# Heart Rate Variability and Blood Pressure Response to Low-Intensity Endurance Exercise Training Plus Blood Flow Restriction in Individuals with Mild Hypertension: A Randomized Controlled Clinical Trial

Maryam Doustaki Zaboli¹, PhD candidate; Siyavash Joukar², PhD; Masoumeh Nouzari⁴, PhD; Soheil Aminizadeh¹, PhD; Masoomeh Kahnooji², MD; Khadijeh Mohammadi¹, MD

<sup>1</sup>Physiology Research Center, Institute of Neuropharmacology, Kerman University of Medical Sciences, Kerman, Iran; <sup>2</sup>Cardiovascular Research Center, Institute

<sup>2</sup>Cardiovascular Research Center, Institute of Basic and Clinical Physiology Sciences, Kerman University of Medical Sciences, Kerman, Iran;

<sup>3</sup>Department of Physiology and Pharmacology, Afzalipour Medical Faculty, Kerman University of Medical Sciences, Kerman, Iran:

<sup>4</sup>Neuroscience Research Center, Institute of Neuropharmacology, Kerman University of Medical Sciences, Kerman, Iran; <sup>5</sup>Department of Cardiology, Afzalipour Medical Faculty, Kerman University of Medical Sciences, Kerman, Iran

#### Correspondence:

Tel: +98 34 33257671

Siyavash Joukar, PhD; Department of Physiology and Pharmacology, Afzalipour Medical School, Pazhoohesh Sq., 22 Bahman Blvd., Postal code: 7616914115, Kerman, Iran

Email: sjokar@gmail.com jokar@kmu.ac.ir Received: 05 January 2025 Revised: 19 March 2025 Accepted: 05 May 2025

## What's Known

• Endurance exercise improves heart rate variability (HRV) and blood pressure (BP), but the effects of combining low-intensity endurance training with blood flow restriction (BFR) in mild hypertension are unclear

#### What's New

 Low-intensity endurance exercise combined with BFR reduces BP and HRV similar to exercise and increases HRV more effectively, without causing adverse effects.

#### Abstract

**Background:** Given limited available data and information gaps related to the effects of endurance exercise along with blood flow restriction (BFR) on the heart. This study examined the effects of low-intensity endurance exercise training (Ex) alone and BFR on blood pressure (BP), electrocardiogram (ECG), heart rate variability (HRV), and heart rate recovery time (HRRT) in participants with grade 1 hypertension.

**Methods:** In this randomized double-blind clinical trial, 43 hypertensive participants, 50-65 years old, were randomly divided into three groups: Ex+BFR, Ex, and the control (Con) group. The training program was conducted three times weekly for 10 weeks in spring 2024 at Kerman University of Medical Sciences. Before and 24 hours after the intervention, HRV parameters, BP, ECG, and HRRT were assessed.

**Results:** The Ex and Ex+BFR groups showed a significant increase in Root Mean Square of Successive Differences between normal heartbeats (RMSSD) (P=0.008, P=0.002), Standard Deviation of Successive Differences (SDSD) (P=0.008, P=0.002), and the standard deviation of the Poincaré plot ratio (SD1/SD2) (P=0.0004, P=0.0002), and a reduced low frequency to high frequency ratio (LF/HF) (P=0.013 and P=0.007) compared to Con group, respectively. The Ex+BFR group demonstrated a greater positive effect on frequency-domain parameters of HRV. In addition, both the Ex and Ex+BFR groups showed a significant reduction in HRRT (P=0.0001 vs. relevant baseline), mean arterial blood pressure (MAP) (P=0.0001), and prolonged PR interval (P=0.038 and P=0.035, respectively) and shortened QRS complex compared to the Con group.

Conclusion: This study demonstrates that combining lowintensity endurance exercise with BFR exerts a positive effect on cardiovascular parameters such as BP, ECG, HRRT, and demonstrates superior effects on HRV compared to exercise alone in individuals with mild hypertension.

A preprint version of this manuscript is available at DOI: https://doi.org/10.21203/rs.3.rs-5347658/v1.

