ORIGINAL ARTICLE

Effect of different doses of supervised aerobic exercise on heart rate recovery in inactive adults who are overweight or obese: results from E-MECHANIC

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Abstract

Purpose Heart rate recovery (HRR) after exercise is an independent risk factor for cardiovascular disease and mortality. Regular aerobic exercise can improve HRR, yet little is known regarding the dose necessary to promote increases. The aim was to assess the impact of different doses of vigorous-intensity aerobic exercise on HRR in individuals with overweight/obesity.

Methods Data from 137 sedentary adults with overweight/obesity from E-MECHANIC were analyzed. Participants were randomized to either a moderate-dose exercise group (8 kcal/kg body weight/week; KKW), a high-dose exercise group (20 KKW), or a non-exercise control group. HRR was defined as the difference between peak heart rate (HR) during a graded exercise test and the HR after exactly 1 min of active recovery at 1.5 mph and level grade.

Results Change in HRR did not differ significantly by exercise group; therefore, the data from both exercise groups were combined. The combined exercise group showed an improvement in HRR of 2.7 bpm (95% CI 0.1, 5.4; $p = 0.04$) compared to the control group. Those participants who lost more weight during the intervention (non-compensators) increased HRR by 6.2 bpm (95% CI 2.8, 9.5; $p < 0.01$) compared to those who lost less weight (compensators). Multiple linear regression models indicated that improvements in HRR are independently associated with increases in VO_{2peak} ($\beta = 0.4$; 95% CI 0.1, 0.7; $p = 0.04$) but also influenced by concomitant weight loss ($\beta = 0.6$; 95% CI 0.2, 1.1; $p = 0.01$).

Conclusion Exercise-induced improvements in 1-min HRR are likely due to increases in cardiorespiratory fitness as well as concomitant weight loss.

Keywords Heart rate recovery · Exercise · Aerobic capacity · Weight loss · Autonomic function

Abbreviations

ANCOVA	Analysis of covariance
BMI	Body mass index
bpm	Beats per minute
CI	Confidence interval
E-MECHANIC	The Examination of Mechanisms of Exercise-Induced Weight Compensation
HR	Heart rate
HRR	Heart rate recovery
KKW	Kilocalories per kilogram of body weight per week
METS	Metabolic equivalents
mph	Miles per hour
RPE	Ratings of perceived exertion
SD	Standard deviation
VO_{2peak}	Peak oxygen uptake

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Introduction

Heart rate recovery (HRR) refers to the rate at which heart rate (HR) decreases after exercise, reflecting autonomic nervous system function (Cole et al. 1999). Early HRR is thought to be primarily caused by vagal reactivation,

whereas later recovery (≥ 2 min) is likely attributed to sympathetic withdrawal (Borresen and Lambert 2008). Due to its simple and noninvasive assessment, HRR is commonly used to monitor exercise-induced adaptions in autonomic function as well as changes in training status (Bellenger et al. 2016). Beyond the use for training monitoring, it has been shown that an attenuated HRR is associated with an increased risk of cardiovascular events and all-cause mortality, making HRR an increasingly recognized prognostic health marker in clinical practice (Savonen et al. 2011; Carnethon et al. 2012; Johnson and Goldberger 2012; Qiu et al. 2017). A recent meta-analysis of 14 prospective cohort studies ($N = 75,867$) further suggested that the relationship between attenuated HRR and the risk of cardiovascular events and all-cause mortality is dose-dependent, estimating hazard ratios of 1.13 (cardiovascular events) and 1.09 (all-cause mortality) for every 10 beats per minute (bpm) reduction in HRR, independent of traditional cardiovascular risk factors (Qiu et al. 2017). In addition, impaired HRR has been shown to be strongly associated with higher body mass index (BMI) and greater waist circumference, demonstrating a generally prevalent autonomic dysfunction in obese individuals (Dimkpa and Oji 2010; Barbosa Lins et al. 2015).

