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Acute and chronic effects of high-intensity interval and moderate-intensity continuous exercise on heart rate and its variability after recent myocardial infarction: A randomized controlled trial

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ABSTRACT

Background: Resting heart rate (HR) and HR variability (HRV) are known to predict mortality in patients after myocardial infarction (MI).
Objective: We assessed acute and chronic effects of high-intensity interval training (HIIT) versus moderate-intensity continuous exercise (MICE) on HR and HRV in individuals after acute ST-segment elevation MI (STEMI).
Methods: Participants within 7 weeks after MI were randomly assigned to HIIT or MICE groups for a 9-week intervention. HR and the power spectrum of HRV were measured pre- and post-intervention by using orthostatic challenge and during sleep to assess chronic effects. Sleep measurements were performed at night after HIIT, MICE or no training to assess acute effects. Mixed models assessed time*group interaction for differences in chronic and acute effects, adjusted for beta-blocker dose and number of training sessions.
Results: Overall, 34 of 37 and 35 of 36 participants in the HIIT and MICE groups completed the study. We found a trend for an acute increase in HR of 2.5 bpm (4%, $P = 0.023$) during sleep after HIIT. We found a trend for a chronic decrease in HR during supine and standing position as well as during sleep in the MICE group but a trend for an increase in HR during supine and standing position in the HIIT group. Low- and high-frequency power (LF, HF) of the standing segment increased from pre- to post-intervention in the MICE group but decreased in the HIIT group (group*time interaction $P = 0.005$ and $P = 0.026$, respectively).
Conclusion: HR during sleep tended to be increased acutely during the night after HIIT but not after MICE as compared with controls. Chronic effects on resting HR, HF and LF tended to be more beneficial after MICE than HIIT in individuals with recent STEMI.

1. Introduction

Secondary prevention via comprehensive cardiac rehabilitation has been considered the most cost-effective intervention to ensure favourable outcomes across a wide spectrum of cardiovascular disease, reducing cardiovascular mortality, morbidity and disability, and to increase quality of life [1]. Because mortality is an outcome measure that requires long follow-up times in study settings, surrogate measures for mortality are often reported instead for interventional studies. In cardiovascular patients, resting heart rate (HR) and HR recovery (HRR), quantified as the slowing of HR within 60 sec after peak exercise cessation, have been found to predict mortality [2–5]. Likewise, low HR variability (HRV) can predict mortality after MI [6,7]. HRR and various HRV parameters have been found improved with exercise training in cardiovascular patients [8–11]. Furthermore, interventions with exercise or drugs that lower resting HR can reduce cardiovascular risk [12].

In the last decades, evidence has grown to support the beneficial effect of high-intensity interval training (HIIT) on exercise capacity, cardiovascular function and quality of life

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[13,14]. However, only few studies have assessed chronic effects of different exercise modalities on HR, HRV, and/or HRR, with conflicting results: some studies have found no difference between HIIT and moderate-intensity continuous exercise (MICE) [15,16], whereas others have found HIIT more beneficial [9,10]. No study has investigated the effect of HIIT and MICE on HRV and HRR after acute ST-segment elevation myocardial infarction (STEMI). Furthermore, to the best of our knowledge, the acute effects of different exercise modalities on these parameters have not been investigated at all in people with coronary artery disease.

The aim of the present study was to assess acute and chronic effects of HIIT and MICE on HR and HRV in people after recent STEMI.

2. Methods

2.1. Study population

Individuals were included in the HIIT-Early study between November 30, 2015 and November 30, 2019 if they started outpatient cardiac rehabilitation at the University Hospital Bern within 4 weeks after a first STEMI and underwent primary percutaneous coronary intervention. For the present study, HRV data available on July 19, 2019 were used.

Exclusion criteria were known chronic heart failure with left ventricular ejection fraction $\leq 45\%$ before the acute MI, recent valve surgery, musculoskeletal limitations, thrombus formation or permanent atrial fibrillation. The study was approved by the ethics committee of the Canton of Bern. Written informed consent was obtained from all participants. The reporting of results follows the Consort statement [17].

2.2. Study design

The HIIT-Early study (NCT02627586) was a single-centre, prospective, randomized controlled trial with a parallel arm design. It was integrated in a 12-week multidisciplinary outpatient CR program at the Inselspital Bern. The cardiac rehabilitation program consisted of 3 supervised 90-min exercise training sessions per week and nutrition counseling, psychotherapy and smoking cessation according to individual needs. The exercise sessions usually included 38 min of endurance training on a cycling ergometer, followed by 45 min of coordination training, resistance training, water therapy, stretching or relaxation.

After regular CR baseline testing, participants completed a 3-week run-in period with 3 weekly MICE training sessions (Supplement Figure 1). They then completed the pre-intervention testing, after which they were randomly allocated (1:1, block size 2, using sealed envelopes) by research personnel not involved in the intervention delivery to the HIIT or MICE group for the 9-week intervention. Blinding to allocation was not possible, but investigators analysing outcome data were blinded to group allocation. Participants allocated to the HIIT group performed two HIIT sessions and one MICE session per week and those allocated to the MICE group performed three MICE sessions per week during the 9-week intervention, after which they underwent the post-intervention measurements. After this, participants were given physical activity recommendations based on current guidelines. The choice of the HIIT protocol was based on the one most widely used for patients with coronary artery disease (CAD), 4×4 min-protocol [18,19], and the MICE protocol was designed to suit patient preference and achieve isocaloric energy expenditure with HIIT [20].

