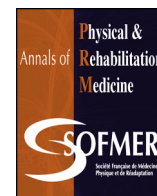




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Original article

Heart rate recovery of individuals undergoing cardiac rehabilitation after acute coronary syndrome



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ABSTRACT

Background: An efficient cardiac rehabilitation programme (CRP) can improve the functional ability of patients after acute coronary syndrome (ACS).

Objective: To examine the effect of a CRP on parasympathetic reactivation and heart rate recovery (HRR) measured after a 6-min walk test (6MWT), and correlation with 6MWT distance and well-being after ACS.

Methods: Eleven normoweight patients after ACS (BMI < 25 kg/m²; 10 males; mean [SD] age 61 [9] years) underwent an 8-week CRP. Before (pre-) and at weeks 4 (W4) and 8 (W8) during the CRP, they performed a 6MWT on a treadmill, followed by 10-min of seated passive recovery, with HRR and HR variability (HRV) recordings. HRR was measured at 1, 3, 5 and 10 min after the 6MWT (HRR1, HRR3, HRR5, HRR10), then modeled by a mono-exponential function. Time-domain (square root of the mean of the sum of the squares of differences between adjacent normal R-R intervals [RMSSD]) and frequency-domain (with high- and low-frequency band powers) were used to analyse HRV. Participants completed a mental and physical well-being questionnaire at pre- and W8. Exhaustion after tests was assessed by the Borg scale. Pearson correlation was used to assess correlations.

Results: HRR3, HRR5 and HRR10 increased by 37%, 36% and 28%, respectively, between pre- and W8 ($P < 0.05$), and were positively correlated with change in 6MWT distance ($r = 0.58, 0.66$ and 0.76 ; $P < 0.05$). Percentage change in HRR3 was positively correlated with change in well-being ($r = 0.70$; $P = 0.01$). Parasympathetic reactivation (RMSSD) was improved only during the first 30 sec of recovery ($P = 0.04$).

Conclusion: Among patients undergoing a CRP after ACS, increased HRR after a 6MWT, especially at 3 min, was positively correlated with 6MWT distance and improved well-being. HRR raw data seem more sensitive than post-exercise HRV analysis for monitoring functional and autonomic improvement after ACS.

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1. Introduction

Cardiovascular diseases remain the most common cause of death among Europe and accounted for 45% of all deaths in 2015 [1]. Alteration of the autonomic nervous system has a key pathophysiological role in the development of most cardiovascular

risk factors such as hypertension and metabolic syndrome as well as in the onset of acute coronary syndrome (ACS) and the development of chronic heart failure [2]. Indeed, poor vital prognosis related to an exaggerated sympathetic tone is well demonstrated in these patients and triggers threatening cardiac arrhythmias and sudden death [3].

The R-R variability is a strong predictor of the autonomic nervous modulation of the heart and is extensively used for monitoring patients after ACS or predicting cardiac events [4–6]. Moreover, when assessing exercise capacity, heart rate recovery (HRR) 1 min into recovery provides insight into the speed of parasympathetic reactivation. An abnormally low HRR (< 12 bpm

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after 1 min) can be a marker of poor prognosis and greater disease severity [7]. Conversely, an increased parasympathetic tone has been associated with reduced mortality after ACS [8]. This increased parasympathetic activity is one of the protective mechanisms of exercise training implemented during cardiac rehabilitation, in addition to pharmacological treatment and invasive non-pharmacological interventions [9]. Indeed, cardiac rehabilitation was shown to positively modulate autonomic balance in post-ACS patients [10–12], leading to increased HRR after a maximal symptom-limited exercise test [8].

However, the high costs, required medical supervision, and safety concerns with evaluating maximal exercise capacity is sometimes impossible, especially among patients with chronic heart failure. Thus, several submaximal walking protocols have been developed to estimate cardiorespiratory fitness (CRF). The 6-min walk test (6MWT) is a common method used to estimate CRF in clinical settings lacking cardiovascular exercise testing ability. Indeed, studies have reported poor performance on the 6MWT being associated with poor prognosis. Additionally, the 6MWT may be able to detect differences attributable to therapy, especially in cardiac rehabilitation programmes (CRPs). Finally, even if the 6MWT does not provide an accurate estimation of CRF, it provided a clinically meaningful estimate of CRF and was similar to treadmill exercise testing in predicting cardiovascular events over a median follow-up of 8.0 years among outpatients with stable coronary heart disease [13]. In addition, the 6MWT appears to better reflect daily activity than a laboratory maximal exercise test [14].

An efficient CRP can improve the functional ability of patients after ACS, with a reported increase from 12% and 40% in walking distance on the 6MWT [15,16]. Conversely, the effect of such a programme on modulating the autonomic nervous system of the heart is debated, and some studies reported conflicting results [17,18]. Moreover, to our knowledge, no study has clarified a possible relation between HRR or heart rate variability (HRV) changes during a CRP and functional improvement during a submaximal exercise test such as the 6MWT.

The aim of the present study was to investigate the effect of a CRP on parasympathetic modulation, then the relation between HRV and HRR and any improvement in functional walking performance by the 6MWT and well-being in patients after ACS.

2. Materials and methods

2.1. Participants

We consecutively enrolled 11 normoweight patients (BMI < 25 kg/m²; 10 males; mean [SD] age 61 [9] years). Inclusion criteria were an acute cardiac event within the previous 2 months and undergoing cardiac surgery and agreeing to participate in an 8-week rehabilitation programme including three training sessions per week. Exclusion criteria were significant cognitive disorders that hampered participation in the tests (Mini Mental State Examination score ≤ 24), acute or chronic respiratory failure, any associated disease that substantially limited walking capacity, acute or chronic heart failure (left-ventricular ejection fraction < 45% by the echocardiographic Simpson method), residual myocardial ischemia, absence of supraventricular premature ectopy able to alter HRV analysis, and modification of drug therapy affecting adaptation to effort (diuretics, angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, beta-blockers, anti-aldosterones, ivabradine) within the 15 days preceding the tests. However, the drug class, even those affecting HR (e.g., beta-blockers), was not an exclusion criterion. Participants were asked to maintain their usual medication throughout the study. They signed a written informed consent before data

collection. The experiment was approved by a medical ethics committee (Commission cantonale d'éthique sur la recherche humaine du Canton-de-Vaud, CCER-VD, Lausanne, Switzerland; Agreement 165/14) and was performed in accordance with the Declaration of Helsinki.