Aerobic exercise training has been shown to result in beneficial increases in HRR in a wide range of target groups, such as cardiac patients (MacMillan et al. 2006; Medeiros et al. 2018), cancer survivors (Giallauria et al. 2015; Niederer et al. 2015), patients with chronic obstructive pulmonary disease (Gimeno-Santos et al. 2014) or insulin resistance (Álvarez et al. 2017) as well as obese individuals (Kim et al. 2009). It has further been shown that patients with abnormal HRR (≤ 12 bpm reduction during the first minute post-exercise) at baseline, who normalized their HRR in response to a 12-week supervised aerobic exercise program, had a mortality risk after the intervention that was similar to that of individuals with normal HRR at baseline (Jolly et al. 2011). Despite the benefits of aerobic exercise, considerable ambiguity remains regarding the optimal training load to improve HRR. While some studies have shown significant increases in HRR only for vigorous aerobic exercise but not for moderate exercise (Matsuo et al. 2014; Stöggl and Björklund 2017; Villelabeitia-Jaureguizar et al. 2017), other studies have found significant increases after moderate-intensity exercise training for different target groups (Kim et al. 2009; Moholdt et al. 2009). It has yet to be elucidated, however, whether different doses of vigorous-intensity aerobic exercise influence HRR differently.

Therefore, we assessed the impact of different weekly doses of aerobic exercise training on HRR in an overweight/obese target group. Since increased cardiorespiratory fitness is related to improved HRR (Watson et al. 2017); and given higher exercise doses are associated with greater cardiorespiratory fitness in a dose-dependent manner (Church et al. 2007; Martin et al. 2019), we hypothesized the effect of aerobic exercise on HRR would be dose-dependent.

Methods

Participants and design

The Examination of Mechanisms of Exercise-induced Weight Compensation (E-MECHANIC) study (ClinicalTrials.gov ID: NCT01264406) was approved by the Institutional Review Board and conducted between November 2010 and December 2015 at Pennington Biomedical Research Center (Baton Rouge, LA, USA). The 24-week randomized controlled trial recruited 198 healthy, sedentary [≤ 20 min of exercise on ≤ 3 days/week (self-report) and < 8000 steps/day (Tudor-Locke et al. 2011), based on 1 week of accelerometer data (SenseWear Armband, Body-Media, Pittsburgh, PA, USA)] men and women with overweight/obesity (BMI ≥ 25 to ≤ 45 kg/m^2) that were randomly allocated in a 1:1:1 ratio to either a moderate-dose exercise group (8 kcal/kg body weight/week; 8 KKW), a high-dose exercise group (20 KKW), or a non-exercise control group (Myers et al. 2014). The selected exercise doses reflect current recommendations for general health (8 KKW) and for weight loss (20 KKW) (West Suitor et al. 2007). Exclusion criteria were current participation in a weight loss program, pregnancy (current or within the past 6 months), diabetes or cardiovascular disease, and arrhythmia. Further, participants taking β-blockers were excluded, as β-blockers are known to lower heart rate (American College of Sports Medicine 2014). No other medication or supplements with a possible impact on heart rate (American College of Sports Medicine 2014) was reported. All participants provided written informed consent prior to inclusion in the study. The primary aim of the E-MECHANIC study was to identify mechanisms of exercise-induced weight compensation (i.e., less than expected weight loss) by examining the effect of the two different doses of exercise training on energy intake over the 24-week intervention period. A significantly higher weight compensation in the high-dose exercise group compared to the moderate-dose exercise group was found that resulted from increased energy intake and concomitant increases in appetite (Martin et al. 2019).

The assessment team and investigators were blinded with respect to group allocation. Exercise intensity of the supervised treadmill exercise sessions was self-selected between 65–85% of peak oxygen uptake (VO_{2peak}), i.e., vigorous (Garber et al. 2011), and sessions varied in length to meet participant's group-dependent energy expenditure goals. The detailed study protocol is described elsewhere (Myers et al. 2014).

Exercise test and heart rate recovery

At baseline and follow-up, participants underwent a standardized graded exercise test on a treadmill (Trackmaster 425, Newton, KS). Participants were instructed to refrain from exercise and other vigorous physical activity in the 24 h leading up to the exercise test. On the day of the exercise test, participants arrived approximately 3 h prior to test at the laboratory to undergo several additional measurements (Myers et al. 2014) preceding the exercise test. During this time, participants did not eat and only drank water. Exercise testing began at 2.4 miles per hour (mph) and a 0% grade, equal to 2.8 metabolic equivalents (METS). Every 2 min, intensity increased by altering speed (0.2 mph increments), grade (increments of 2% points), or both to achieve a ~ 1MET change at each stage. The test continued until individual maximal exertion. Respiratory gas parameters were analyzed breath-by-breath (Parvomedics True Max 2400 Metabolic Measurement Cart, Salt Lake City, UT) and ratings of perceived exertion (RPE) according to the 6–20 Borg Scale (Borg 1982) were obtained. Throughout the entire duration of the test, including the immediate recovery period, cardiac function was monitored with a 12-lead electrocardiogram.

