2024 13th Conference of the European Study Group on Cardiovascular Oscillations (ESGCO) | 979-8-3503-9205-0/24/$31.00 ©2024 IEEE | DOI: 10.1109/ESGCO63003.2024.10767063

Cardiorespiratory Coupling and Exercise Capacity in Patients with Chronic Heart Failure

Raphael Martins de Abreu[1,2], Beatrice Cairo[3], Vlasta Bari[3,4], Francesca Gelpi[3], Giulia Paglione[5], Beatrice De Maria[6], Francesco Bandera[3,7] and Alberto Porta[3,4]

Email: {alberto.porta, beatrice.cairo, vlasta.bari, francesca.gelpi, francesco.bandera}@unimi.it {rmartinsdeabreu}@lunex.lu {beatrice.demaria}@icsmaugeri.it {giulia.paglione}@grupposandonato.it

[1]Department of Physiotherapy, LUNEX University, International University of Health, Exercise & Sports S.A., Differdange, Luxembourg

[2]LUNEX ASBL Luxembourg Health & Sport Sciences Research Institute, Differdange, Luxembourg

[3]Department of Biomedical Sciences for Health, University of Milan, Milan, Italy

[4]Department of Cardiothoracic, Vascular Anesthesia and Intensive Care, IRCCS Policlinico San Donato, San Donato Milanese, Milan, Italy

[5]Clinical Research Service, IRCCS Policlinico San Donato, San Donato Milanese, Milan, Italy

[6]IRCCS Istituti Clinici Scientifici Maugeri, Milan, Italy

[7]Cardiac Rehabilitation and Heart Failure Unit, Cardiology University Department, Scientific Institute for Research, Hospitalization and Healthcare MultiMedica, Sesto San Giovanni, Milan, Italy

***Abstract* – Cardiopulmonary exercise testing (CPET) is crucial for assessing exercise capacity in chronic heart failure (CHF) patients, with peak oxygen consumption (VO_2peak) being the gold standard for cardiorespiratory fitness. This study explores the correlation between VO_2peak and cardiorespiratory coupling (CRC). The CRC was calculated via the power of heart period (HP) variability in the high frequency (HF, from 0.15 to 0.4 Hz) band expressed in absolute units (HFa_{HP}) and the squared coherence (K^2) between HP variability and respiration (RESP) in the HF band (K^2_{HF}). We computed the difference between CRC markers measured after CPET with respect to those before CPET in 25 CHF patients (age: 62±9 yrs, NYHA class: I to III, 15 males). A positive correlation between variation of CRC markers and VO_2peak (r = 0.5; p = 0.007) was observed. No correlation was found between HFa_{HP} and VO_2peak. The findings suggest CRC analysis as a supplementary method for evaluating exercise capacity in CHF patients, providing insights beyond traditional measures.**

Keywords—Squared coherence, heart rate variability, autonomic nervous system, exercise testing.

I. Introduction

The determination of exercise capacity based on cardiopulmonary exercise testing (CPET) is part of the clinical routine for the physical evaluation and prognosis of patients with chronic heart failure (CHF). CPET provides comprehensive data on the integrative responses of the pulmonary, cardiovascular, and skeletal muscle systems during exercise. It measures parameters such as peak oxygen consumption (VO_2peak), which is a function of the cardiac output and arterial-mixed venous oxygen difference, and offers valuable insights related to the severity of CHF and prognostic outcomes. However, VO_2peak measurement via CPET is not always feasible in clinical practice. Correlating VO_2peak with other biological markers such as those assessing cardiorespiratory coupling (CRC), can be useful for more detailed understanding of a patient's physiological status and predicting exercise capacity, when CPET is not available.

The CRC analysis is based on the interactions between heart activity and respiration (RESP). CRC analysis offers information on autonomic nervous system function and the efficiency of cardiovascular and respiratory integration [1]. In recreational athletes higher CRC values have been found correlated with higher exercise capacity during maximal exercise, *i.e.*, higher VO_2peak [2]. Increased CRC might be linked to enhanced diffusion capacity at the alveolar level, thereby improving the ventilation-perfusion ratio during exercise, and to a reduced cardiac workload due to a more efficient oxygen transport and utilization in the muscles [2]. Moreover, central command mechanisms could be more effectively activated in individuals with higher CRC, resulting in more synchronized and efficient heart function during exercise [3]. However, the link between CRC and exercise capacity in patients with CHF, as well as potential physiological mechanism has not been explored in the literature.

Thus, this study aims to verify whether there is any relationship between CRC indexes and VO_2peak reached during CPET in patients diagnosed with CHF. Traditional CRC indexes were utilized based on the assessment of respiratory sinus arrhythmia (RSA) and degree of association between cardiac activity and respiration.

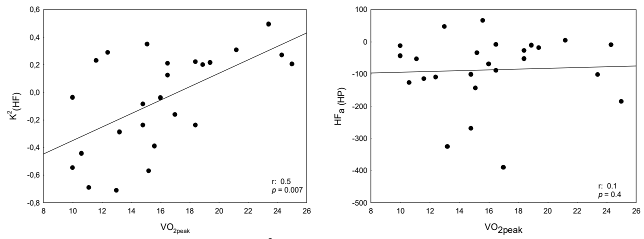

Figure 1. Scatterplots of delta K^2_{HF} versus VO_2peak (left panel) and delta HFa_{HP} versus VO_2peak (right panel).