Please cite this article as: Doustaki Zaboli M, Joukar S, Nouzari M, Aminizadeh S, Kahnooji M, Mohammadi K. Heart Rate Variability and Blood Pressure Response to Low-Intensity Endurance Exercise Training Plus Blood Flow Restriction in Individuals with Mild Hypertension: A Randomized Controlled Clinical Trial. Iran J Med Sci. 2025;50(11):775-787. doi: 10.30476/ijms.2025.105405.3916.

**Keywords** • Heart rate • Endurance training • Blood flow restriction • Blood pressure

## Introduction

Heart rate variability (HRV) refers to variations in time intervals between successive heartbeats. These variations reflect the balance between the sympathetic and parasympathetic divisions of the autonomic nervous system (ANS).1 Aging is associated with an increase in sympathetic nervous system (SNS) activity and a decrease in parasympathetic nervous system (PNS) activity, which leads to reduced HRV.2 HRV reduction plays a role in the progression of hypertension and raises the long-term danger of cardiovascular diseases and mortality.3, 4 Exercise training is a non-pharmacological intervention to improve cardiovascular function and HRV.5,6 It enhances cardiovascular health by increasing capillary density, mitochondrial function, and oxygen delivery.6,7 Blood flow restriction (BFR) involves partial arterial and complete venous occlusion. Enhances the benefits of resistance exercise at low intensities and is particularly beneficial for elderly populations unable to perform highintensity exercise.8,9

A study reported that 12 weeks of low-intensity resistance training with BFR reduced blood pressure in elderly adults but had no effect on HRV.<sup>10</sup> Additionally, 6 weeks of walking with BFR improved time-domain HRV parameters and reduced systolic blood pressure in middle-aged men.11, 12 Considering that endurance exercise is more effective in improving cardiovascular function, combining this type of exercise with BFR may yield beneficial or adverse effects due to increased nervous system stimulation and additional metabolic stress. Due to limited information and insufficient knowledge of the benefits and disadvantages of this exercise model on the cardiovascular system, the present study investigated the effects of 10 weeks of endurance training on a cycle ergometer with blood flow restriction on HRV, ECG parameters, mean arterial pressure (MAP), resting heart rate, and heart rate recovery time (HRRT) in individuals aged 50 to 65 with grade 1 hypertension.

## **Materials and Methods**

This randomized double-blind clinical trial was registered with the Iranian Registry of Clinical Trials (IRCT20230528058311N1) and received approval from the Ethics Committee of Kerman University of Medical Sciences (IR. KMU.AH.REC.1402.029). It was conducted in spring 2024 at Kerman University of Medical Sciences. All participants were fully aware of the study events, and written informed consent was

obtained from each participant.

Participants, Sample Size, and Study Design

Participants in this study were aged between 50-65 years and had a body mass index (BMI) of less than 30. The participants were assessed by a cardiologist in the Javad-al-Aeme Hospital in Kerman (Iran). Persons were assessed by 48-hour ambulatory blood pressure monitoring. Based on the American Heart Association's guidelines, a systolic pressure of 130-139 mmHg and/or a diastolic pressure of 80-89 mmHg was measured as grade 1 hypertension.<sup>13</sup> Exclusion criteria include regular exercise for the previous 6 months, consuming any medicines that lesser blood pressure, positive history of joint or bone disorders, cancer, cardiovascular, liver, kidney, or pulmonary diseases, diabetes, and being overweight.

The sample size was calculated using G\*Power software (version 3.1.9.2, Heinrich-Heine-Universität Düsseldorf, Germany) based on the number of groups and a one-way ANOVA design (α=0.05, power=0.80, effect size=0.5), resulting in a total sample size of 43 participants. Participants were randomly assigned to three groups: Ex+BFR (n=15) performed cycle ergometer sessions with blood flow restriction, Ex (n=15) performed identical training without BFR, and Control (Con) (n=13) maintained usual activity. In the Ex+BFR group, a cuff was applied to the thigh to restrict blood flow. Complete arterial occlusion pressure (AOP) for the femoral artery was estimated using the formula:<sup>14</sup>

Lower body arterial occlusion pressure (mmHg)=(5.893×thigh circumference)+(0.912 systolic pressure)(0.734 diastolic blood pressure)-220.046

The cuff pressure was set at 30% of AOP and maintained throughout the exercise program. The exercise duration was increased by five to 10 min each week. The control group continued their normal lifestyle without participating in any exercise activities.