After peak exercise, participants underwent a 2-min cool-down period at 1.5 mph and a 0% grade, similar to the procedure used in previous studies assessing HRR (Nishime et al. 2000; Jolly et al. 2011). HRR, measured as bpm, was defined as the difference between the highest observed HR (peak HR) during the graded exercise test and the heart rate after exactly 1 min of active recovery (1-min HRR) (Cole et al. 1999). Participants were encouraged to reach maximum exertion during the exercise test and were included in the analyses if they reached ≥ 90% of their age-predicted maximum HR [208 − 0.7 × age (years) (Tanaka et al. 2001)] as well as at least one of the following two criteria in both exercise tests: (1) respiratory exchange ratio ≥ 1.1 and/or (2) RPE (Borg 1982) ≥ 18.

As the primary analyses reported for E-MECHANIC (Martin et al. 2019) followed a per-protocol approach, including all participants that (1) provided follow-up data and (2) achieved ≥ 75% adherence to the exercise condition prescribed to them, as randomized, some participants were included in the analysis of VO_{2peak} who did in fact not reach maximal exertion during the graded exercise test. Therefore, the analyses reported in this paper additionally serve as a sensitivity analysis, reducing a potential type I error (i.e., mistakenly assuming maximal exertion) (Knaier et al. 2018) to gain a more precise understanding of the dose-dependent effects of supervised aerobic vigorous-intensity exercise on VO_{2peak}.

Statistical analysis

A power analysis based on the primary outcome was conducted for E-MECHANIC (Myers et al. 2014). As 1-min HRR is a secondary outcome, the corresponding analyses presented herein are considered exploratory. Normality was checked using normal quantile–quantile plots of the residuals and variance homogeneity was assessed using Tukey–Anscombe Plots. We used analyses of covariance (ANCOVA) to compare 1-min HRR (bpm), resting HR (bpm), and relative VO_{2peak} (mL/kg/min) and absolute VO_{2peak} (L/min) at follow-up between the three groups, adjusted for baseline values (Vickers and Altman 2001). Weight change (kg) during the intervention (follow-up weight minus baseline weight) was added as an additional covariate for the HRR and resting HR comparisons; the E-MECHANIC intervention elicited significant group differences in weight change (Martin et al. 2019) and it has previously been shown that weight loss can improve HRR even in the absence of changes in physical activity levels (Brinkworth et al. 2006). Results of analyses that included age, sex, and ethnicity did not differ meaningfully; therefore, the models without these covariates are reported. Pearson product–moment correlation analysis was used to assess the association between changes in resting HR and changes in 1-min HRR. In additional analyses, we used simple and multiple linear regression models to estimate the effect of the change in cardiorespiratory fitness, measured as VO_{2peak} (mL/kg/min), on the change in 1-min HRR (bpm). Covariates in the multiple linear regressions were 1-min HRR at baseline and weight change (kg) during the intervention. Further, we used multiple linear regression models to estimate the effect of weight change (kg) on 1-min HRR (bpm) with 1-min HRR at baseline and change in VO_{2peak} (L/min) as covariates. Post-hoc comparisons for ANCOVAs were Bonferroni-adjusted. For each analysis, we report the estimated mean difference in outcome with 95% CI between the three groups.

Due to the prevalence of compensation in E-MECHANIC and following the trial's primary analyses (Martin et al. 2019), we classified participants in the exercise groups as compensators and non-compensators based on a median split with compensators > − 58.5%, and non-compensators ≤ − 58.5% weight compensation. Percent compensation was calculated using data from the two exercise groups according to the following formula:

Percent compensation
$$= (actual − predicted\ weight\ loss)/predicted\ weight\ loss.$$

