HRR was defined as the difference between peak HR and HR 1 minute following test termination. An active cool-down period for at least 1 minute was employed for all tests. In addition, minute ventilation [VE, body temperature, pressure, and saturated (BP)], oxygen uptake [VO2, standard temperature, pressure, and dry (STPD)], and carbon dioxide output (VCO2, STPD) were acquired breath-by-breath, averaged over 30 seconds, and printed using rolling averages every 10 seconds. The V-slope method was used to determine the first ventilatory threshold (VT1). Peak VO2 and peak respiratory exchange ratio (RER) were expressed as the highest 10-second averaged sample obtained during the last 20 seconds of testing. VE and VCO2 values, acquired from
the initiation of exercise to peak, were input into spreadsheet software (Excel; Microsoft, Bellevue, WA, USA) to calculate the VE/VCO₂ slope via least squares linear regression \( y = mx + b \), where \( m \) is slope. Exercise oscillatory ventilation (EOV) during CPX was defined as previously described in detail.⁵,²⁴ Briefly, criteria for EOV included the presence of three or more regular oscillatory fluctuations in VE with a minimal average amplitude of 5 l/min persisting for at least 60% of the entire exercise.

**Echocardiography**

Left ventricular chamber dimensions were evaluated using standard procedures including the LV mass index.²⁵ Left ventricular ejection fraction was calculated from 2D apical images according to Simpson’s method.

**Conventional Doppler and tissue Doppler imaging measurements**

Mitrail inflow measurements were obtained with the standard pulse-Doppler technique and included peak early (E) and peak late (A) flow velocities, and the E/A ratio. The tissue Doppler imaging of the mitral annulus was obtained from the apical four-chamber view. A 1.5 sample was placed sequentially at the lateral and septal annular sites. Analysis was performed for the early (E’) and late (A’) diastolic peak velocities. The ratio of early transmitial flow velocity to annular mitral velocity of the lateral LV wall (E/E’) was taken as an estimate of LV filling pressure.²⁶

**Statistical analysis**

A statistical software package (SPSS 19.0; Chicago, IL, USA) was used to perform all analyses. Continuous and categorical data are reported as mean ± standard deviation and percentages, respectively. Independent t-tests and chi-squared tests were used to assess differences in patient characteristics, 6MWT variables, and CPX variables between patients with HFrEF and HFrEF. Correlation analysis using Spearman’s rho statistic was performed to examine relationships between HRR and patient characteristics, 6MWT variables, and CPX variables for the entire cohort and between patients with HFrEF and HFrEF except for LVEF and RER, which were both significantly greater in patients with HFrEF.

**Results**

**Baseline characteristics**

Table 1 lists patient characteristics as well as 6MWT and CPX variables for the entire cohort and between subjects with HFrEF and HFrEF. There were no significant differences between patients with HFrEF and HFrEF except for LVEF and RER, which were both significantly greater in patients with HFrEF.

**6-minute walk test and cardiopulmonary exercise testing performance**

The 6MWT was performed without complication and no test was terminated prematurely. The mean 6MWT distance ambulated was 354 ± 90 metres and the mean percentage of the age-predicted maximal HR achieved during the 6MWT was 77 ± 10% with a mean peak HR of 121.9 ± 16 bpm. The mean resting HR, peak HR, HRreserve and percentage of age-predicted maximal HR achieved during the 6MWT were not significantly different between patients with HFrEF vs. HFrEF. There was no significant difference in HRR after the 6MWT between patients with HFrEF and HFrEF (Table 1).

All CPX assessments were performed without complication and with good effort. The mean percentage of age-predicted maximal HR achieved was 82 ± 10%. There was no significant difference in peak VO₂, VO₂ at VAT, or the VE/VCO₂ slope between patients with HFrEF and HFrEF. The mean resting HR, peak HR, HRreserve, and percentage of age-predicted maximal HR achieved during CPX were not significantly different between patients with HFrEF vs. HFrEF. There was no significant difference in HRR after CPX between patients with HFrEF and HFrEF (Table 1).