Measurement of Heart Rate (HR) and Calculation of MAP and VO, Peak

Participants were instructed to avoid alcohol, caffeine, intense physical activity, and stressful situations for at least 1 day before measurements. They were allowed to rest for 10 min to stabilize their heart rate. A Polar smartwatch (Polar, Finland) was utilized to automatically measure the resting heart rate. Arterial BP was measured using a digital monitoring device (Omron M2 Comfort, Japan). Measurement of arterial BP was calculated from the left hand for two periods with an intermission of 10 min, and the mean

of these two values was recorded. MAP was calculated using the formula: MAP=DBP+1/3 (SBP-DBP) where SBP is systolic BP, and DBP is diastolic BP.

Maximal oxygen consumption (VO, Peak) was assessed by the Astrand test to calculate aerobic capacity. This test includes participants cycling for 6 min on a cycle ergometer (Monark, Ergomedic 839 E, Sweden) connected to a gas analyzer (Cortex, Metalyzer 3B, Germany), maintaining a cycling rate of 50±5 rebellions per min and a HR between 120 and 140 bpm.15 The test measured oxygen saturation (SpO<sub>2</sub>) using a pulse oximeter (Beurer, Germany), HR, oxygen uptake (VO<sub>2</sub>), and respiratory exchange ratio (RER). Mean HR and output wattage were used to estimate the VO<sub>2</sub> peak, with age adjustment. The test was considered valid if the participants maintained HRs between 120 and 140 bpm throughout the 6-min protocol.

## Training Protocol

The 10-week exercise program consisted of three weekly sessions on a bicycle ergometer. The initial exercise duration was set at 15 min at 50-60% VO<sub>2</sub> peak intensity, which corresponded to the target heart rate zone, and gradually increased by 5-10 min per week, reaching 55 minutes by week 10. Exercise intensity was adjusted every 2 weeks based on heart rate and

rating of perceived exertion (RPE scale). For the Ex+BFR group, cuff pressure was adjusted based on RPE level during the sessions and temporarily released/reapplied as needed to ensure safety and comfort while maintaining exercise efficacy. A 10-min warm-up and cooldown period was included in each session.

#### Measurement of HRRT

Before the first exercise session, resting HR was measured as described above. Then, immediately after the exercise ended, the time it took for the heart rate to return to resting levels was recorded and considered as the baseline HRRT for each participant. This procedure was repeated in the last session of the protocol, and the final HRRT was recorded.

# ECG Recording and HRV Assessment

Before and after the exercise program, participants were instructed to abstain from caffeinated beverages for 24 hours and strenuous exercise for 48 hours. Lead II electrocardiograms (ECGs) were recorded in the supine position after 10 min of rest at 25 °C using a PowerLab system (ADInstruments, Australia). ECG parameters, including PR interval, QRS duration, JT interval, and heart rate-corrected QT (QTc), as well as HRV parameters such as time domains (RMSSD,

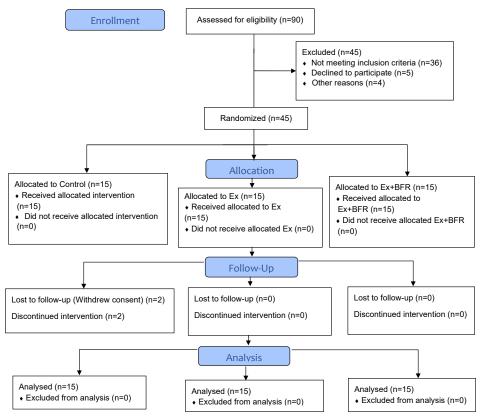


Figure 1: The diagram depicts the CONSORT flow diagram of the investigation.