2.3. Training intervention

The individual workload of MICE training for every participant was determined on the basis of data from the baseline cardiopulmonary exercise test. MICE training consisted of a 38-min cycling ergometer endurance exercise at a constant workload starting at the first ventilatory threshold (VT1). Of the 38 min, five min of warm-up and 3 min of cool-down were performed at 50% of this workload. HIIT consisted of four 4-min intervals at a workload starting at the second ventilatory threshold (VT2), each interval separated by 3-min intervals at an intensity half way between zero and VT1. This same workload was used for the 8 min of warm-up and 3 min of cool-down. Both training modalities were adjusted weekly according to participants' reported rate of perceived exertion on the Borg scale and aiming at a Borg score 13 to 14 for MICE and 15 to 16 for the high-intensity intervals of the HIIT sessions.

2.4. Measurements

The primary outcome was cardiac remodeling. The secondary outcomes were acute and chronic effects on HRV. The measurements are described in Supplement 1.

2.5. Data analysis

For statistical analyses, R v3.5.2 was used. Baseline values were analyzed with descriptive statistics and Mann–Whitney U test for between-group differences. Chronic changes in predicted oxygen consumption (VO_2 predicted), peak HR, HRR, blood pressure and any of the HR and HRV parameters from the supine and standing segments of the orthostatic challenge test from pre- to post-intervention were analyzed by using mixed models with patient as a random intercept and group and time effects as fixed factors for main and interaction effects. The number of completed training sessions in any training modality during the intervention and beta-blocker dose were covariates added to these models. Night measurements were used to assess acute and chronic effects of HIIT and MICE. Mixed models with patient as a random intercept were used, including training modality of the preceding day (with no training as reference) for acute effects and time (nights 1 to 3 vs. nights 4 to 6) for chronic effects. Number of completed training sessions, beta-blocker dose and order of night with each training modality (within the 3 nights of each visit) were entered into the models as covariates (fixed effects). HRV parameters were log-transformed to reduce heteroscedasticity of model residuals. Significance level was adjusted by Bonferroni adjustment for 4 models, so alpha was set at ≤ 0.0125.

For the present study, a per-protocol analysis (PP) was used because we were interested in the actual effects of HIIT versus MICE on chronic and acute HRV when properly performed. Of the scheduled 18 HIIT and 9 MICE sessions for participants allocated to the HIIT group, a minimum of 12 HIIT sessions needed to be completed; otherwise, the HIIT:MICE training session ratio was assessed, and if this ratio was < 1, these participants were allocated to the MICE group for the PP analysis.

Sample size calculation was performed for the primary outcome of the main study (cardiac function) and was set at 144 participants.

3. Results

After 4.5 years, the study was terminated without achieving the target enrolment because many otherwise eligible patients were already enrolled in other studies. Of 75 enrolled participants,

Table 1
Age, percentage of maximal beta-blocker doses, number of training sessions and time between visits by group according to per-protocol analysis for patients with moderate-intensity continuous exercise (MICE) and high-intensity interval training (HIIT).

Group	*n*	MICE	*n*	HIIT	*P* value
Age (years)	35	59 (52–62)	34	53 (49–66)	0.795
BMI (kg/m^2)	35	27.4 (26.2–29.0)	34	26.4 (24.4–28.7)	0.074
ß-blocker dose of maximal (%)	35	18.8 (12.5–25.0)	34	25.0 (12.5–37.5)	0.146
Number of total training sessions	35	21 (18–24)	34	20 (18–25)	0.640
Number of HIIT training sessions	1	1 (1–1)	34	17 (14–18)	0.000
Time between pre-intervention to post-intervention (days)	35	77 (75–85)	34	75 (70–83)	0.214
Time between nights 1–3 to nights 4–6 (days)	21	49 (44–56)	21	49 (39–62)	0.965

Data are median (interquartile range). *P*-values were calculated by Mann-Whitney U test. BMI: body mass index.

73 were randomized to HIIT (n = 37) and MICE (n = 36, Supplement Figure 2). The present PP analysis finally included 34 and 35 participants in the HIIT and MICE groups because 1 participant completed fewer HIIT (n = 1) than MICE (n = 19) sessions. Depending on assessed parameters, data for fewer participants were analysed as indicated in Tables because of missing measurements or low-quality data.

Most participants were on beta-blockers during the intervention phase, except 3 in the MICE group and 1 in the HIIT group, with the same median beta-blocker dose in both groups (Table 1). Participants in the HIIT and MICE groups completed a median of 20 and 21 training sessions over 9 weeks; in both groups, participants achieved 1.2 Watts/kg during training sessions (data not shown). Detailed characteristics of the 2 training modalities achieved in this study will be published elsewhere (data not shown). The groups did not differ in age, beta-blocker dose, number of completed training sessions (completed by each participant) and time between visits (Table 1). Owing to the reallocation of one participant from the HIIT to MICE group in the PP analysis, 1 participant had one HIIT training session in the MICE group.