3. Experimental protocol

3.1. Rehabilitation programme

Patients followed an 8-week rehabilitation programme with three sessions/week. Each session included a 1-hr aerobic exercise training on a treadmill or cycle ergometer followed by a 1-hr session of gymnastics or water aerobic exercises in the swimming pool when scars were healed. They also had 1-hr relaxation sessions once a week and attended education sessions on cardiovascular risk-factor control (2 hr) and healthy nutrition advice (2 hr).

4. Measurements

4.1. 6MWT

The tests were performed on the first day (pre-), half way (W4) and at the end (W8) of the CRP on a treadmill (HP Cosmos[®] running machine series mercury, Nussdorf, Germany) with a 0% incline. The speed was self-selected by the participant and could be changed at any time. Before the test, blood pressure was measured by use of an armband (Welch Allyn[®], Bronze Series DS44 Integrated Aneroids, New York, USA) and a stethoscope. With abnormal blood pressure or HR before the training session, the doctor was informed and the test was postponed if needed. The participant was equipped with an HR monitor (T6d, Suunto, Vantaa, Finland) and HR belt. After a familiarization period, the participant walked on the treadmill, self-selecting the walking speed, in order to achieve the greatest distance during 6 min.

The modified Borg scale (CR10) was used to quantify the rate of perceived exhaustion after each test [19]. At pre- and W8, participants also completed the in-house-developed well-being questionnaire that is used routinely for clinical purposes at the hospital for investigating physical and emotional changes. Scores for “mental well-being” and “physical well-being” were obtained.

5. Post-exercise HRV

At the end of exercise, the participant immediately sat on a chair placed adjacent to the treadmill. The time between the end of exercise and sitting was < 3 sec. The patient was asked not to move or talk while on the chair. All HRR and HRV analyses have been described in detail elsewhere [20,21]. Briefly, all R-R series recorded by the Suunto[®] T6d were exported in an Excel compatible file and data for the 10-min recovery period after the 6MWT were extracted. Occasional ectopic beats were visually identified and manually replaced with interpolated adjacent R-R interval values.

6. Post-exercise HRR

HRR was defined as the difference (exercise–recovery) after 1, 2, 3, 5 or 10 min of exercise cessation (i.e., when HRR increases, the recovery is improved) and was calculated from the end of the 6MWT to the end of 1, 3, 5 and 10 min after the test: HRR1, HRR3, HRR5, and HRR10, respectively. The results are obtained in beat per minutes (bpm). We also gathered the time constant (HRR_τ) of the

HR decay by fitting the 10-min post-exercise HRR into a first-order exponential decay curve.

7. HRV analyses

7.1. Post-exercise parasympathetic reactivation

We calculated the square root of the mean of the sum of the squares of differences between adjacent normal R-R intervals (RMSSD) for each 30-sec segments of recovery (RMSSD30s).

7.2. Post-exercise HRV

HRV was analyzed for the last 5 min of the 10-min recovery period with the participant in the seated position by using Kubios HRV v2.2 (University of Kuopio, Finland). The mean HR ($HR_{5-10 \text{ min}}$) and RMSSD ($RMSSD_{5-10 \text{ min}}$) were calculated for this 5-min period. The power spectrum of the band frequency (high and low [HF, LF]) was calculated with fast Fourier transform based on a nonparametric algorithm with a Welch periodogram (256-sec window with 50% overlap) after the ectopic-free data were detrended and resampled. We calculated HF and LF power in normalized units (nu) for this 5-min period (i.e., $HFnu_{5-10 \text{ min}}$, $LFnu_{5-10 \text{ min}}$) as follows:

HF power in normalized units: $HF / (\text{total power} - VLF) \times 100$

LF power in normalized units: $LF / (\text{total power} - VLF) \times 100$

Finally, the total power (HF + LF) and the LF/HF ratio were calculated.

8. Statistical analysis

With previous data [22] reporting an HRR increase from 18 to 22 bpm in post-ACS patients during a 12-week rehabilitation programme, we needed 10 participants for this study. All data are presented as mean (SD). One-factor repeated-measure ANOVA was used to compare the variables at the 3 times of the CRP (pre-, W4, W8). Pearson product moment correlation was used to examine correlation between change in 6MWT and changes in HRR (in percentage), HRV, and well-being. In addition, we analysed the responses of 6 patients receiving beta-blockers and 5 not receiving this medication. Data were analyzed by using SigmaStat 3.5 (Systat Software, Inc, San Jose, CA). $P < 0.05$ was considered statistically significant.

9. Results

9.1. Walk performance, HRR, and HRV after CRP

Among the 11 participants, the 6MWT distance increased by a mean (SD) of 88 (91) m ($P = 0.009$) between pre- and W4 and 59 (59) m ($P = 0.008$) (Fig. 1) between W4 and W8. Overall, the mean 6MWT distance increase was 147 (83) m (+30%; $P < 0.001$). The mean (SD) walk speed during 6MWT at pre-, W4 and W8 was 3.5 (1.8), 4.4 (1.0) and 5.0 (2.3) km/h, respectively. We found an inverse correlation between initial CRF (6MWT speed or distance measured at pre-) and percentage increase at both W4 ($r = -0.61$; $P < 0.05$) and W8 ($r = -0.65$; $P < 0.05$).