Table 1 Baseline characteristics of the 137 included participants

	Control (*n* = 45)	8 KKW (*n* = 49)	20 KKW (*n* = 43)
Female, *n* (%)	31 (69%)	36 (74%)	30 (70%)
	Mean (SD)	Mean (SD)	Mean (SD)
Age (years)	50.3 (10.7)	48.2 (11.1)	49.0 (12.3)
Height (cm)	167.3 (7.6)	166.7 (8.6)	167.2 (7.3)
Weight (kg)	90.5 (13.8)	86.9 (15.2)	87.0 (14.5)
BMI (kg/m^2)	32.3 (4.5)	31.2 (4.6)	31.1 (4.6)
Fat mass (kg)	38.8 (9.9)	36.2 (9.5)	36.3 (10.2)
Fat-free mass (kg)	48.6 (9.8)	47.8 (8.9)	48.0 (10.1)
Systolic blood pressure (mm Hg)	121.6 (10.6)	118.7 (10.1)	121.6 (9.8)
Diastolic blood pressure (mm Hg)	78.8 (8.1)	77.1 (6.1)	77.7 (8.1)
Resting HR (bpm)	65.8 (6.7)	67.8 (7.6)	67.6 (8.0)
Maximum HR (bpm)	176 (13)	178 (12)	179 (15)
HRR at 1 min (bpm)	21.7 (5.4)	24.1 (7.3)	24.6 (7.6)
VO_{2peak} (mL/kg/min)	23.1 (5.3)	24.4 (5.4)	23.9 (5.4)
VO_{2peak} (L/min)	2.1 (0.6)	2.1 (0.5)	2.0 (0.5)

Data are mean (standard deviation) if not stated otherwise. ANOVA (continuous variables) and a Chi-square test (categorical variable) were used to test for baseline differences between the three groups. The control, 8 KKW, and 20 KKW groups did not differ significantly in any of the baseline measures presented in the table

KKW kilocalories per kilogram of body weight per week, *SD* standard deviation, *BMI* body mass index, *HR* heart rate, *bpm* beats per minute, *HRR* heart rate recovery, *VO_{2peak}* peak oxygen uptake

We used IBM SPSS Statistics for Windows version 25 (IBM Corp., Armonk, NY, USA) for the statistical analyses with the significance level set to 0.05 (two-sided).

Results

Participant characteristics

Thirty-four of the originally analyzed 171 participants did not reach the defined exhaustion criteria during both exercise tests and were subsequently excluded from the analyses reported in this paper. Baseline characteristics of all 137 included participants are shown in Table 1.

Average self-chosen exercise intensity during the intervention was 76.2 [standard deviation (SD) 0.5] % of HR reserve in the 20 KKW group and 76.3 (SD 0.5) % of HR reserve in the 8 KKW group with a non-significant difference between the two groups (*p* = 0.95). These average exercise intensities correspond to 69.1 (SD 0.7) % of VO_{2peak} in the 20 KKW group and to 69.2 (SD 0.8) % of VO_{2peak} in the 8 KKW group. Maximum HR did not change significantly in either of the three groups between baseline and 24-week follow-up (all *p* values ≥ 0.26).

Changes in heart rate recovery and resting heart rate

One-min HRR for the entire sample was normal at baseline with a mean of 23.5 (SD 6.9) bpm; however, based on previously published studies that used a similar cool-down procedure after maximal exertion during a graded exercise test (Cole et al. 1999; Nishime et al. 2000), 17 participants (20 KKW: *n* = 7; 8KKW: *n* = 4; control: *n* = 6) had an abnormal 1-min HRR of ≤ 12 bpm at baseline. In the 20 KKW group, 1-min HRR showed a tendency towards an increase of 2.7 bpm (95% CI − 0.1, 5.5; *p* = 0.06) during the 24-week intervention (Table 2). In the 8 KKW and in the control group, 1-min HRR did not change significantly (all *p* values ≥ 0.33). Figure 1 illustrates the individual changes in HRR across the control and two treatment groups. There was no significant difference in HRR change between the three groups (all *p* values ≥ 0.35). Weight change was a significant covariate (partial η^2 = 0.043; *p* = 0.02) for 1-min HRR at follow-up. In the 20 KKW group, body weight changed by − 1.9 kg (95% CI − 2.7, − 1.1; *p* < 0.01), with a significant difference of − 1.7 kg (95% CI − 3.2, − 0.3; *p* = 0.02) compared to the control group and of − 1.5 kg (95% CI − 2.9, − 0.1; *p* = 0.04) compared to the 8 KKW group. When pooling both exercise groups together, 1-min HRR increased by 2.0 bpm (95% CI 0.1, 3.9; *p* = 0.045) in the exercise condition, with an adjusted difference between the exercise condition and the non-exercise control condition of