3.1. Chronic changes in HR parameters on cardiopulmonary exercise test

Training response with regard to cardiorespiratory fitness will be reported elsewhere. Briefly, for the present PP analysis, exercise capacity expressed as VO_2 predicted (according to Wassermann [21]) improved during cardiac rehabilitation by 10%, with no significant difference between groups (Table 2). Peak HR increased over time ($P < 0.001$), with no difference between groups. HRR was lower but not significantly in the HIIT than MICE group (P = 0.089, Table 2).

3.2. Chronic effects of training modality on HR and HRV by orthostatic challenge test

Chronic changes from pre- to post-intervention for HR and HRV parameters from the orthostatic challenge test are shown for group and time effects in Fig. 1. HRV parameters for the supine and standing time segments from the orthostatic challenge test were available for 29 HIIT and 29 MICE participants for pre-intervention testing and for 28 HIIT and 29 MICE participants for post-intervention testing. Because of time constraints or equipment failure, 12 measurements were not performed (pre-intervention: 2 MICE and 2 HIIT; post-intervention: 2 MICE and 6 HIIT), and another 11 measurements had to be excluded because of poor signal quality. Results from the mixed models indicated a significant group*time interaction effect for low-frequency (LF) power for the standing segment adjusted for number of training session and beta-blocker dose (Fig. 1). The full model outputs are shown in Supplement Table 1. We also found trends for group*time interactions for LF power for the supine segment and high-frequency (HF) power for the standing segment. This was accompanied by a concomitant slight decrease in HR for the supine and standing segments in the MICE group but increases in HR in the HIIT group (Fig. 1).

3.3. Chronic effects of training modality on HR and HRV during sleep

Among the 286 night recordings, 44 had poor signal quality and had to be excluded. Results from the mixed models based on night measurements indicated that HR decreased significantly over time, with a decrease of 3% from nights 1 to 3 to nights 4 to 6 (P = 0.005) but no difference between groups (Table 3). None of the other HRV parameters showed an effect of group or time. Unadjusted chronic changes of frequency domain HRV parameters are shown in Supplement Figure 3.

3.4. Acute effects of training modality on HR and HRV during sleep

Among the 242 valid measurements, 129 night measurements after a day without training, 37 measurements after a day with HIIT, and 76 after a day with MICE training were included in the mixed models. Fig. 2 shows individual data and quartiles of HR measured during the night after HIIT, MICE, or no preceding training session. HR was 4% higher after HIIT sessions than during a night following a day without training (P = 0.023), whereas HR after MICE training was only 1% higher than during a night following a day without training (P = 0.368, Table 3).

Table 2
Patient characteristics and cardiopulmonary exercise test parameters at pre- and post-intervention as well as changes between pre- and post-intervention.

Group (n)	MICE [35] Pre-Intervention	HIIT [34] Pre-Intervention	MICE [35] Post-Intervention	HIIT [34] Post-Intervention	*P*-value for interaction
VO2 peak of predicted (%)	99 (84–112)	99 (89–112)	108 (89–123)	109 (92–121)	0.225
Systolic BP (mmHg)	113 (110–120)	110 (110–125)	120 (110–130)	120 (111–130)	0.189
Diastolic BP (mmHg)	75 (70–80)	75 (70–80)	75 (75–80)	80 (70–80)	0.021
Maximal HR (min^{-1})	142 (128–152)	140 (126–155)	150 (134–161)	148 (137–158)	0.502
60-sec HRR (n of beats)	24 (21–29)	26 (20–31)	24 (18–30)	21 (16–27)	0.089

Data are median (interquartile range) at pre- and post-intervention as well as absolute and relative changes from pre- to post-intervention. Indicated are p-values for group*time interactions of mixed models adjusted for beta-blocker dose and number of training sessions. HIIT: high intensity interval training group; MICE: moderate intensity continuous exercise group; VO_2 peak: peak oxygen consumption; BP: blood pressure; HR: heart rate; HRR: heart rate recovery.