**Correlation analyses**

Table 2 lists the results of bivariate correlation analyses of HRR and a variety of echocardiographic and exercise measurements from the 6MWT and CPX. All 6MWT HRR and CPX HRR correlations were statistically significant except for 6MWT HRR and LVEF and CPX HRR and diabetes. The highest correlations were between 6MWT HRR and 6MWT peak HR and CPX HRR and CPX HRreserve. Figure 1 illustrates the relationships of 6MWT HRR and CPX HRR to several key measures from each respective mode of exercise in patients with HFrEF and HFrEF.

The relationships between CPX HRR and CPX respiratory gas analysis measures were modest, with EOV and peak VO₂ having the greatest correlation to CPX HRR (Figure 1). Figure 1E shows the very good
correlation between CPX HRR and 6MWT HRR ($r = 0.91; p < 0.001$).

The correlation between LVEF and HRR was significant for both patients with HFrEF and HfPEF, but the direction of the relationships were different. The relationship between 6MWT and CPX HRR to LVEF in HFrEF patients was positively correlated ($r = 0.20; p < 0.01$ and $r = 0.29; p < 0.001$), but 6MWT and CPX HRR were negatively correlated to LVEF in HfPEF patients ($r = -0.43$ and $r = -0.49; p < 0.01$). Significant negative relationships between 6MWT and CPX HRR and E/E' were found in both HFrEF and HfPEF patients, but with higher correlation coefficients in patients with HfPEF ($r = -0.52$ and $-0.56$ vs. $r = -0.39$ and $-0.42$, respectively; $p < 0.001$).

**Multivariate logistic regression analyses**

The multivariate logistic regression results predicting abnormal HRR (i.e. ≤12 beats at 1-minute post exercise) after the 6MWT and CPX are shown in Table 3. Significant predictors of abnormal HRR after the 6MWT while controlling for HF type and several other patient characteristics included 6MWT peak HR, LV mass, and E/E’, with peak HR and E/E’ being the strongest predictors. Patients with greater peak HR during the 6MWT were less likely to have an abnormal HRR while patients with greater LV mass and E/E’ were more likely to have an abnormal HRR. In fact, patients with elevated E/E’ were 1.3-times more likely to have an abnormal HRR (Table 3).

Significant predictors of abnormal HRR after CPX while controlling for HF type and several other patient characteristics included CPX peak HR, LV mass, E/E’, and EOV, with E/E’ and EOV being the strongest predictors. Patients with greater peak HR during CPX were less likely to have an abnormal HRR, while patients with greater LV mass and E/E’ were more likely to have an abnormal HRR. Patients with elevated E/E’ were 1.4-times more likely to have
Table 2. Correlation analysis of 6MWT and CPX HRR with key CPX and 6MWT variables

<table>
<thead>
<tr>
<th></th>
<th>6MWT HRR (n = 240)</th>
<th>CPX HRR (n = 240)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>-0.22</td>
<td>-0.19</td>
</tr>
<tr>
<td>Diabetes</td>
<td>-0.14</td>
<td>-0.07</td>
</tr>
<tr>
<td>COPD</td>
<td>-0.32</td>
<td>-0.33</td>
</tr>
<tr>
<td>LVESV</td>
<td>-0.19</td>
<td>-0.14</td>
</tr>
<tr>
<td>LV mass</td>
<td>-0.41</td>
<td>-0.38</td>
</tr>
<tr>
<td>LVEF</td>
<td>0.09</td>
<td>-0.16</td>
</tr>
<tr>
<td>E/E</td>
<td>-0.43</td>
<td>-0.46</td>
</tr>
<tr>
<td>6MWT distance</td>
<td>0.37</td>
<td>0.40</td>
</tr>
<tr>
<td>6MWT peak HR</td>
<td>0.65</td>
<td>0.61</td>
</tr>
<tr>
<td>6MWT HFrsev</td>
<td>0.61</td>
<td>0.61</td>
</tr>
<tr>
<td>6MWT %APMHR</td>
<td>0.58</td>
<td>0.56</td>
</tr>
<tr>
<td>CPX RER</td>
<td>-0.43</td>
<td>-0.31</td>
</tr>
<tr>
<td>CPX peak VO₂</td>
<td>0.47</td>
<td>0.50</td>
</tr>
<tr>
<td>CPX VO₂ @AT</td>
<td>0.44</td>
<td>0.47</td>
</tr>
<tr>
<td>VE/VO₂ slope</td>
<td>-0.41</td>
<td>0.41</td>
</tr>
<tr>
<td>CPX EOV</td>
<td>-0.51</td>
<td>-0.51</td>
</tr>
<tr>
<td>CPX resting HR</td>
<td>-0.18</td>
<td>-0.22</td>
</tr>
<tr>
<td>CPX peak HR</td>
<td>0.63</td>
<td>0.62</td>
</tr>
<tr>
<td>CPX HFrsev</td>
<td>0.62</td>
<td>0.63</td>
</tr>
<tr>
<td>CPX %APMHR</td>
<td>0.55</td>
<td>0.56</td>
</tr>
</tbody>
</table>