HRR was improved between pre- and W8 (Fig. 2): mean (SD) increases were 8 (6) bpm ($P = 0.002$), 11 (11) bpm ($P = 0.007$), and 10 bpm ($P = 0.013$ and 0.016) for HRR1, HRR3, and both HRR5 and HRR10, respectively. Moreover, only HRR1 increased between W4 and W8 (mean 6 (8) bpm; $P = 0.023$). HRR increase was significantly larger between pre- and W8 for patients receiving beta-blockers ($n = 5$) for HRR1 ($P < 0.001$) and HRR3, HRR5 and HRR10 ($P < 0.05$ for all). For those not receiving beta-blockers, the

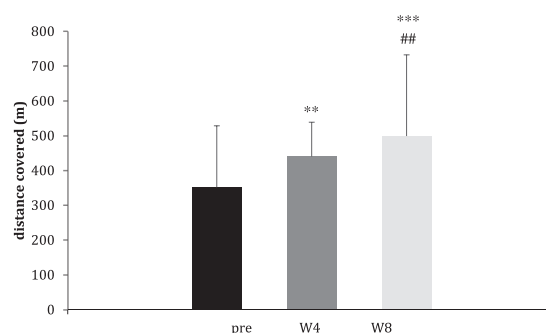


Fig. 1. Performance during a 6-min walk test before (pre-) and at week 4 (W4) and week 8 (W8) during an 8-week cardiac rehabilitation program in patients after

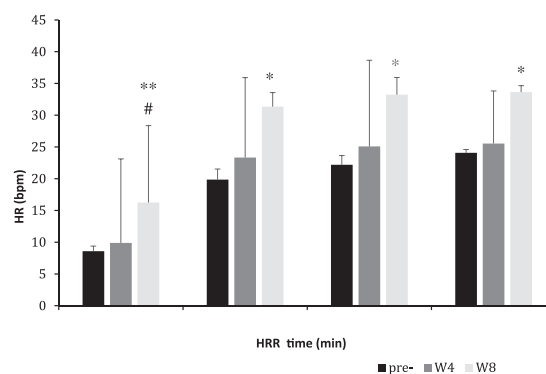


Fig. 2. Heart rate recovery (HRR) at 1- (HRR1), 3- (HRR3), 5- (HRR5) and 10-min (HRR10) after a 6-min walk test, before (pre-) and at week 4 (W4) and week 8 (W8) during an 8-week rehabilitation program. * $P \leq 0.05$, ** $P \leq 0.01$ vs pre-. # $P \leq 0.05$ vs W4.

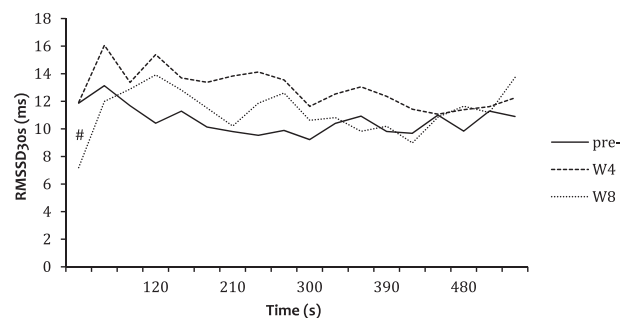


Fig. 3. RMSSD30s after a 6-min walk test, before (pre-) and at week 4 (W4) and week 8 (W8) during an 8-week rehabilitation program. # $P = 0.04$ vs W4.

improvement did not reach significance ($P = 0.09$ to 0.23). The mean (SD) HRR_{τ} decreased from pre- to W4 or W8 (107 (48) vs 79 (12) and 75 (35) sec; $P < 0.05$).

Participants showed no change in parasympathetic reactivation, except that RMSSD30s for the first 30-sec window was improved between W4 and W8 only ($P = 0.04$) (Fig. 3). Mean (SD) $RMSSD_{5-10 \text{ min}}$ did not change significantly between pre- and W4 or W8 (6.3 [0.8] vs 12.3 [1.3] or 11.7 [1.7]), and mean $HR_{5-10 \text{ min}}$ was improved between pre- and W4, although not significantly ($P = 0.06$): the mean (SD) reduction was 5 (14) bpm. We observed no differences for all frequency-domain parameters during the CRP (Table 1).

10. Mental and physical well-being and exhaustion

Participants showed significant improvement in scores for mental (by 34%, $P < 0.001$) and physical (by 22%, $P = 0.012$) well-

Table 1

Frequency-domain heart rate variability (HRV) parameters measured between 5 and 10 min after a 6-min walk test, prior (pre-) and at week 4 (W4) and 8 (W8) after an 8-week rehabilitation programme in patients with acute coronary syndrome.

	Pre-	W4	W8
HF (ms ²)	10.2 (1.4)	31.5 (7.2)	38.3 (11.9)
LF (ms ²)	16.7 (16.4)	91.2 (89.9)	91.9 (82.7)
HF (n.u)	45.5 (24.2)	5.3 (38.1)	39.2 (13.3)
LF (n.u)	53.3 (25.6)	64.4 (38.5)	60.5 (13.7)
LH/HF	1.5 (1.3)	3.0 (3.3)	2.7 (2.3)
HF + LF	27.0 (17.8)	123.6 (97.1)	130.3 (94.6)

Data are mean (SD). n.u.: normalized units; HF: high frequency; LF: low frequency.

being between pre- and W8. The mean (SD) rate of perceived exhaustion for the 6MWT was not modified during the CRP (3.8 [0.7], 3.7 [0.7] and 4.0 [0.7] for pre-, W4 and W8, respectively).