Table 2 Analysis of covariance to determine the effects of two different doses of 24-week supervised aerobic exercise on heart rate recovery, resting heart rate, and VO_{2peak} compared to a non-exercise control condition

	Control (n=45)		8 KKW (n=49)		20 KKW (n=43)		8 KKW vs control	20 KKW vs control	20 KKW vs 8 KKW
	Pre	Post	Pre	Post	Pre	Post	Adjusted difference[a] (95% CI)	Adjusted difference[a] (95% CI)	Adjusted difference[a] (95% CI)
HRR at 1 min (bpm)	21.7 (5.4)	22.2 (6.3)	24.1 (7.3)	25.4 (9.6)	24.6 (7.6)	27.3 (8.9)	1.8 (− 2.0, 5.6)[b]	2.6 (− 1.4, 6.6)[b]	0.8 (− 3.1, 4.7)b
Resting HR (bpm)	65.8 (6.7)	64.8 (7.6)	67.8 (7.6)	64.8 (7.4)	67.6 (8.0)	64.7 (6.5)	− 1.1 (− 4.1, 1.9)[b]	− 0.5 (− 3.8, 2.8)b	0.6 (− 2.6, 3.8)b
VO_{2peak} (mL/kg/min)	23.1 (5.3)	22.0 (6.2)	24.4 (5.4)	25.3 (7.1)	23.9 (5.4)	27.2 (6.5)	1.9 (0.2, 3.6)†	4.4 (2.7, 6.1)*	2.5 (0.8, 4.2)*
VO_{2peak} (L/min)	2.1 (0.6)	2.0 (0.6)	2.1 (0.5)	2.2 (0.6)	2.0 (0.5)	2.3 (0.6)	0.2 (0.1, 0.3)*	0.4 (0.3, 0.5)*	0.2 (0.1, 0.3)*

Data are mean (standard deviation) and adjusted differences with 95% confidence intervals

KKW kilocalories per kilogram of body weight per week, *CI* confidence interval, *HRR* heart rate recovery, *bpm* beats per minute, *HR* heart rate, VO_{2peak} peak oxygen uptake

*$p < 0.01$

†$p < 0.05$

[a]Analysis of covariance comparing post-intervention values between groups adjusted for the corresponding values at baseline

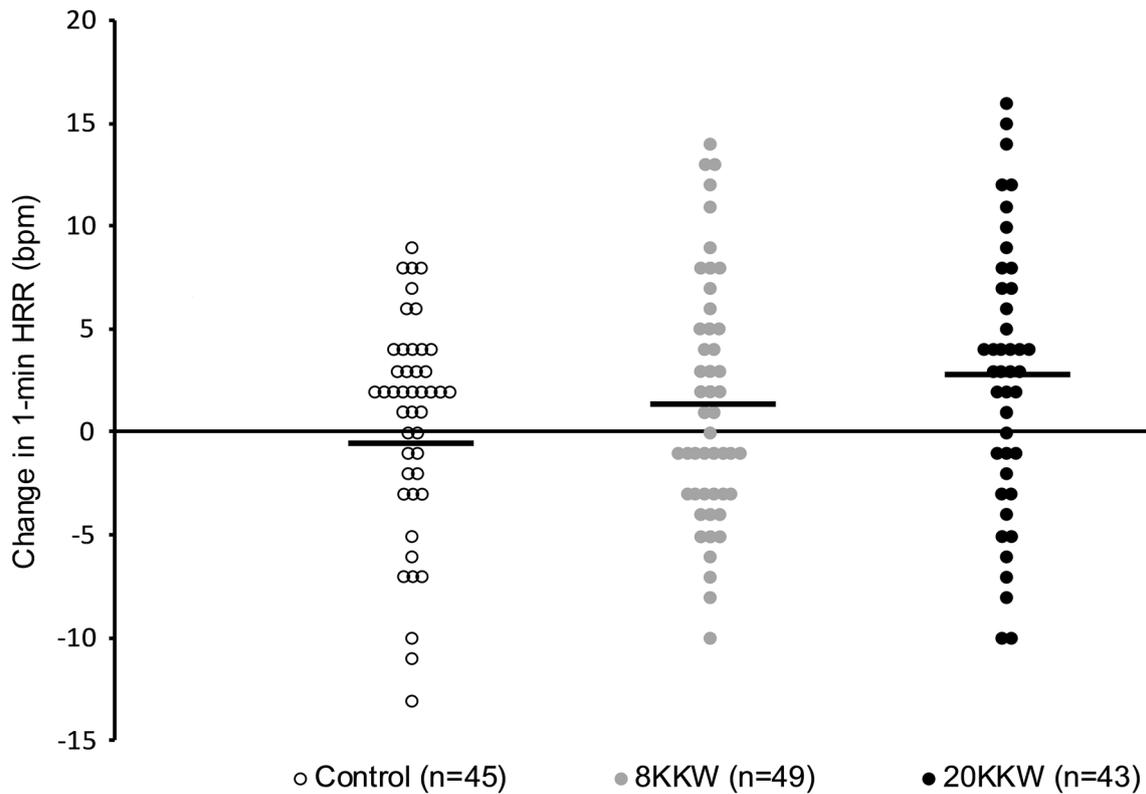[b]Weight change as an additional covariate