*All 6MWT HRR and CPX HRR correlations are statistically significant (p < 0.05) except for 6MWT HRR and LVEF and CPX HRR and diabetes; 6MWT, 6-minute walk test; APMHR, age predicted maximal heart rate; AT, anaerobic threshold; COPD, chronic obstructive pulmonary disease; CPX, cardiopulmonary exercise testing; E/E', mitral flow early (E) velocity to mitral annulus early velocity (E'); EOV, exercise oscillatory ventilation; HR, heart rate; HRR, heart rate recovery; LV, left ventricular; LVEF, left ventricular ejection fraction; RER, respiratory exchange ratio; VE/VO₂ slope, minute ventilation/carbon dioxide production/VE/VO₂ slope, minute ventilation/carbon dioxide production; VO₂, oxygen consumption.

an abnormal HRR and patients demonstrating EOV were 6.5-times more likely to have an abnormal HRR (Table 3).

Discussion

This study is the first to examine predictors of abnormal HRR using data obtained from both submaximal and maximal exercise. Patients demonstrating EOV during CPX were 6.5-times more likely to have an abnormal HRR. The finding that EOV predicts abnormal HRR so strongly and the finding that potentially valuable prognostic information may be obtained during a submaximal exercise test like the 6MWT are clinically important and novel results from this study. Additionally, the very good correlation between CPX HRR and the 6MWT HRR (r = 0.91) is clinically important and suggests that HRR after the 6MWT may be as prognostic as HRR after maximal CPX.

Finally, in the multivariate logistic regression analyses, HF type was not observed to be a significant predictor of abnormal HRR after submaximal or maximal exercise. Therefore, HRR appears to demonstrate the potential for comparable clinical utility in HFrEF and HFrEF after both submaximal and maximal exercise.

Despite our finding that HRR was not significantly different between patients with HFrEF and HFrEF after both submaximal and maximal exercise, a previous study examining predictors of HRR after maximal exercise found that patients with HFrEF had a significantly lower HRR at minutes 1 and 2 of recovery compared to HFrEF patients. These results are markedly different from HRR 1 minute after both submaximal and maximal in HFrEF and HFrEF patients in our study and may be partly explained by the poorer cardiorespiratory fitness of our HFrEF and HFrEF patients as well as our larger sample size that may be more representative and generalizable of patients with HF.

Also, although weaker, the results of our bivariate correlation analyses are mostly in keeping with the above previous study except for the relationship between HRR and LVEF which was positive in the previous study and in our study was found to be negatively correlated for the entire cohort (r = -0.16; p < 0.05), positively correlated in the HFrEF patients, and negatively correlated in patients with HFrEF. No separate subanalysis of the relationship between LVEF and HRR in patients with only HFrEF or HFrEF was performed in the previous study which is surprising given the fact that the LVEF is markedly different between HFrEF and HFrEF patients. Nonetheless, our significant positive correlation of HRR 1 minute after maximal exercise to LVEF in patients with HFrEF is similar in direction, but much weaker than that previously reported (r = 0.29 vs. 0.70).