11. Correlation between change in HRR and 6MWT distance and well-being

We found significant positive correlations between change in HRR (in percentage) between pre- and W8 and change in 6MWT distance: HRR3 ($r = 0.58$; $P = 0.05$), HRR5 ($r = 0.66$; $P = 0.02$) and HRR10 ($r = 0.76$; $P = 0.006$; Fig. 4). Change in HRR3 between pre- to W8 was positively correlated with change in mental well-being ($r = 0.70$; $P = 0.01$) (Fig. 5), and changes in HRR3 and HRR5 were positively correlated with change in physical well-being but not significantly ($r = 0.53$, $P = 0.08$; and $r = 0.52$, $P = 0.09$).

12. Discussion

To our knowledge, this is the first study to investigate changes in functional ability, HRR or HRV variables, after a 6MWT and subjective factors in patients after ACS undergoing a CRP. We found a 30% functional improvement in 6MWT distance after 8 weeks of the CRP, which was significant after 4 weeks (+20%). HRR was improved between pre- and W8 after the 6MWT at all measurement times (1, 3, 5 and 10 min). In addition, the magnitude of the change in HRR was correlated with improved functional ability, as measured by the 6MWT distance, and with improved mental or physical well-being. Finally, parasympathetic reactivation was not modified during the CRP.

13. Functional performance improvement

6MWT distance improvement was greater during the first 4 weeks of the CRP (20% vs 12% for pre- to W4 vs W4 to W8). These results agree with the published literature in people with cardiac and/or pulmonary failure [15] and are of clinical importance. The significant improvement in walking speed is of high clinical importance. Walking speed has been proposed as a potential “vital sign” of aging and disease and is a useful prognostic marker (<https://www.cdc.gov/vitalsigns/pdf/2012-08-vitalsigns.pdf>).

Moreover, walking speed during extended walk in patients with cardiovascular disease undergoing CRPs has been found a valid tool to assess the results of these interventions [23]. This improvement is larger than the 54-m improvement threshold needed to validate the relevance of the rehabilitation programme, as suggested by the American Thoracic Society [16]. It also exceeds the minimal clinically significant difference previously determined among patients after ACS [24]. Finally, the improved walking speed during moderate and perceptually regulated treadmill walk tests seems a clinical marker of interest, strongly linked with long-term prognosis and morbidity in aging people and those with cardiovascular diseases [25,26]. As is commonly reported with

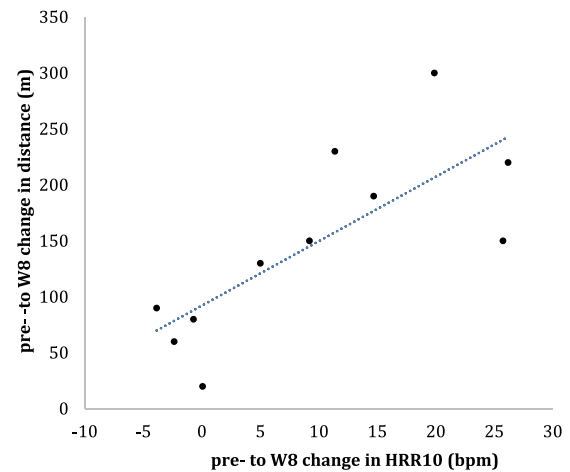


Fig. 4. Correlation between improved performance from pre- to W8 during a 6-min walk test and HRR over 10 min (HRR10) after the end of the test.

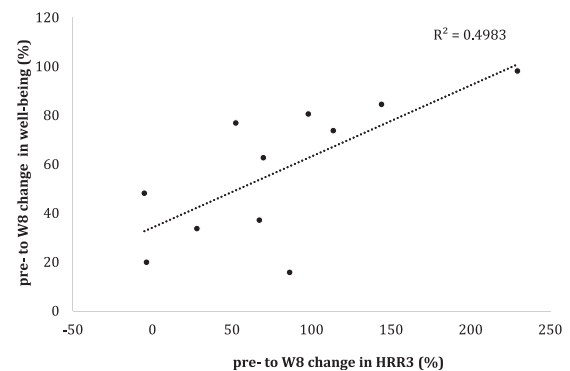


Fig. 5. Correlation between percent change from pre- to W8 in HRR at 3 min (% HRR3) after a 6-min walk test and percentage improvement in well-being during an 8-week rehabilitation program.

exercise training in patients or healthy people, the lower the initial CRF (estimated from the average walking speed at pre-), the larger the improvement at both W4 and W8.

One potential limitation of our findings is that the 6MWT was performed on a treadmill, but the cut-off value reported above was validated for 6MWT performed in a corridor. However, such a test has been found reproducible in patients with chronic heart failure [27]. In addition, we cannot completely rule out a potential learning effect because patients did not perform a complete familiarization test. However, they all had a familiarization walking session on treadmill, and the size effect of the improvement was large (1.77).

14. HRR

The 77% improvement in HRR1 we found is larger than previous reported: 27% [28] or 14% [29], both following a sub-maximal test after 12 weeks of rehabilitation. In the present study, HRR1 was further improved between W4 and W8, whereas improvement in 6MWT distance was greater between pre- and W4. This discrepancy might be related to the time from surgery [17], but we cannot confirm the effects related to the intervention and the natural history in the absence of a control group.

When considering subgroup analysis, only patients receiving beta-blockers showed a significant improvement in HRR. These results must be interpreted with caution because the sample size is small, but they contradict previous studies finding HRR not

affected by this treatment [17]. However, more recent advances in medical treatment for the acute phase of ACS might explain our results. Moreover, one must remember that most patients take beta-blockers after ACS, in line with the latest recommendations in this field [30]. Overall, this finding emphasizes the relevance of this drug, especially during the first year after ACS, as suggested by a recent meta-analysis [31].