SDSD, pRR50), frequency domains (LF: 0.04–0.15 Hz; HF: 0.15–0.4 Hz; LF/HF ratio), and nonlinear parameters (SD1, SD2, SD1/SD2) from Poincaré plots were calculated using dedicated software. To calculate the percentage changes in HRV, ECG, and MAP variables, the following formula was used:

Percentage Change=
$$\left(\frac{\text{Final Value-Initial Value}}{\text{Initial Value}}\right) \times 100^{\circ}$$

#### Statistical Analysis

Statistical analyses were conducted using Prism software (version 9, GraphPad Software, USA). Data were presented as mean±SEM. The normality of the data was evaluated by the Shapiro-Wilk test. One-way ANOVA compared pre- and post-intervention values among groups. Significant group differences were examined using Tukey's *post hoc* test. Intragroup changes were analyzed with a paired *t* test. P value less than 0.05 was considered the level of significance.

## Results

Of the 90 screened patients, 45 were randomized (15/group). Attrition occurred only in controls (n=2 withdrew; final n=13). Both Ex and Ex+BFR groups maintained full retention (n=15 each) (figure 1).

Table 1 presents demographic characteristics, medication, and clinical history of each group. No differences across groups were detected at baseline.

#### MAP and HRRT

One-way analysis of variance showed a significant difference in the percentage change in MAP between groups (F [2, 40]=27, P=0.0001). MAP decreased by 11% in the Ex-group and by 13% in the Ex+BFR group (P=0.0001, vs. Con group). No significant difference was observed between the Ex and Ex+BFR groups (figure 2a). According to paired t tests, MAP reduced significantly in both the Ex (P=0.0002, t=7.3) and Ex+BFR (P=0.0001, t=9.1) groups compared to their respective baselines (figure 2b).

Table 1: Demographic and baseline characteristics of participants					
Parameter		Ex group (n=15)	Ex+BFR group (n=15)	Control group (n=13)	P value
Age (years, mean±SEM)	,	54.2±5.8	59.1±6.3	57.4±5.5	0.124
Sex, n (%)	Male	3 (20)	3 (20)	3 (23.07)	0.975
	Female	12 (80)	12 (80)	10 (76.92)	0.975
Weight (Kg, mean±SEM)		72.3±9.1	78.6±8.7	75.2±9.4	0.231
BMI (Kg/m², mean±SEM)		25.8±2.5	28.3±2.7	27.1±2.6	0.092
SBP (mmHg, mean±SEM)		132.58±0.66	134.23±0.54	133.06±0.73	0.20
DBP (mmHg, mean±SEM)		81±1.92	81.63±1.87	83.08±1.34	0.68
Ethanol intake (%)		0	0	0	-
Current smoker, (%)		0	0	0	-
Family history of HTN, n (%)		5 (38.5%)	7 (46.7%)	6 (40.0%)	0.714

BFR: Blood Flow Restriction; SEM: Standard Error of Mean; HTN: Hypertension; BMI: Body mass index; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; Con: Control group; Ex: Exercise training group; Ex+BFR: Exercise training+Blood flow restriction group

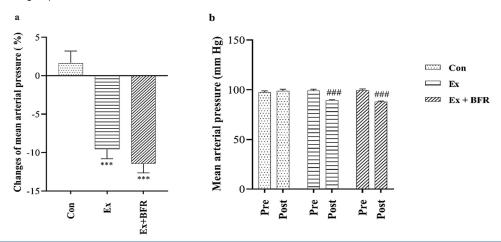


Figure 2: The effect of endurance exercise training with/without blood flow restriction on mean arterial pressure (MAP): a) The percentage changes in MAP among the study groups are shown, and b) shows the MAP before and after the intervention in the study groups a. Data are presented as mean±SEM, \*\*\*P<0.001 in comparison with Con, ####P<0.001 in comparison with pre-intervention. Con: Control group; Ex: Exercise training group; Ex+BFR: Exercise training+Blood flow restriction group; Pre: pre-intervention; Post: post- intervention