The results of our multivariate logistic regression analyses for submaximal exercise identified 6MWT peak HR and several echocardiographic measurements (E/E' and LV mass) while multivariate logistic regression analyses for CPX identified EOV and peak HR and the same echocardiographic measurements to be significant predictors of abnormal HRR. The only significant predictor observed in the previous study using linear regression analysis was peak VO₂. Peak VO₂ along with several other CPX variables were included in our maximal exercise logistic regression model, but peak VO₂ was not found to be a significant predictor of abnormal HRR. It is likely that the predictive strength of EOV (OR = 6.5) decreased the prognostic utility of peak VO₂ in our study which reinforces the need for further investigation of EOV in predicting abnormal HRR as well as prognosis in HF. Although the
The aetiology of EOV is poorly understood, it appears to keenly reflect cardiorespiratory performance.\textsuperscript{27–29} Our current results and those of others highlight the intimate relationship between the cardiorespiratory and neurohumeral systems. Although HRR does appear to reflect overall health of the autonomic nervous system and the influence of parasympathetic reactivation and sympathetic deactivation,\textsuperscript{1–15} very little is known about the specific characteristics of the autonomic nervous system responsible for HRR.\textsuperscript{30} Our results and those of others suggest that chronotropic incompetence may be partly responsible for abnormal HRR.\textsuperscript{9,16,31} In our

\textbf{Figure 1.} Scatter plots of the relationship between 6MWT HRR and LV mass (A), 6MWT HRR and 6MWT peak HR (B), CPX HRR and CPX EOV (C), CPX HRR and peak VO\textsubscript{2} (D), and 6MWT HRR and CPX HRR (E).

0.00, heart failure reduced ejection fraction; 1.00, heart failure preserved ejection fraction; 6MWT, 6-minute walk test; CPX, cardiopulmonary exercise testing; EOV, exercise oscillatory ventilation; HR, heart rate; HRR, heart rate recovery; LV, left ventricular.
study, peak HR during both submaximal and maximal exercise was significantly correlated positively to HRR and a significant positive correlation was observed previously in patients with HF. Additionally, our logistic regression results revealed that peak HR during both the 6MWT and CPX was a significant predictor of being less likely to have an abnormal HRR. Thus, patients with a greater peak HR were less likely to have an abnormal HRR. Furthermore, in patients with idiopathic pulmonary fibrosis, HR reserve was observed to be a significant univariate and multivariate predictor of abnormal HRR after the 6MWT. Therefore, chronotropic incompetence does appear to be related to abnormal HRR and further investigation of the underlying mechanisms after submaximal and maximal exercise is warranted.

**Study limitations**

The major potential limitation to this study is that only 17% of the patients studied were patients with HFrEF. Despite our subanalyses finding almost identical bivariate correlations and the finding that HF type was not a significant predictor of abnormal HRR in our submaximal and maximal exercise logistic regression analyses, further investigation of HRR in a larger population of patients with HFrEF is warranted. Moreover, our study enrolled a greater number of patients with both HFrEF and HFrEF than previous studies examining HRR in HF.

**Conclusions**

To our knowledge, this is the first study that has examined predictors of abnormal HRR in patients with HF after both submaximal and maximal exercise and it appears to be the first study to identify the significant relationship between EOV and abnormal HRR. Patients demonstrating EOV during CPX were 6.5-times more likely to have an abnormal HRR. The very good correlation between CPX HRR and 6MWT HRR is also clinically important and suggests that HRR after the 6MWT may be as prognostic as HRR after maximal CPX which may be clinically useful and requires further examination. Furthermore,