15. Parasympathetic reactivation

Overall, parasympathetic reactivation was not improved during the CRP, which agrees with previous studies [16,32]. However, conflicting results were reported among healthy older people (mean [SD] age 75 [2] years), finding RMSSD and HF values improved with a moderate-intensity exercise training programme [33]. This finding suggests a specific post-exercise response to retraining in ACS patients versus healthy older people.

16. HRV

Frequency-domain variables remained unchanged during the CRP. Because 75% of the testing sessions were performed in the morning, these results could be related to the testing schedule. Indeed, circadian variations in variables have been demonstrated, with an upper sympathetic activity level in the morning, and a greater risk of cardiovascular events with a sympathetic dominance and reduced HRV in the morning [34]. Moreover, some patients experienced difficulties being relaxed during the testing sessions because of various factors such as early wake-up or pre-exercise anxiety. All these factors may have participated in overactivation of the sympathetic branch. However, another study evidenced a 30% reduction in LF/HF ratio ($P < 0.01$), meaning a parasympathetic dominance, when tests began, but with a 15 min recovery session [35], which is an important difference from our protocol.

It is intuitive to expect an association between resting HRV, parasympathetic reactivation and HRR. However, the relations between these three types of data are very low [36]. For example, parasympathetic reactivation after intense exercise has been found largely lowered despite an almost preserved HRR [37]. The lack of association between HRR and HRV is due to many factors such as sympathetic activity, ventilation or environmental conditions (noise, light, temperature, etc.) that might interfere with parasympathetic outflow during the post-exercise period but also, and probably to a larger extent, during resting conditions. For these reasons, resting HRV is moderately reliable [38], whereas HRR reliability when expressed from raw HR (and not with an exponential fitting) was considered satisfactory. Altogether the main aim of the present study was to investigate parasympathetic reactivation and HRR and not resting HRV.

17. Rate of perceived exhaustion, mental and physical well-being

Rating of perceived exhaustion did not change in our study, whereas 6MWT distance improved; that is, at W8, participants walked faster for the same level of perceived effort. In contrast, the rate was reduced after a 12-week rehabilitation programme for post-ACS patients, with no changes in HRR or HRV [18]. These results might be explained by methodological differences between the studies: the Currie et al. training programme included high-intensity interval training, and patients were enrolled a long time after the cardiac event (4 to 5 months). Indeed, Munk et al. reported alteration in the autonomic nervous system activity, with a shift toward increased parasympathetic activity and decreased

sympathetic activity among participants performing a high-intensity interval training programme initiated 11 days after a percutaneous coronary intervention for angina pectoris [39].

We found a large (34%) improvement in subjective well-being, which is higher than the 22% improvement in physical well-being. This result agrees with a previous study reporting such effects after a shorter intervention (4 weeks) [40] and appears clinically important in that improved psychological well-being is now seen important in assessing the efficiency of an exercise intervention in cardiac patients [41] and other chronic diseases such as cancer [42].

18. HRR relationships

An important finding is that change in HRR was correlated with changes in both 6MWT distance and well-being. To our knowledge, no studies have shown these associations in post-ACS patients. The role of the autonomic nervous system in submaximal performance improvement and psychological well-being in this population is probably underestimated. Indeed, HRR is an indicator of cardiac autonomic function and demonstrates a strong correlation with mortality risk in healthy [43] and post-ACS patients [44]. Moreover, psychological status was shown to alter HRR after a psychologically stressing test [45]. However, data regarding the interest of HRR after a submaximal exercise in post-ACS patients are scarce. Myers et al. [46] previously observed a correlation between exercise capacity and improvement in HRR in post-ACS patients after 8 weeks of a rehabilitation programme, but performance assessment was based on peak $\dot{V}O_2$. In our study, HRR3, a simple variable measured over a short time after 6MWT, seems the best marker of these improvements. From a clinical perspective, the present results highlight that this accessible and simple HRR measurement is valid for monitoring improvement in functional ability and subjective well-being, both key variables for assessing the effectiveness of a rehabilitation programme. This assessment could be useful to help clinicians tailor the exercise programme to improvement and also for prognosis: both HRR and 6MWT seem good markers of prognosis for morbidity and mortality in patients with stable coronary artery disease and preserved left-ventricular function. In particular, the distance of 300 m was recently confirmed to be discriminant in elderly people undergoing cardiac rehabilitation after coronary artery bypass grafting [47].

19. HRR versus post-exercise HRV

To the best of our knowledge, this is the first study quantifying post-exercise HRV and HRR variables after a 6MWT in post-ACS patients. This study highlights that HRR is more sensitive and convenient than post-exercise HRV for monitoring such patients during a CRP. Analysing HRR takes less time (for both recording and analysis phases) than does post-exercise HRV. This aspect was also noted with healthy people, in whom HRR improved first [48]. HRV is less reliable and more largely affected by non-alterable factors such as age, sex, and heredity as compared with HRR [49–51]. This finding might explain in part why we observed improvement in only HRR and not post-exercise HRV. However, future study should investigate the potential interest of a more frequent measure of post-exercise HRV during a CRP. Indeed, such measures might also be of interest in monitoring short-term adaptations to exercise training and thus better individualising training intensity, as was shown among healthy people [52].

20. Conclusion

This study provides further evidence of the association between improved HRR and improved walking ability and perceived well-

being in patients with ACS after an exercise-based CRP. Our findings have interest from a clinical point of view because HRR is easily measurable with these patients and was found reproducible. HRR was the most clinically relevant variable for people with ACS as compared with HRV. Moreover, HRR3 was the most relevant, because it was correlated with both improved mental well-being and performance. These results and their clinical relevance to monitor improvements and individualize exercise training in cardiac rehabilitation should be further investigated with a larger sample.

Disclosure of interest

The authors declare that they have no competing interest..