Fig. 1 Individual changes in heart rate recovery across the control and two treatment groups. Black lines indicate the mean change

Table 3 Analysis of covariance to determine the changes in heart rate recovery, resting heart rate, and VO_{2peak} for compensators and non-compensators

	Non-compensators ($n = 45$)		Compensators ($n = 47$)		Adjusted difference[a] (95% CI)
	Pre	Post	Pre	Post	
HRR at 1 min (bpm)	25.0 (6.3)	29.8 (9.3)	23.6 (8.3)	23.0 (8.0)	6.2 (2.8, 9.5)*
Resting HR (bpm)	68.8 (8.6)	65.0 (7.0)	66.5 (6.7)	64.4 (6.9)	− 0.6 (− 3.1, 2.0)
VO_{2peak} (mL/kg/min)	24.6 (4.9)	27.7 (6.1)	23.8 (5.8)	24.8 (7.3)	2.0 (0.4, 3.5)*
VO_{2peak} (L/min)	2.1 (0.5)	2.3 (0.6)	2.1 (0.6)	2.2 (0.6)	0.2 (0.1, 0.3)†

Data are mean (standard deviation) and adjusted differences with 95% confidence intervals

CI confidence interval, *HRR* heart rate recovery, *bpm* beats per minute, *HR* heart rate, *VO_{2peak}* peak oxygen uptake

*$p < 0.01$

†$p < 0.05$

[a]Analysis of covariance comparing post-intervention values between groups adjusted for the corresponding baseline values

2.7 bpm (95% CI 0.1, 5.4; $p = 0.04$). Non-compensators (i.e., participants with $\leq − 58.5\%$ weight compensation) showed significant improvements in 1-min HRR of 4.8 bpm (95% CI 1.6, 7.8; $p < 0.01$) (Table 3), whereas compensators (i.e., participants with $> − 58.5\%$ weight compensation) showed non-significant changes of − 0.6 bpm (95% CI − 2.9, 1.6; $p = 0.56$), with a significant adjusted difference between the median split-defined groups of 6.2 bpm (95% CI 2.8, 9.5; $p < 0.01$) in favor of the non-compensators.

Resting HR changed significantly by − 2.9 bpm (95% CI − 5.0, − 0.7; $p = 0.01$) in the 20 KKW group and by − 3.0 bpm (95% CI − 5.2, − 0.9; $p = 0.01$) in the 8 KWW group with a non-significant adjusted difference of 0.6 bpm (95% CI − 2.6, 3.8; $p > 0.99$) between the two groups (Table 2). In the non-exercise control condition, resting HR did not change significantly over the course of the intervention. Pearson product–moment correlation analysis indicated that the changes in 1-min HRR were not significantly correlated with the changes in resting HR ($r = 0.02$, $p = 0.84$).

Changes in cardiorespiratory fitness

VO_{2peak} increased significantly by 3.3 mL/kg/min (95% CI 2.4, 4.2; $p < 0.01$) in the 20 KKW group, with a significant difference (adjusted for baseline values) of 4.4 mL/kg/min (95% CI 2.7, 6.1; $p < 0.01$) compared to the control group and of 2.5 mL/kg/min (95% CI 0.8, 4.2; $p < 0.01$) compared to the 8 KKW group (Table 2). The 8 KKW group did not show any significant changes in relative VO_{2peak} and the control group showed significant decreases of 1.1 mL/kg/min (95% CI 0.3, 2.0; $p < 0.01$), with an adjusted difference between the two groups of 1.9 mL/kg/min (95% CI 0.2, 3.6; $p = 0.02$). Similar to the changes in 1-min HRR, we found a significant adjusted difference in VO_{2peak} between non-compensators and compensators of 2.0 mL/kg/min (95% CI 0.4, 3.5, $p < 0.01$). Non-compensators showed significant improvements of 3.1 mL/kg/min (95% CI 2.1, 3.9; $p < 0.01$),

whereas compensators did not change VO_{2peak} significantly during the 24-week intervention.