---

**Table 3. Logistic regression results of abnormal 6MWT HRR and CPX HRR**

<table>
<thead>
<tr>
<th>Variable</th>
<th>B ± SE</th>
<th>Exp(B) (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>6MWT HRR (n = 240) Pseudo R² = 0.60</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Variables of key interest</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6MWT distance</td>
<td>−0.001 ± 0.003</td>
<td>0.999 (0.994–1.004)</td>
</tr>
<tr>
<td>6MWT peak HR</td>
<td>−0.102 ± 0.019</td>
<td>0.903 (0.870–0.937)***</td>
</tr>
<tr>
<td>Demographic variables</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>0.007 ± 0.021</td>
<td>1.007 (0.967–1.049)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>0.115 ± 0.458</td>
<td>1.122 (0.457–2.754)</td>
</tr>
<tr>
<td>COPD</td>
<td>0.266 ± 0.499</td>
<td>1.305 (0.491–3.468)</td>
</tr>
<tr>
<td>HF type</td>
<td>0.675 ± 0.792</td>
<td>1.964 (0.416–9.276)</td>
</tr>
<tr>
<td>Echocardiography variables</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LVESV</td>
<td>0.007 ± 0.010</td>
<td>1.007 (0.987–1.026)</td>
</tr>
<tr>
<td>LV mass</td>
<td>0.027 ± 0.009</td>
<td>1.027 (1.008–1.046)**</td>
</tr>
<tr>
<td>LVEF</td>
<td>1.453 ± 2.787</td>
<td>4.278 (0.018–1008.150)</td>
</tr>
<tr>
<td>E/E'</td>
<td>0.286 ± 0.066</td>
<td>1.330 (1.170–1.513)**</td>
</tr>
<tr>
<td><strong>CPX HRR (n = 240) Pseudo R² = 0.65</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Variables of key interest</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peak VO₂</td>
<td>0.014 ± 0.067</td>
<td>1.014 (0.889–1.157)</td>
</tr>
<tr>
<td>VE/VCO₂ slope</td>
<td>0.045 ± 0.042</td>
<td>1.047 (0.964–1.136)</td>
</tr>
<tr>
<td>EOV</td>
<td>1.871 ± 0.431</td>
<td>6.497 (2.790–15.131)***</td>
</tr>
<tr>
<td>Peak HR</td>
<td>−0.062 ± 0.019</td>
<td>0.940 (0.906–0.975)***</td>
</tr>
<tr>
<td>Demographic variables</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>−0.012 ± 0.022</td>
<td>0.988 (0.947–1.031)</td>
</tr>
<tr>
<td>COPD</td>
<td>−0.228 ± 0.570</td>
<td>0.796 (0.261–2.430)</td>
</tr>
<tr>
<td>HF type</td>
<td>1.331 ± 0.850</td>
<td>3.785 (0.716–20.011)</td>
</tr>
<tr>
<td>Echocardiography variables</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LV mass</td>
<td>0.019 ± 0.009</td>
<td>1.019 (1.002–1.036)*</td>
</tr>
<tr>
<td>LVEF</td>
<td>−1.342 ± 2.974</td>
<td>0.261 (0.001–88.790)</td>
</tr>
<tr>
<td>E/E'</td>
<td>0.324 ± 0.066</td>
<td>1.383 (1.214–1.575)**</td>
</tr>
</tbody>
</table>

*p < 0.05; **p < 0.01; ***p < 0.001; 6MWT, 6-minute walk test; COPD, chronic obstructive pulmonary disease; CPX, cardiopulmonary exercise testing; E/E', mitral inflow early (E) velocity to mitral annulus early velocity (E'); EOV, exercise oscillatory ventilation; HF, heart failure; HR, heart rate; HRR, heart rate recovery; LV, left ventricular; LVEF, left ventricular ejection fraction; LVESV, left ventricular end-systolic volume; VE/VCO₂, minute ventilation/carbon dioxide production; VO₂, oxygen consumption.
the above correlations were similar and at times identical in patients with HFrEF and HfP EF suggesting equal clinical utility of HRR in patients with HFrEF and HfP EF after both submaximal and maximal exercise. Further investigation of HRR in patients with HF after submaximal and maximal exercise is warranted.

**Funding**

This research received funding from The Monzino Foundation, Milano, Italy.

**References**