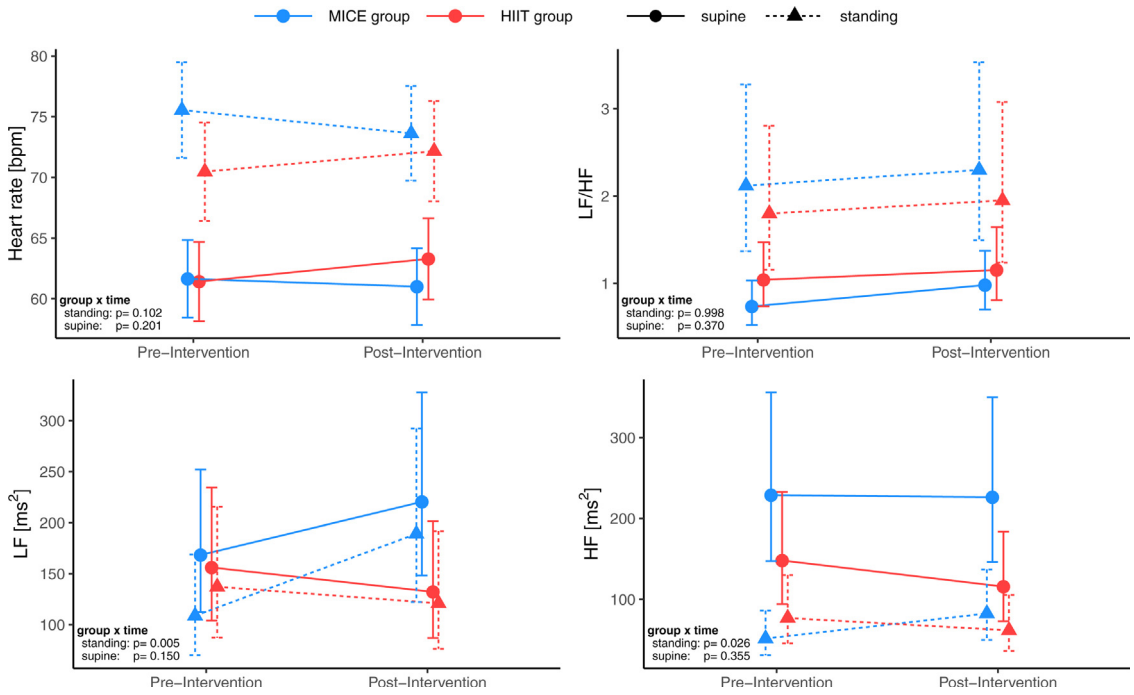

Fig. 1. Interaction plots for heart rate (HR; upper left panel), low-frequency (LF) power (lower left panel), LF/high-frequency (HF) power ratio (upper right panel) and HF power (lower right panel) from supine (circles) and standing (triangles) segments for the moderate-intensity continuous exercise (MICE; blue) and high-intensity interval training (HIIT; red) groups. Mixed models were used for HR, with logarithms of HR variability (HRV) parameters with patients as random effects and group, time, group*time interaction, beta-blocker dose and number of completed training sessions as fixed effects. Model effects for HRV parameters were transformed back to linear scales.

Table 3
Estimates and (99% confidence intervals) of mixed models with patients as a random factor and training modality (with no training as the reference), group (with MICE as the reference) and visit (nights 1–3 as the reference) as fixed factors, adjusted for percentage of maximal beta-blocker dose and total number of training sessions and order of day. Interactions between group and training, and training and visit were non-significant and were omitted from the model.

	ln(HR)	ln(HF)	ln(LF)	ln(LF/HF)
MICE training on preceding day	0.01 (−0.02; 0.04)	0.09 (−0.28; 0.47)	0.12 (−0.23; 0.46)	−0.02 (−0.31; 0.34)
HIIT training on preceding day	0.04 (−0.00; 0.08)	−0.04 (−0.55; 0.46)	0.15 (−0.32; 0.61)	0.18 (−0.26; 0.62)
HIIT group	−0.03 (−0.13; 0.08)	0.29 (−0.47; 1.05)	0.36 (−0.48; 1.21)	0.07 (−0.61; 0.75)
Nights 4–6	−0.03 (−0.06; −0.00)*	0.19 (−0.13; 0.52)	0.15 (−0.15; 0.45)	−0.05 (−0.33; 0.24)

HIIT: high intensity interval training group; MICE: moderate intensity continuous exercise group; HR: heart rate; HF: high frequency; LF: low frequency.
* $P < 0.0125$.

4. Discussion

We found a trend for an acute increase in HR during sleep after a day with HIIT and a trend for a chronic decrease in HR during the supine and standing position in the MICE group but an increase in the HIIT group. HF and LF power for the standing segment increased from pre- to post-intervention in the MICE group but decreased in the HIIT group. HRR remained stable in the MICE group but tended to worsen by 19% in the HIIT group.

The effects of our training interventions on increases in VO_2 peak and peak HR were comparable to findings from several previous studies [15,22–24]. Likewise, the chronic decrease in HR of 3% (corresponding to 2 bpm) during deep sleep we found is comparable to findings from a previous study, [25] although smaller than the decrease of 5 bpm during sleep found after 6 months of HIIT in 20 cardiac patients [10]. HRR did not change significantly over time in our study, which agrees with one study of CAD patients [15] but contrasts with studies finding increases of 1 and 3 bpm with HIIT and MICE after 12 weeks of training in CAD patients [16] and 3 and 5 bpm with 4-week training after coronary artery bypass grafting [26].

4.1. Chronic effects of training modalities on HR and HRV

Our results contrast with a small study finding shorter intervals (2 min) of HIIT more successful than MICE at lowering resting HR and increasing HRV [9] and another small pilot study finding HIIT and MICE similarly beneficial for lowering HR but HIIT more beneficial for increasing HF (in normalized units) [25]. The effect of HIIT and MICE on HRV and HRR did not differ in studies of 14 CAD patients, [15] 31 CAD patients, [16] or 22 CAD patients [27].