The unadjusted linear regression model showed that every 1 mL/kg/min increase in VO_{2peak} is associated with an estimated improvement in HRR of 0.4 bpm (95% CI 0.1, 0.8; $p = 0.04$) during the first minute after maximal physical exertion. If adjusted for baseline 1-min HRR, the estimated improvement was 0.5 bpm (95% CI 0.1, 0.8; $p < 0.01$) and if additionally adjusted for weight change, every 1 mL/kg/min increase in VO_{2peak} was associated with an improvement in 1-min HRR of 0.4 bpm (95% CI 0.1, 0.7; $p = 0.04$). For absolute VO_{2peak}, the fully adjusted regression model showed an estimated improvement in 1-min HRR of 5.4 bpm (95% CI 0.3, 11.1; $p = 0.04$) for every 1 L/min increase in VO_{2peak}. Further, when adjusted for baseline 1-min HRR and change in VO_{2peak} (L/min), the multiple linear regression model showed that for every 1 kg weight loss, 1-min HRR improves by 0.6 bpm (95% CI 0.2, 1.1; $p = 0.01$).

Discussion

The present analysis from the E-MECHANIC randomized controlled trial aimed to assess the effects of different doses of aerobic vigorous-intensity exercise on 1-min HRR and VO_{2peak} during a 24-week supervised exercise intervention. While the results suggest that vigorous-intensity exercise (8 KKW and 20 KKW pooled together) encourages greater improvements in 1-min HRR than a non-exercise control condition, reconfirming previously reported exercise-induced improvements in autonomic function (Kim et al. 2009; Gimeno-Santos et al. 2014; Giallauria et al. 2015; Niederer et al. 2015; Álvarez et al. 2017), the hypothesized dose-dependent effect was not unequivocally confirmed. Consequently, high-dose aerobic exercise (20 KKW) that markedly exceeds general health recommendations (+150%) did not elicit significantly greater improvements in 1-min

HRR compared to guideline-concordant moderate-dose aerobic exercise (8 KKW), and only a tendency towards a dose-dependent benefit was detected. The sensitivity analyses for relative VO_{2peak} confirmed the findings from our main outcomes paper that included all 171 per-protocol analyzed participants, but found an approximately 6.5% greater improvement in the 20 KKW group compared to the previously published results (Martin et al. 2019). The changes in VO_{2peak} in the 8 KKW group, though significantly different from the non-exercise control condition, remained statistically non-significant in the present analyses.

The suggested effect on 1-min HRR for the 20 KKW group (11% improvement) is comparable to the exercise-induced improvements in 1-min HRR reported for a 12-week exercise intervention in obese men (12%) (Kim et al. 2009). However, the previous study was able to elicit improvements of this magnitude with a markedly lower-volume exercise program (three 60-min sessions per week), more comparable to 8 KKW, which in our study elicited improvements in 1-min HRR of only around 6%. It is noteworthy that in the present study, only 17 participants (12%) had an abnormal 1-min HRR at baseline (≤ 12 bpm) and it is conceivable that a stronger and more dose-dependent effect would have been found if HRR had been more impaired at baseline. It has been shown that, particularly in patients with abnormal HRR, increases in exercise capacity following an aerobic exercise program predict a subsequent improvement of HRR (Kim et al. 2009). The clinical relevance of the suggested effect on 1-min HRR in our study can be conjectured based on previous work. It has been shown that every 10 beats per minute decrement in HRR is associated with a 13% risk increase for cardiovascular events and 9% risk increase for all-cause mortality (Qiu et al. 2017). Applying these findings to our results, it can be speculated that the improvement in HRR in the 20KKW group of 2.7 bpm would correspond to a risk reduction for cardiovascular events of around 4% and for all-cause mortality of around 2.5%. Interestingly, and in contrast to previous findings (Kim et al. 2009), we did not find a significant correlation between changes in 1-min HRR and changes in resting HR. As significant reductions in resting HR in both exercise groups, as well as a tendency towards an improved 1-min HRR at least in the 20 KKW group, was found, this is surprising since both early (≤ 1 min) HRR and a reduction in resting HR are thought to be driven by parasympathetic activity (Borresen and Lambert 2008; Coote and White 2015).