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References

- [1] Townsend N, Nichols M, Scarborough P, Rayner M. Cardiovascular disease in Europe – epidemiological update 2015. *Eur Heart J* 2015;36:2696–705. <http://dx.doi.org/10.1093/eurheartj/ehv428> [PubMed PMID: 26306399].
- [2] Besnier F, Labrunee M, Pathak A, Pavy-Le Traon A, Gales C, Senard JM, et al. Exercise training-induced modification in autonomic nervous system: an update for cardiac patients. *Ann Phys Rehabil Med* 2017;60:27–35. <http://dx.doi.org/10.1016/j.irehab.2016.07.002> [PubMed PMID: 27542313].
- [3] Vaseghi M, Shivkumar K. The role of the autonomic nervous system in sudden cardiac death. *Prog Cardiovasc Dis* 2008;50:404–19. <http://dx.doi.org/10.1016/j.pcad.2008.01.003> [PubMed PMID: 18474284; PubMed Central PMCID: PMC2752648].
- [4] Song T, Qu XF, Zhang YT, Cao W, Han BH, Li Y, et al. Usefulness of the heart-rate variability complex for predicting cardiac mortality after acute myocardial infarction. *BMC Cardiovasc Disord* 2014;14:59. <http://dx.doi.org/10.1186/1471-2261-14-59> [PubMed PMID: 24886422; PubMed Central PMCID: PMC4023175].
- [5] La Rovere MT, Pinna GD, Maestri R, Mortara A, Capomolla S, Febo O, et al. Short-term heart rate variability strongly predicts sudden cardiac death in chronic heart failure patients. *Circulation* 2003;107:565–70 [PubMed PMID: 12566367].
- [6] La Rovere MT, Mortara A, Sandrone G, Lombardi F. Autonomic nervous system adaptations to short-term exercise training. *Chest* 1992;101:299S–303S [PubMed PMID 1576853].
- [7] Guazzi M, Adams V, Conraads V, Halle M, Mezzani A, Vanhees L, et al. EACPR/AHA scientific statement. Clinical recommendations for cardiopulmonary exercise testing data assessment in specific patient populations. *Circulation* 2012;126:2261–74. <http://dx.doi.org/10.1161/CIR.0b013e31826b946> [PubMed PMID: 22952317; PubMed Central PMCID: PMC4777325].
- [8] La Rovere MT, Bigger Jr JT, Marcus FI, Mortara A, Schwartz PJ. Baroreflex sensitivity and heart-rate variability in prediction of total cardiac mortality after myocardial infarction. ATRAMI (autonomic tone and reflexes after myocardial infarction) Investigators. *Lancet* 1998;351:478–84 [PubMed PMID: 9482439].
- [9] Task Force, Piepoli MF, Hoes AW, Agewall S, Albus C, Brotons C, et al. 2016 European Guidelines on cardiovascular disease prevention in clinical practice: the sixth joint task force of the European Society of Cardiology and other societies on cardiovascular disease prevention in clinical practice (constituted by representatives of 10 societies and by invited experts): developed with the special contribution of the European Association for Cardiovascular Prevention & Rehabilitation (EACPR). *Eur J Prevent Cardiol* 2016;23. <http://dx.doi.org/10.1177/2047487316653709> [NP1-NP96, PubMed PMID: 27353126].
- [10] Klimov D, Lysy C, Berteau S, Dutrançois J, Dereppe H, Brohet C, et al. Biofeedback on heart rate variability in cardiac rehabilitation: practical feasibility and psycho-physiological effects. *Acta Cardiol* 2014;69:299–307. <http://dx.doi.org/10.2143/AC.69.3.3027833> [PubMed PMID: 25029875].
- [11] Sandercock GR, Grocott-Mason R, Brodie DA. Changes in short-term measures of heart rate variability after eight weeks of cardiac rehabilitation. *Clin Auton Res* 2007;17:39–45. <http://dx.doi.org/10.1007/s10286-007-0392-5> [PubMed PMID: 17285225].
- [12] Tygesen H, Wettervik C, Wennerblom B. Intensive home-based exercise training in cardiac rehabilitation increases exercise capacity and heart rate variability. *Int J Cardiol* 2001;79:175–82 [PubMed PMID: 11461739].
- [13] Ross R, Blair SN, Arena R, Church TS, Despres JP, Franklin BA, et al. Importance of assessing cardiorespiratory fitness in clinical practice: a case for fitness as a clinical vital sign: a scientific statement from the American Heart Association. *Circulation* 2016;134:e653–99. <http://dx.doi.org/10.1161/CIR.0000000000000461> [PubMed PMID: 27881567].
- [14] Casillas JM, Hannequin A, Besson D, Benaim S, Krawcow C, Laurent Y, et al. Walking tests during the exercise training: specific use for the cardiac rehabilitation. *Ann Phys Rehabil Med* 2013;56:561–75. <http://dx.doi.org/10.1016/j.irehab.2013.09.003> [PubMed PMID: 24126080].
- [15] Enright PL. The six-minute walk test. *Respir Care* 2003;48:783–5 [PubMed PMID: 12890299].
- [16] Jelinek HF, Huang ZQ, Khandoker AH, Chang D, Kiat H. Cardiac rehabilitation outcomes following a 6-week program of PCI and CABG patients. *Front Physiol* 2013;4:302. <http://dx.doi.org/10.3389/fphys.2013.00302> [PubMed PMID: 24198786; PubMed Central PMCID: PMC3812547].
- [17] Hao SC, Chai A, Kligfield P. Heart rate recovery response to symptom-limited treadmill exercise after cardiac rehabilitation in patients with coronary artery disease with and without recent events. *Am J Cardiol* 2002;90:763–5 [PubMed PMID: 12356394].