We found consistent inverse chronic changes for HR and HRV in the supine and standing positions. Changes in HRV are often paralleled by changes in HR, and in fact, the prognostic information for HRV has been found completely contained in HR [28]. However, the increase in HRV parameter values with exercise training is mostly argued to be due to a change in autonomic tone, but the decrease in resting HR may be due to altered activity of the autonomic nervous system or a change in intrinsic HR due to remodeling of the sinus node [29–33]. Nevertheless, the reduction in resting HR by exercise training has commonly been ascribed to increased vagal activity [10,25,26]. Likewise, the increase in HRR with exercise training found in older MI patients was also ascribed

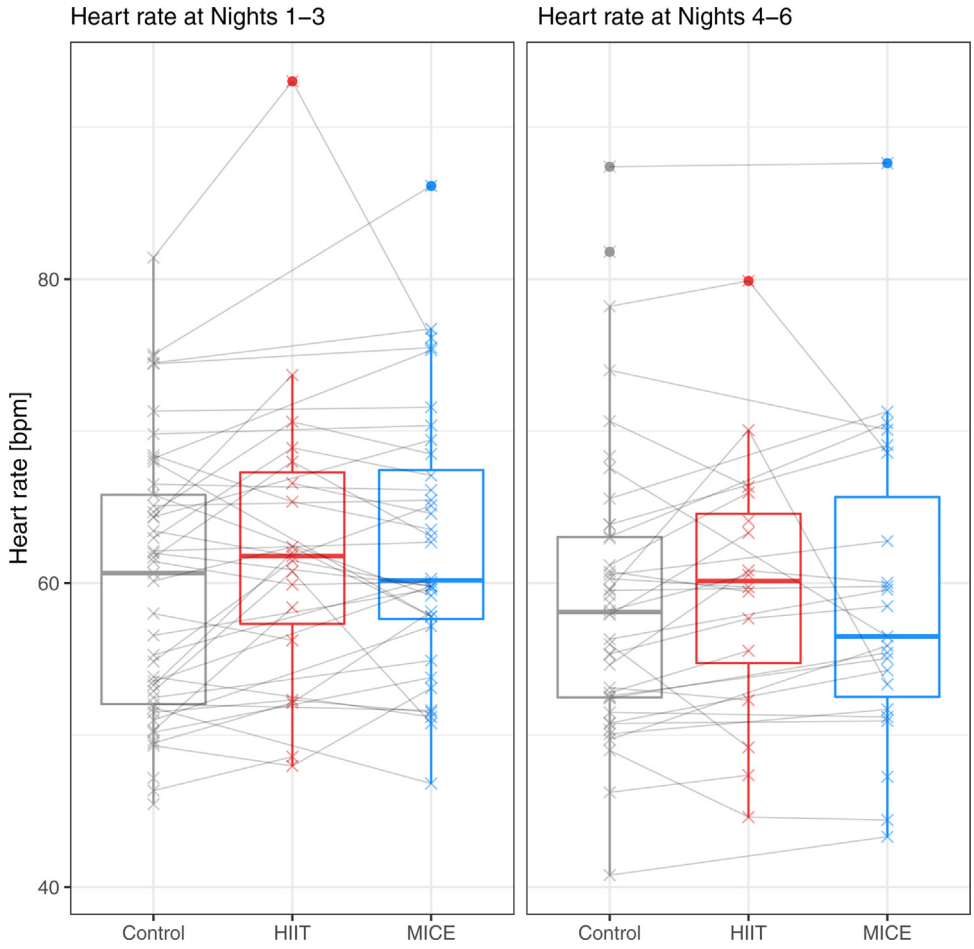

Fig. 2. Boxplots showing the acute effect of training modality on HR during deep sleep and individual unadjusted data points after days with different training modalities for patients from the pooled group during nights 1 to 3 (left) and 4 to 6 (right). Data from nights after no training session are in gray, after HIIT in red, and after MICE in blue. When more than one sleep measurement was available for treatment of any one participant (as was often the case for MICE sessions of participants in the MICE group and also for days without training [control] due to missed sessions), medians were calculated and used.

to increased vagal activity [8]. Sympathetic activity is likely increased in patients after MI and can be lowered by exercise training to values comparable to healthy people, [27,34] which supports a beneficial effect of exercise on the autonomic nervous system. In CAD patients, HIIT has been suggested to be superior to MICE in improving HRV [9] and HRR [35]; however, we found the opposite, with a trend toward better effects with MICE than HIIT for HRV and HRR.

We found increases in HF and LF power in supine and standing position with MICE but decreases with HIIT. The LF spectral band is most likely regulated by the parasympathetic nervous system and reflects modulation of the vasomotor control (for review see [36]). Unfortunately, training effects on orthostatic challenge tests have mostly been assessed in athletes, with controversial results depending on training load and duration, and on time since training. Therefore, we may only suggest that changes in HRV were less beneficial in our HIIT group than MICE group. This is supported by the increase in HR during the orthostatic test and decrease in HRR with HIIT.