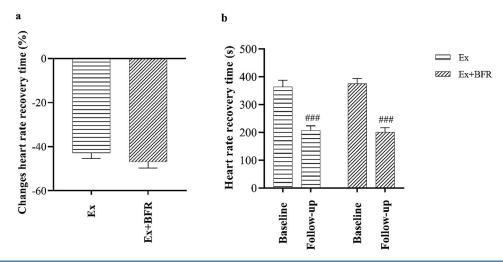


Figure 3: The effect of endurance exercise training with/without blood flow restriction on heart rate recovery time (HRRT):
a) The percentage changes in HRRT, which is defined as the time required for the heart rate to return to resting levels after exercise, are shown. (b) HRRT before and after a ten-week exercise program is displayed. Data are presented as mean±SEM. ###P<0.001 indicates statistically significant differences compared to baseline values; s: Second; Con: Control group; Ex. Exercise training group; Ex+BFR: Exercise training+Blood flow restriction group; Pre: Pre-intervention; Post: Post- intervention

Percent changes in HRRT did not differ significantly between exercise groups (figure 3a). Paired *t* tests showed a significant reduction in HRRT in both Ex (P=0.0001, t=11) and Ex+BFR groups (P=0.0001, t=15) compared to corresponding baselines (figure 3b).

#### Heart Rate Variability (HRV)

There was no significant difference in baseline HRV parameters between the groups. One-way ANOVA analysis revealed a significant increase in percentage changes of RMSSD and SDSD between groups (F [2, 40]=9.7, P=0.0001). Specifically, RMSSD and SDSD improved by 13% in the Ex-group and 14% in the Ex+BFR group (P=0.008 and P=0.002, respectively, vs. Con group) (figure 4a, c). No significant differences were observed between Ex and Ex+BFR groups. Paired t test analysis revealed that RMSSD and SDSD significantly increased after intervention in both the Ex (P=0.0001, t=11) and Ex+BFR (P=0.0003, t=4.3) groups (figure 4b, d). The exercise intervention did not alter the percentage of adjacent R-R intervals that varied by 50% or more (pRR50) (figure 4e, f).

No significant differences were observed in percentage changes in low frequency power normalized (LF [nu]) among groups (F [2,40]=0.13, P=0.881) (figure 5a). LF decreased in the Ex+BFR group compared to baseline (P=0.045, t=2.2) (figure 5b). High frequency power normalized (HF [nu]) increased by 16% in the Ex-group and by 19% in the Ex+BFR group (P=0.011 and P=0.002) vs. the Con group (figure 5c). In addition, HF significantly increased in both the Ex (P=0.017, t=2.7) and Ex+BFR (P=0.0009, t=4.5) groups compared to corresponding

baselines (figure 5d). Percentage changes in the LF/HF ratio (as an indicator of sympathovagal balance) were 19% in the Ex-group and 21% in the Ex+BFR group (P=0.013 and P=0.007, respectively, vs. Con group) (figure 5e). In comparison to the respective baseline, this parameter also diminished significantly in both the Ex (P=0.003, t=3.6) and Ex+BFR (P=0.004, t=3.5) groups (figure 5f).

Percentage changes in SD1 differed significantly among groups (F [2, 40]=15, P=0.0001). SD1 increased by 23% in the Ex-group and by 25% in the Ex+BFR group (P=0.0004 and P=0.0002, respectively, vs. the Con group). No significant change was found between the Ex and Ex+BFR groups (P=0.877, figure 6a). SD1 significantly improved in both the Ex (P=0.0009, t=8.7) and Ex+BFR (P=0.007, t=7) groups compared to relative baselines (figure 6b). SD2 decreased by 14% in the Ex-group and by 15% in the Ex+BFR group (P=0.012 and P=0.005, respectively, vs. Con), but no significant change was found between the Ex and Ex+BFR groups (P=0.951, figure 6c). This parameter decreased in both the Ex (P=0.005, t=3.3) and Ex+BFR (P=0.006, t=3.3) groups compared to relative baselines (figure 6d). SD1/SD2 ratio changes differed significantly between groups (F [2, 40]=9.5, P=0.0002, figure 6e). Post-hoc analyses showed SD1/ SD2 changes of 44% in the Ex group and 55% in the Ex+BFR group, significantly greater than Con (P=0.005 and P=0.0009, respectively). Exercise training significantly increased SD1/ SD2 in both Ex (P=0.0007, t=5.9) and Ex+BFR (P=0.0008, t=7.1) groups compared to baseline (figure 6f).