When considering the significant adjusted difference of 6.2 bpm between non-compensators and compensators, and especially the independent effect of weight change on 1-min HRR as demonstrated by the multiple linear regression model, it seems that the changes in 1-min HRR are affected by weight loss (−2% in 20 KKW and −0.5% in 8 KKW) during the 24-week intervention. This assumption is further supported by the fact that previous studies reporting comparable exercise-induced improvements in HRR in individuals with overweight/obesity likewise reported these improvements in the presence of concurrent weight reductions [−0.8% (Álvarez et al. 2017) and −3% (Kim et al. 2009)], and that improvements in HRR have even been reported for weight loss trials in sedentary individuals without any changes in physical activity levels (Brinkworth et al. 2006). It is noteworthy that for exercise interventions, there seems to exist a dose–response relationship between concurrent weight loss and improvements in HRR, in which trials with greater concurrent percent weight loss elicit greater improvements in HRR (Kim et al. 2009; Álvarez et al. 2017). It can be speculated that greater weight loss, as an indirect result of the exercise training, would have translated to greater and statistically significant improvements in HRR to confirm the hypothesized dose–response relationship.

The direct results of the exercise training are demonstrated clearly by the significant and dose-dependent improvements in VO_{2peak} of 3.3 mL/kg/min or 15% in the 20 KKW group. The magnitude of these improvements of approximately one metabolic equivalent (3.5 mL oxygen/kg/min) has been shown to be associated with a mortality risk reduction of 14% in 29,257 middle-aged adults, independent of age, sex, ethnicity, concomitant medication, hypertension, smoking, and BMI (McAuley et al. 2016), highlighting the clinical importance of the improvements in cardiorespiratory fitness. While weight loss likely supports and potentially even moderates the beneficial effect of aerobic exercise on HRR, the multiple linear regression analyses also showed that increases in VO_{2peak}, which are likely the direct result of exercise training, are to some extent also independently associated with improvements in 1-min HRR. This suggests an independent predictive value of cardiorespiratory fitness with regard to autonomic function, as has been shown previously (Curfman and Hillis 2003; Kim et al. 2009), and further underlines the importance of cardiorespiratory fitness as a comprehensive health parameter.

A limitation of this study is the predominantly female-based cohort which does not allow for generalizability of the results for both sexes independently. To account for the sex imbalance, sex was included in the ANCOVAs. As it was found to be a non-significant covariate, the models without sex as a covariate were reported. Further, the E-MECHANIC trial was powered to detect differences in the trial's primary outcomes of 'energy intake' and 'weight loss'. It is possible that failure to detect significant group differences in 1-min HRR is at least partly due to insufficient power, as is often the case in explorative subset analyses. The results with regard to changes in 1-min HRR remain inconclusive and more research is needed to determine the effect of different doses of vigorous-intensity aerobic exercise on 1-min HRR as a measure of autonomic function.

In conclusion, this subset analysis to the E-MECHANIC study was able to show that vigorous-intensity exercise can induce improvements in 1-min HRR, but that a higher dose (20 KKW) of the same-intensity aerobic exercise only tended to yield additional benefits in 1-min HRR compared to the standard dose (8 KKW) that is recommended for general health. Similar to the findings reported in our main outcomes paper, the sensitivity analysis showed that improvements in VO_{2peak} are dose-dependent and that consequently, 20 KKW leads to greater improvements in cardiorespiratory fitness than the guideline-concordant moderate dose of aerobic exercise (8 KKW). Although a dose–response relationship was not unequivocally confirmed, our regression models suggest that aerobic exercise drives improvements in HRR both directly via improvements in cardiorespiratory fitness and indirectly via weight reduction caused by the exercise-induced energy expenditure.

Author contributions CKM and TSC conceptualized and designed the study. DSH, NMJ, and JWA were responsible for data collection. CH performed statistical analyses and wrote the manuscript. CH, JD, and CKM interpreted the data and prepared the results for publication. All authors reviewed and edited the manuscript and approved the final version for publication.

Compliance with ethical standards

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