4.2. Acute effects on HR and HRV during sleep

We found a trend for an acute effect of HIIT on HR, with HR 2.5 bmp ($P = 0.023$) higher during a night after a day with HIIT as compared with a night after no training. None of the other HRV parameters were significantly changed after training sessions with any training modalities. Acute effects of exercise on HR have been well established, with increased sympathetic activity after acute exercise identified as a main cause [37–39]. Higher HR and associated lower HF and LF powers were documented during sleep after a day with exercise than a day without exercise [40]. Our results indicate that HIIT may have led to greater physical stress and fatigue as compared with MICE. This contrasts with to a study of 18 chronic heart failure patients who had lower HR during the 24 hours after a HIIT session than no training, [41] with only a lesser effect found with MICE. However, the authors used 16 high-intensity intervals of only 30 sec totaling 8 min as compared with 16 min (4×4 min) with our protocol. A study of healthy individuals found no difference between HIIT and MICE in elevation in resting HR and changes in HRV at 24 and 48 hr after exercise [39]. The HIIT consisted of nine 1-min high-intensity intervals interspersed by low-intensity intervals of 4 min, and the population was young and healthy, so short intervals in young people likely do not exert the same physical stress as longer bouts in CAD patients after recent MI. Namely, in athletes completing a 91-km recreational mountain-bike race, the duration of elevated HR during the race was an important predictor of physiological exercise-elevated cardiac troponin level [42] An elevated HR during the night after a long distance running race was also

associated with cardiac damage quantified by high-sensitivity cardiac troponin T level [43].

4.3. Limitations

The main limitation of our study was the lack of statistical power. However, we found a consistent pattern of more beneficial effects with MICE than HIIT on resting HR, HRV and HRR. The number of individuals we included was comparable to or larger than in previous studies. Furthermore, because of no control group performing no exercise training, we cannot exclude that the decrease in resting HR over time may have been caused by effects other than exercise, namely recovery after MI. However, the acute effects of increased HR after HIIT were found by within-subject comparison with control nights. We had to exclude some orthostatic challenge tests and more so, some night measurements because of low-quality data. Furthermore, not all participants completed the night measurements as instructed, so measurements after HIIT were available for analysis for only 21 participants for nights 1 to 3 and 16 for nights 4 to 6. The measurements of HRR were poorly standardized in that participants continued to pedal at low intensity because CAD patients should not rest completely after maximal exercise in order to avoid hypotension and ventricular ectopy [44].

Furthermore, both HRR and HRV are only surrogate parameters for autonomic nervous system activity, so we cannot conclude on changes in autonomic nervous system activity. Of interest, 2 studies measuring autonomic nervous system activity by microneurography of peroneal nerve sympathetic activity found reduced burst frequency at rest and in response to muscle contraction after 6 months of exercise training in CAD patients [27] and patients after acute MI [34]. At the same time, the former study found no difference in resting HR or any measured HRV parameters.

4.4. Strengths

The main strength of this study was the combined assessment of acute and chronic effects of the 2 training modalities on HR and HRV. Additionally, the method used to identify deep sleep phases has been found valid, with deep sleep providing autonomic stability and a regular breathing frequency [45]. Another strength was the 3-week run-in period, which allowed participants to become familiar with the laboratories and cardiac rehabilitation exercise rooms before the intervention. All training sessions were supervised by experienced physiotherapists, and the workload was individually adapted for each participant. HIIT and MICE were prescribed to be isocaloric and resulted in similar increases in peak VO_2 and peak HR, thus allowing for an unbiased comparison of exercise modalities.

4.5. Clinical implications

In MI individuals, resting HR $\geq$ 65 bpm and HRR $<$ 12 bpm in the first minute after MI has been found associated with increased mortality [46]. In our population, only 16 participants had a HR $\geq$ 65 and 3 had HRR $<$ 12 bpm, so our participants did not belong to a high-risk group within the post-STEMI population. In our study, HIIT had no superior effects on acute or chronic HR and HRV parameters as compared with MICE. In contrast, the trend we found for acutely increased HR during sleep after HIIT as well as for chronically increased HR and decreased HRR suggests that HIIT may be physically more demanding and possibly less beneficial in this patient group than MICE. Although the overall risk of acute CV events is low after both HIIT and MICE, cardiac arrests occur approximately 5 times more often after HIIT [47]. The clinical relevance of slightly elevated HR for the healing process of the myocardium after acute MI remains to be established.

5. Conclusion

HIIT was not superior to MICE in improving HR and HRV parameters acutely or chronically. In contrast, HIIT tended to acutely increase HR during deep sleep as compared with nights after no training in patients with recent STEMI. MICE tended to result in more beneficial chronic changes of HR, HRV and HRR as compared with HIIT (with a trend for values for all of these parameters to deteriorate in the HIIT group). The clinical relevance of these changes warrants further investigation.

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Disclosure of interest

The authors declare that they have no competing interest.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.rehab.2020.09.008.