- [18] Currie KD, Rosen LM, Millar PJ, McKelvie RS, MacDonald MJ. Heart rate recovery and heart rate variability are unchanged in patients with coronary artery disease following 12 weeks of high-intensity interval and moderate-intensity endurance exercise training. *Appl Physiol Nutr Metab* 2013;38:644–50. <http://dx.doi.org/10.1139/apnm-2012-0354> [PubMed PMID: 23724882].
- [19] Borg GA. Psychophysical bases of perceived exertion. *Med Sci Sports Exerc* 1982;14:377–81 [PubMed PMID: 7154893].
- [20] Buchheit M, Millet GP, Parisy A, Pourchez S, Laursen PB, Ahmadi S. Supramaximal training and postexercise parasympathetic reactivation in adolescents. *Med Sci Sports Exerc* 2008;40:362–71. <http://dx.doi.org/10.1249/mss.0b013e318151815> [Epub 2008/01/19. PubMed PMID: 18202564].
- [21] Task Force. Heart rate variability. Standards of measurement, physiological interpretation, and clinical use. *Eur Heart J* 1996;17:354–81 [PubMed PMID: 8737210].
- [22] Tiukinhoy S, Beohar N, Hsie M. Improvement in heart rate recovery after cardiac rehabilitation. *J Cardiopulm Rehabil* 2003;23:84–7 [PubMed PMID: 12668927].
- [23] Chiaranda G, Myers J, Mazzoni G, Terranova F, Bernardi E, Grossi G, et al. Peak oxygen uptake prediction from a moderate, perceptually regulated, 1-km treadmill walk in male cardiac patients. *J Cardiopulm Rehabil Prev* 2012;32:262–9. <http://dx.doi.org/10.1097/HCR.0b013e3182663507> [PubMed PMID: 22936157].
- [24] Gremeaux V, Troisgros O, Benaim S, Hannequin A, Laurent Y, Casillas JM, et al. Determining the minimal clinically important difference for the six-minute walk test and the 200-meter fast-walk test during cardiac rehabilitation program in coronary artery disease patients after acute coronary syndrome. *Arch Phys Med Rehabil* 2011;92:611–9. <http://dx.doi.org/10.1016/j.apmr.2010.11.023> [PubMed PMID: 21440707].
- [25] Grazzi G, Mazzoni G, Myers J, Codeca L, Pasanisi G, Napoli N, et al. Improved walking speed is associated with lower hospitalisation rates in patients in an exercise-based secondary prevention programme. *Heart* 2016;102:1902–8. <http://dx.doi.org/10.1136/heartjnl-2015-309126> [PubMed PMID: 27390367].
- [26] Chiaranda G, Bernardi E, Codeca L, Conconi F, Myers J, Terranova F, et al. Treadmill walking speed and survival prediction in men with cardiovascular disease: a 10-year follow-up study. *BMJ Open* 2013;3:e003446. <http://dx.doi.org/10.1136/bmjopen-2013-003446> [PubMed PMID: 24163203; PubMed Central PMCID: PMC3808890].
- [27] Guimaraes GV, Carvalho VO, Bocchi EA. Reproducibility of the self-controlled six-minute walking test in heart failure patients. *Clinics (Sao Paulo)* 2008;63:201–6 [PubMed PMID: 18438574; PubMed Central PMCID: PMC2664221].
- [28] Kligfield P, McCormick A, Chai A, Jacobson A, Feuerstadt P, Hao SC. Effect of age and gender on heart rate recovery after submaximal exercise during cardiac rehabilitation in patients with angina pectoris, recent acute myocardial infarction, or coronary bypass surgery. *Am J Cardiol* 2003;92:600–3 [S0002914903007331, Epub 2003/08/29 PubMed PMID: 12943886].
- [29] MacMillan JS, Davis LL, Durham CF, Matteson ES. Exercise and heart rate recovery. *Heart Lung* 2006;35:383–90. <http://dx.doi.org/10.1016/j.hrtlng.2006.07.003> [[pii]S0147-9563(06)00181-6 PubMed PMID: 17137939].
- [30] Smith Jr SC, Benjamin EJ, Bonow RO, Braun LT, Creager MA, Franklin BA, et al. AHA/ACCF secondary prevention and risk reduction therapy for patients with coronary and other atherosclerotic vascular disease: 2011 update: a guideline from the American Heart Association and American College of Cardiology Foundation endorsed by the World Heart Federation and the Preventive Cardiovascular Nurses Association. *J Am Coll Cardiol* 2011;58:2432–46. <http://dx.doi.org/10.1016/j.jacc.2011.10.824> [PubMed PMID: 22055990].
- [31] Bangalore S, Makani H, Radford M, Thakur K, Toklu B, Katz SD, et al. Clinical outcomes with beta-blockers for myocardial infarction: a meta-analysis of randomized trials. *Am J Med* 2014;127:939–53. <http://dx.doi.org/10.1016/j.amjmed.2014.05.032> [PubMed PMID: 24927909].
- [32] Oliveira NL, Ribeiro F, Teixeira M, Campos L, Alves AJ, Silva G, et al. Effect of 8-week exercise-based cardiac rehabilitation on cardiac autonomic function: A randomized controlled trial in myocardial infarction patients. *Am Heart J* 2014;167:753–61. <http://dx.doi.org/10.1016/j.ahaj.2014.02.001> [PubMed PMID: 24766987].
- [33] Buchheit M, Simon C, Viola AU, Doutreleau S, Piquard F, Brandenberger G. Heart rate variability in sportive elderly: relationship with daily physical activity. *Med Sci Sports Exerc* 2004;36:601–5 [00005768-200404000-00008 pii, Epub 2004/04/06. PubMed PMID: 15064587].
- [34] Boudreau P, Yeh WH, Dumont GA, Boivin DB. A circadian rhythm in heart rate variability contributes to the increased cardiac sympathovagal response to awakening in the morning. *Chronobiol Int* 2012;29:757–68. <http://dx.doi.org/10.3109/07420528.2012.674592> [PubMed PMID: 22734576].

