

## Abnormal heart rate recovery in patients with heart failure: an important target for exercise training treatment

The important prognostic role of abnormalities in the autonomic nervous system (ANS) in patients with chronic heart failure (CHF) has been clearly demonstrated over the last three decades. ANS imbalance with predominant sympathetic overactivation and parasympathetic withdrawal is of particular importance in CHF pathophysiology and is strongly associated with the poor outcome of this population. Growing evidence during the last decade has shown that an abnormal chronotropic response to exercise and early heart rate recovery (HRR) after exercise (1 min) are accurate and reliable indices of sympathetic overactivation and parasympathetic withdrawal, respectively, in patients with CHF having significant prognostic validity (1, 2). In particular, HRR has been included in the risk stratification of patients with CHF according to the recent clinical recommendations for cardiopulmonary exercise testing (CPET) by the American Heart Association (3). This easy-to-obtain parameter from CPET has also been shown to further risk stratify patients with intermediate exercise capacity, a population of uncertain prognosis (peak oxygen uptake of 10–18 mL/kg/min, the “gray area”) (1). In a previous study (4), we reported that even after left ventricle assist device (LVAD) implantation, HRR still remains abnormal, possibly reflecting poor prognosis for a selected population with more pronounced HRR abnormalities. Interestingly, HRR has also been found to be significantly impaired in patients with pulmonary arterial hypertension, indicating marked ANS abnormalities with prominent parasympathetic withdrawal (5).

Over the last decade, exercise training has been progressively established as part of the treatment of patients with CHF due to multiple beneficial effects in terms of exercise capacity, cardiovascular mortality, and quality of life (6, 7) as well as in terms of its anti-depressive effects (8). In particular, it has been demonstrated that exercise training can restore ANS abnormalities. However, so far, only few studies have investigated the effects of exercise training on HRR in CHF (9–12). In a recent study by Yaylali et al. (13), it was found that HRR at the 1<sup>st</sup> min after exercise was not improved after exercise training with no differences between low-intensity interval and continuous exercise training protocols. However, when the investigators analyzed the data according to the baseline HRR (“abnormal:” <12 bpm versus “normal:” >12 bpm), they found that only patients with CHF having an “abnormal” baseline HRR significantly

improved their HRR post-exercise training by both exercise protocols. This observation is of particular interest because baseline HRR seems to detect the group of patients with CHF that may benefit more from exercise training regardless of exercise capacity improvement.

The findings of this recent study (13) can also be confirmed from the data of a retrospective analysis that we performed in a previously published study (9), and this analysis has not yet been published. These are not proper to 9–10 references. Specifically, on re-analyzing our data, we found that patients with more pronounced HRR abnormalities (HRR ≤ 12 bpm) had a significant improvement in HRR after exercise training (from 5 ± 7 to 19 ± 12 bpm,  $p=0.02$ ) when compared with HRR improvement in patients with an HRR of >12 (from 22 ± 7 to 24 ± 11 bpm,  $p=0.4$ ). Despite the fact that baseline peak exercise capacity was similar between the two exercise groups (continuous versus high-intensity interval training), most of the patients with an “abnormal” HRR were assigned to continuous training. For this reason, there was no possible comparison between the two exercise groups. Further larger randomized studies and meta-analysis would be necessary for confirming these data.

Despite significant findings by the authors, there are some limitations emerging in their study that limit the generalization of their findings. The low number of patients on beta-blocker medications in the interval training group can significantly affect the results, and in particular, the comparison between the groups. Beta-blockers can partially influence HRR, although the degree of this effect is not well clarified yet. In addition, the low number of patients analyzed based on their baseline HRR may render the comparison between the two exercise protocols unreliable and inaccurate (interval versus continuous training).

In the study by Yaylali et al. (13), authors have chosen to use a low-intensity interval training protocol (50%–75% of heart rate reserve at 30 s, followed by rest intervals of 30 s) and a continuous training protocol (50%–75% of heart rate reserve at 30 min), but the two protocols were not estimated to be isocaloric. Authors have also underlined the positive effects of interval training when HRR is assessed at the 2<sup>nd</sup> min after exercise compared with the effects of continuous training; however, a definite conclusion for these effects needs further investigation because the two protocols cannot be reliably compared from that study.



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Accepted Date: 15.05.2015

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DOI:10.5152/AnatolJCardiol.2015.16529

Exercise characteristics are of great importance to determine the optimal beneficial effects during an exercise training program in patients with CHF. Over the last few years, researchers have demonstrated growing interest in the effects of high-intensity interval training with or without the addition of strength training in patients with CHF (9, 14, 15); however, the question as to whether these new modalities of training are more beneficial than those of continuous training with regard to ANS abnormalities still remain unanswered. Further studies targeting the identification of patients with CHF having an "abnormal" baseline HRR as a high-risk population may achieve greater effects in the ANS and possibly improve their prognosis.

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