References

[1] Ambrosetti M, Abreu A, Corra U, Davos CH, Hansen D, Frederix I, et al. Secondary prevention through comprehensive cardiovascular rehabilitation: From knowledge to implementation. 2020 update. A position paper from the Secondary Prevention and Rehabilitation Section of the European Association of Preventive Cardiology. European journal of preventive cardiology 2020 [2047487320913379].
[2] Kapoor JR, Heidenreich PA. Heart rate predicts mortality in patients with heart failure and preserved systolic function. Journal of cardiac failure 2010;16:806–11.
[3] 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.
[4] Watanabe J, Thamilarasan M, Blackstone EH, Thomas JD, Lauer MS. Heart rate recovery immediately after treadmill exercise and left ventricular systolic dysfunction as predictors of mortality: the case of stress echocardiography. Circulation 2001;104:1911–6.
[5] 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.
[6] 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.
[7] Malik M, Bigger JT, Camm AJ, Kleiger RE, Malliani A, Moss AJ, et al. Heart Rate Variability. Standards of measurement, physiological interpretation and clinical use. Task Force of the European Society of Cardiology the North American Society of Pacing Electrophysiology. Circulation 1996;93:1043–65.
[8] Giallauria F, Lucci R, Pietrosante M, Gargiulo G, De Lorenzo A, D'Agostino M, et al. Exercise-based cardiac rehabilitation improves heart rate recovery in elderly patients after acute myocardial infarction. The journals of gerontology Series A Biological sciences and medical sciences 2006;61:713–7.
[9] Ghardashi-Afousi A, Holisaz MT, Shirvani H, Pishgoo B. The effects of low-volume high-intensity interval versus moderate intensity continuous training on heart rate variability, and hemodynamic and echocardiography indices in men after coronary artery bypass grafting: A randomized clinical trial study. ARYA atherosclerosis 2018;14:260–71.
[10] 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.
[11] Routledge FS, Campbell TS, McFetridge-Durdle JA, Bacon SL. Improvements in heart rate variability with exercise therapy. The Canadian journal of cardiology 2010;26:303–12.