- [35] Malfatto G, Facchini M, Bragato R, Branzi G, Sala L, Leonetti G. Short and long term effects of exercise training on the tonic autonomic modulation of heart rate variability after myocardial infarction. *Eur Heart J* 1996;17:532–8 [PubMed PMID: 8733085].
- [36] Buchheit M, Papelier Y, Laursen PB, Ahmaidi S. Noninvasive assessment of cardiac parasympathetic function: postexercise heart rate recovery or heart rate variability? *Am J Physiol Heart Circ Physiol* 2007;293:H8–10. <http://dx.doi.org/10.1152/ajpheart.00335.2007> [PubMed PMID: 17384128].
- [37] Buchheit M, Laursen PB, Ahmaidi S. Parasympathetic reactivation after repeated sprint exercise. *Am J Physiol Heart Circ Physiol* 2007;293:H133–41. <http://dx.doi.org/10.1152/ajpheart.00062.2007> [PubMed PMID: 17337589].
- [38] Sandercock GR, Bromley P, Brodie DA. Reliability of three commercially available heart rate variability instruments using short-term (5-min) recordings. *Clin Physiol Funct Imaging* 2004;24:359–67. <http://dx.doi.org/10.1111/j.1475-097X.2004.00584.x> [PubMed PMID: 15522045].
- [39] Munk PS, Butt N, Larsen AI. High-intensity interval exercise training improves heart rate variability in patients following percutaneous coronary intervention for angina pectoris. *Int J Cardiol* 2010;145:312–4. <http://dx.doi.org/10.1016/j.ijcard.2009.11.015> [PubMed PMID: 19962772].
- [40] Duarte Freitas P, Haida A, Bousquet M, Richard L, Mauriege P, Guiraud T. Short-term impact of a 4-week intensive cardiac rehabilitation program on quality of life and anxiety-depression. *Ann Phys Rehabil Med* 2011;54:132–43. <http://dx.doi.org/10.1016/j.rehab.2011.02.001> [PubMed PMID: 21397582].
- [41] Bedi G, Brown SL. Optimism, coping style and emotional well-being in cardiac patients. *Br J Health Psychol* 2005;10:57–70. <http://dx.doi.org/10.1348/135910704X15266> [PubMed PMID: 15826334].
- [42] Oldervoll LM, Kaasa S, Hjermstad MJ, Lund JA, Loge JH. Physical exercise results in the improved subjective well-being of a few or is effective rehabilitation for all cancer patients? *Eur J Cancer* 2004;40:951–62. <http://dx.doi.org/10.1016/j.ejca.2003.12.005> [PubMed PMID: 15093569].
- [43] Cole CR, Blackstone EH, Pashkow FJ, Snader CE, Lauer MS. Heart-rate recovery immediately after exercise as a predictor of mortality. *N Engl J Med* 1999;341:1351–7. <http://dx.doi.org/10.1056/NEJM199910283411804> [PubMed PMID: 10536127].
- [44] Vivekananthan DP, Blackstone EH, Pothier CE, Lauer MS. Heart rate recovery after exercise is a predictor of mortality, independent of the angiographic severity of coronary disease. *J Am Coll Cardiol* 2003;42:831–8 [PubMed PMID: 12957428].
- [45] Gordon JL, Ditto B, D'Antonio B. Cognitive depressive symptoms associated with delayed heart rate recovery following interpersonal stress in healthy men and women. *Psychophysiology* 2012;49:1082–9. <http://dx.doi.org/10.1111/j.1469-8986.2012.01397.x> [PubMed PMID: 22725718].
- [46] Myers J, Hadley D, Oswald U, Bruner K, Kottman W, Hsu L, et al. Effects of exercise training on heart rate recovery in patients with chronic heart failure. *Am Heart J* 2007;153:1056–63. <http://dx.doi.org/10.1016/j.ahj.2007.02.038> [PubMed PMID: 17540210].
- [47] Cacciatore F, Abete P, Mazzella F, Furgi G, Nicolino A, Longobardi G, et al. Six-minute walking test but not ejection fraction predicts mortality in elderly patients undergoing cardiac rehabilitation following coronary artery bypass grafting. *Eur J Prevent Cardiol* 2012;19:1401–9. <http://dx.doi.org/10.1177/1741826711422991> [PubMed PMID: 21933832].
- [48] Buchheit M, Chivot A, Parouty J, Mercier D, Al Haddad H, Laursen PB, et al. Monitoring endurance running performance using cardiac parasympathetic function. *Eur J Appl Physiol* 2010;108:1153–67. <http://dx.doi.org/10.1007/s00421-009-1317-x> [PubMed PMID: 20033207].
- [49] Pinna GD, Maestri R, Torunski A, Danilowicz-Szymanowicz L, Szwoch M, La Rovere MT, et al. Heart rate variability measures: a fresh look at reliability. *Clin Sci Lond* 2007;113:131–40. <http://dx.doi.org/10.1042/CS20070055> [PubMed PMID: 17381425].
- [50] Bosquet L, Gamelin FX, Berthoin S. Reliability of postexercise heart rate recovery. *Int J Sports Med* 2008;29:238–43. <http://dx.doi.org/10.1055/s-2007-965162> [PubMed PMID: 17614018].
- [51] Sandercock GR, Bromley PD, Brodie DA. The reliability of short-term measurements of heart rate variability. *Int J Cardiol* 2005;103:238–47. <http://dx.doi.org/10.1016/j.ijcard.2004.09.013> [PubMed PMID: 16098384].
- [52] Kiviniemi AM, Hautala AJ, Kinnunen H, Nissila J, Virtanen P, Karjalainen J, et al. Daily exercise prescription on the basis of HR variability among men and women. *Med Sci Sports Exerc* 2010;42:1355–63 [PubMed PMID: 20575165].