II. Experimental Protocol and Data Analysis

A. Experimental Protocol

Data were acquired from a group of 25 patients diagnosed with CHF (62±9 yrs, 15 males, VO_2peak = 15±3 $mL \cdot kg^{-1} \cdot min^{-1}$) who underwent clinical evaluation for CPET at IRCCS Policlinico San Donato, San Donato Milanese, Italy. Distribution of patients in New York Heart Association (NYHA) classes was 10, 11 and 4 in NYHA class I, II and III, respectively. During data acquisition, patients were instructed to remain seated, quiet and to breathe naturally, while electrocardiogram (ECG) and respiratory flow (RF) data were collected, with a sampling frequency of 500 Hz. Recordings were carried out for 3 to 5 minutes just before and after completing CPET. Ethical approval for the study was obtained from the ethical review board of San Raffaele Hospital in Milan, Italy. The study was performed in agreement with the principles outlined in the Declaration of Helsinki. Written informed consent was obtained from all participants.

B. Variability Series Extraction

R-wave peaks were automatically detected on the ECG and the interval between two consecutive R-wave peaks was designated as heart period (HP). The RF signal was sampled at the onset of the HP interval, corresponding to the first R-wave peak to extract the RESP series, which values were expressed in $mL \cdot s^{-1}$. For each subject, sequences of 200 stationary consecutive values were selected at both before and after CPET. The mean and variance of the HP series were calculated, labeled as μ_{HP} and σ^2_{HP}, and expressed in ms and ms², respectively. Power spectral density of the HP series was computed by modeling the series as an autoregressive process, and the power in the high frequency (HF, from 0.15 to 0.4 Hz) band expressed in absolute units (ms²) was calculated and labeled as HFa_{HP}. HFa_{HP} was used as an estimate of RSA [4]. Respiratory frequency (f_{resp}) was computed from the RESP series and expressed in breaths per minute ($breaths \cdot min^{-1}$).

C. CRC Assessment via K^2

The CRC was determined using the squared coherence (K^2), which evaluates the degree of association between HP variability and RESP as a function of frequency. This index, ranging from 0 (no association) to 1 (complete association), was computed as the ratio of the squared cross-spectral density modulus between HP and RESP to the product of their power spectral densities. Bivariate autoregressive model, with coefficients determined through traditional least squares estimation [5], was utilized to compute K^2. The K^2 values were sampled at the weighted average of the central frequency of RESP spectral components in HF band, with weights determined by the power of these components. This index was denoted as K^2_{HF}.

D. Statistical Analysis

Pearson and Spearman correlation analyses were conducted as deemed appropriate, to explore the association of the difference between values of K^2_{HF} and HF_{aHP} derived after CPET with respect to those before CPET with VO_2peak. Statistical analyses were performed using commercial software (Sigmaplot, Systat Software, Inc., Chicago, IL, version 11.0), with statistical significance set at $p<0.05$.

III. Results

Before CPET CHF patients featured μ_{HP} (484±152ms), σ^2_{HP} (950±804ms²), and f_{RF} (17±3 $breaths \cdot min^{-1}$). A positive correlation between delta K^2_{HF} and VO_2peak was observed (Fig.1, left panel), indicating that the more negative the variation in CRC, the worse the exercise capacity ($r = 0.5$; $p = 0.007$). On the other hand, no correlation was observed between delta HF_{aHP} and VO_2peak (Fig.1, right panel, $r = 0.1$; $p = 0.4$).

IV. Discussion and Conclusion

The original finding of this study is that negative K^2_{HP} variation after CPET compared to value before CPET is likely to be related to a low exercise capacity based on VO_2peak. These findings can be attributed to the fact that a high value of CRC after CPET with limited reduction compared to that before CPET might be considered an index of good efficiency in oxygen distribution and carbon dioxide removal. This result might be not surprising given that a greater CRC should assure a better matching between pulmonary perfusion and ventilation during inspiration even after exercise. However, this result is evident only when a marker of HP-RESP association was computed and absent when RSA was considered, thus stressing the importance of coordination between the heart and respiratory system more than the sole activity of the autonomic nervous system via the action of vagal control. The analysis of CRC can be applied in addition to HP variability markers for evaluating exercise capacity in patients with CHF.

References

[1] T. E. Dick et al., “Cardiorespiratory coupling: common rhythms in cardiac, sympathetic, and respiratory activities”, *Prog. Brain Res.*, vol. 209, pp. 191−205, 2014.

[2] R. M. Abreu et al., “Cardiorespiratory coupling is associated with exercise capacity in athletes: A cross-sectional study”, *Resp. Physiol. Neurobi.*, vol. 320, art. no. 104198, 2024.

[3] A. Porta et al., “On the validity of the state space correspondence strategy based on k-nearest neighbor cross-predictability in assessing directionality in stochastic systems: Application to cardiorespiratory coupling estimation,” *Chaos*, vol. 34, art. no. 53115, 2024.

[4] A. Porta et al., “Assessment of cardiac autonomic modulation during graded head-up tilt by symbolic analysis of heart rate variability,” *Am. J. Physiol. Heart Circ. Physiol.*, vol. 293, pp. H702−H708, 2007.

[5] A. Porta, G. Baselli, O. Rimoldi, A. Malliani, M. Pagani, “Assessing baroreflex gain from spontaneous variability in conscious dogs: role of causality and respiration,” *Am. J. Physiol. Heart Circ. Physiol.*, vol. 279, pp. H2558−2567, 2000.