[12] Menown IB, Davies S, Gupta S, Kalra PR, Lang CC, Morley C, et al. Resting heart rate and outcomes in patients with cardiovascular disease: where do we currently stand? Cardiovascular therapeutics 2013;31:215–23.
[13] Ribeiro PAB, Boidin M, Juneau M, Nigam A, Gayda M. High-intensity interval training in patients with coronary heart disease: Prescription models and perspectives. Annals of physical and rehabilitation medicine 2017;60:50–7.
[14] Pattyn N, Beulque R, Cornelissen V. Aerobic Interval vs Continuous Training in Patients with Coronary Artery Disease or Heart Failure: An Updated Systematic Review and Meta-Analysis with a Focus on Secondary Outcomes. Sports Med 2018;48:1189–205.
[15] 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. Applied physiology nutrition and metabolismPhysiologie appliquee nutrition et metabolisme 2013;38:644–50.
[16] Pattyn N, Beckers PJ, Cornelissen VA, Coeckelberghs E, De Maeyer C, Frederix G, et al. The effect of aerobic interval training and continuous training on exercise capacity and its determinants. Acta cardiologica 2017;72:328–40.
[17] Schulz KF, Altman DG, Moher D, Group C.. CONSORT 2010 Statement: updated guidelines for reporting parallel group randomised trials. BMJ [Internet] 2010 [cited 2020 4.8.2020]. Available from: http://www.consort-statement.org/checklists/..
[18] Rognmo O, Hetland E, Helgerud J, Hoff J, Slordahl SA. High intensity aerobic interval exercise is superior to moderate intensity exercise for increasing aerobic capacity in patients with coronary artery disease. Eur J Cardiovasc Prev Rehabil 2004;11:216–22.
[19] Wewege MA, Ahn D, Yu J, Liou K, Keech A. High-Intensity Interval Training for Patients With Cardiovascular Disease-Is It Safe?. A Systematic Review. J Am Heart Assoc 2018;7:e009305.
[20] Pattyn N, Cornelissen VA, Buys R, Lagae AS, Leliaert J, Vanhees L. Are aerobic interval training and continuous training isocaloric in coronary artery disease patients? European journal of preventive cardiology 2016;23:1486–95.
[21] Wasserman K, Hansen J, Sue D. Principles of exercise testing and interpretation, 4th ed, Philadelphia: Lippincott Williams and Wilkins; 2004.
[22] Kong HH, Bang HJ, Ko JU, Lee GJ. The Differences in Cardiac Rehabilitation Outcomes by Age in Myocardial Infarction: A Preliminary Study. Annals of rehabilitation medicine 2017;41:1047–54.
[23] Lee BJ, Go JY, Kim AR, Chun SM, Park M, Yang DH, et al. Quality of Life and Physical Ability Changes After Hospital-Based Cardiac Rehabilitation in Patients With Myocardial Infarction. Annals of rehabilitation medicine 2017;41:121–8.
[24] Choe Y, Han JY, Choi IS, Park HK. Changes in Oxygen Consumption and Heart Rate After Acute Myocardial Infarction During 6-Month Follow-up. PM R 2018;10:587–93.
[25] Besnier F, Labrunee M, Richard L, Faggianelli F, Kerros H, Soukarie L, et al. Short-term effects of a 3-week interval training program on heart rate variability in chronic heart failure. A randomised controlled trial. Annals of physical and rehabilitation medicine 2019;62:321–8.
[26] Moholdt TT, Amundsen BH, Rustad LA, Wahba A, Lovo KT, Gullikstad LR, et al. Aerobic interval training versus continuous moderate exercise after coronary artery bypass surgery: a randomized study of cardiovascular effects and quality of life. Am Heart J 2009;158:1031–7.
[27] Badrov MB, Wood KN, Lalande S, Sawicki CP, Borrell LJ, Barron CC, et al. Effects of 6 Months of Exercise-Based Cardiac Rehabilitation on Autonomic Function and Neuro-Cardiovascular Stress Reactivity in Coronary Artery Disease Patients. Journal of the American Heart Association 2019;8:e012257.
[28] Abildstrom SZ, Jensen BT, Agner E, Torp-Pedersen C, Nyvad O, Wachtell K, et al. Heart rate versus heart rate variability in risk prediction after myocardial infarction. Journal of cardiovascular electrophysiology 2003;14:168–73.
[29] Spinelli L, Petretta M, Marciano F, Testa G, Rao MA, Volpe M, et al. Cardiac autonomic responses to volume overload in normal subjects and in patients with dilated cardiomyopathy. The American journal of physiology 1999;277:H1361–8.
[30] Buchheit M, Laursen PB, Al Haddad H, Ahmaidi S. Exercise-induced plasma volume expansion and post-exercise parasympathetic reactivation. European journal of applied physiology 2009;105:471–81.
[31] D'Souza A, Bucchi A, Johnsen AB, Logantha SJ, Monfredi O, Yanni J, et al. Exercise training reduces resting heart rate via downregulation of the funny channel HCN4. Nat Commun 2014;5:3775.
[32] Bahrainy S, Levy WC, Busey JM, Caldwell JH, Stratton JR. Exercise training bradycardia is largely explained by reduced intrinsic heart rate. Int J Cardiol 2016;222:213–6.
[33] Boyett MR, D'Souza A, Zhang H, Morris GM, Dobrzynski H, Monfredi O, et al. is the resting bradycardia in athletes the result of remodeling of the sinoatrial node rather than high vagal tone? J Appl Physiol (1985) 2013;114:1351–5.
[34] Martinez DG, Nicolau JC, Lage RL, Toschi-Dias E, de Matos LD, Alves MJ, et al. Effects of long-term exercise training on autonomic control in myocardial infarction patients. Hypertension 2011;58:1049–56.
[35] Villelabeitia-Jaureguizar K, Vicente-Campos D, Senen AB, Jimenez VH, Garrido-Lestache MEB, Chicharro JL. Effects of high-intensity interval versus continuous exercise training on post-exercise heart rate recovery in coronary heart-disease patients. Int J Cardiol 2017;244:17–23.
[36] Reyes del Paso GA, Langewitz W, Mulder LJ, van Roon A, Duschek S. The utility of low frequency heart rate variability as an index of sympathetic cardiac tone: a review with emphasis on a reanalysis of previous studies. Psychophysiology 2013;50:477–87.
[37] Roussel B, Buguet A. Changes in human heart rate during sleep following daily physical exercise. European journal of applied physiology and occupational physiology 1982;49:409–16.
[38] Myllymaki T, Rusko H, Syvaoja H, Juuti T, Kinnunen ML, Kyrolainen H. Effects of exercise intensity and duration on nocturnal heart rate variability and sleep quality. Eur J Appl Physiol 2012;112:801–9.
[39] Mourot L, Bouhaddi M, Tordi N, Rouillon JD, Regnard J. Short- and long-term effects of a single bout of exercise on heart rate variability: comparison between constant and interval training exercises. Eur J Appl Physiol 2004;92:508–17.
[40] Yoshida Y, Yuda E, Yokoyama K, Hayano J. Evaluation of nocturnal heart rate variability for strenuous exercise day using wearable photoelectric pulse wave sensor. Journal of exercise rehabilitation 2018;14:633–7.
[41] Guiraud T, Labrunee M, Gaucher-Cazalis K, Despas F, Meyer P, Bosquet L, et al. High-intensity interval exercise improves vagal tone and decreases arrhythmias in chronic heart failure. Medicine and science in sports and exercise 2013;45:1861–7.
[42] Bjørkavoll-Bergseth M, Kleiven Ø, Auestad B, Eftestøl T, Oskal K, Nygård M, et al. Duration of Elevated Heart Rate Is an Important Predictor of Exercise-Induced Troponin Elevation. Journal of the American Heart Association 2020;9:e014408.
[43] Aagaard P, Sahlen A, Bergfeldt L, Braunschweig F. Heart rate and its variability in response to running-associations with troponin. Medicine and science in sports and exercise 2014;46:1624–30.
[44] Fletcher GF, Ades PA, Kligfield P, Arena R, Balady GJ, Bittner VA, et al. Exercise standards for testing and training: a scientific statement from the American Heart Association. Circulation 2013;128:873–934.
[45] Herzig D, Eser P, Omlin X, Riener R, Wilhelm M, Achermann P. Reproducibility of Heart Rate Variability Is Parameter and Sleep Stage Dependent. Front Physiol 2017;8:1100.
[46] Hai JJ, Siu CW, Ho HH, Li SW, Lee S, Tse HF. Relationship between changes in heart rate recovery after cardiac rehabilitation on cardiovascular mortality in patients with myocardial infarction. Heart rhythm 2010;7:929–36.
[47] Rognmo O, Moholdt T, Bakken H, Hole T, Molstad P, Myhr NE, et al. Cardiovascular risk of high- versus moderate-intensity aerobic exercise in coronary heart disease patients. Circulation 2012;126:1436–40.