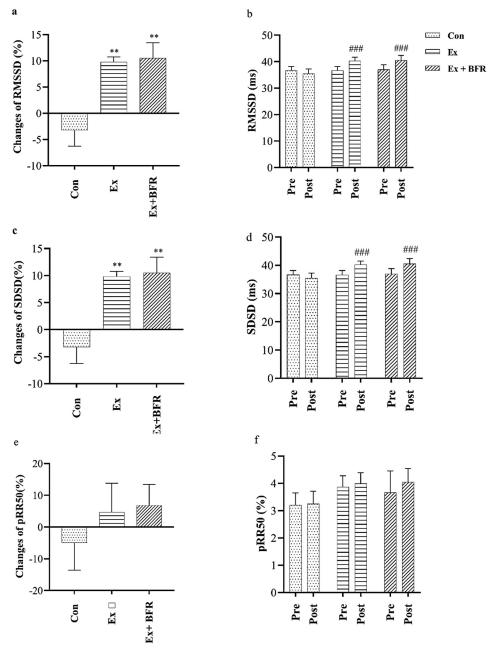


Figure 4: The effects of endurance exercise training with/without blood flow restriction on root mean square of successive differences (RMSSD) between normal heartbeats and standard deviation of successive differences (SDSD): The values of RMSSD (a), SDSD (c), and Percentage of successive R-R intervals that differ by more than 50 ms (pRR50) (e) before and after the intervention are presented in the study groups. The percentage changes in RMSSD (b), SDSD (d), and pRR50 (f) within the study groups are illustrated. Data are expressed as mean±SEM. \*\*P<0.01in comparison with Con, ###P<0.001 in comparison with pre-intervention. Con: Control group; Ex: Exercise training group; Ex+BFR: Exercise training+Blood flow restriction group, Pre: pre-intervention; Post: post- intervention

#### ECG Parameters

Compared to the Con group, both Ex and Ex+BFR groups showed a significant increase in PR interval percentage changes (P=0.038, P=0.035, respectively) with no significant difference between the Ex and Ex+BFR groups (P=0.99) (figure 7a). Moreover, exercise training significantly increased PR interval in Ex and Ex+BFR groups (P=0.019 and P=0.002, vs. relative baselines, respectively) (figure 7b). The percentage changes

in QRS time in the Ex and Ex+BFR groups were significant compared to the Con group (P=0.023 and P=0.005, respectively). No significant change was found between the Ex and Ex+BFR groups (P=0.75) (figure 7c). QRS interval decreased significantly in both Ex and Ex+BFR groups after the intervention (P=0.0009, P=0.0008, respectively) (figure 7d). HR reduction was significantly greater in Ex and Ex+BFR groups than Con group (P=0.021 and P=0.004, respectively) (figure 7e).

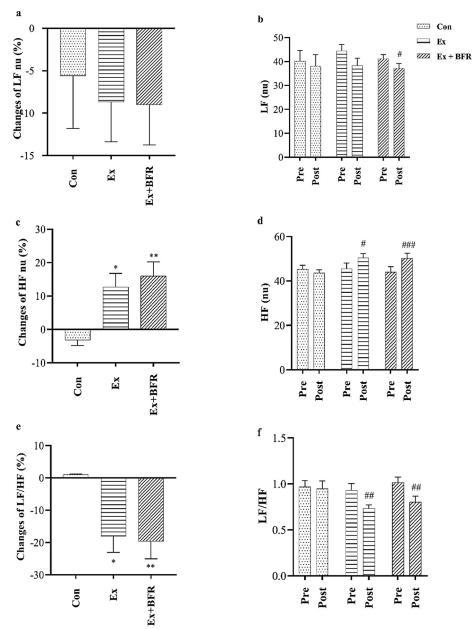


Figure 5: The effects of endurance exercise training with/without blood flow restriction on low frequency power (LF), high frequency power (HF) and LF/HF: (a) Percentage change in LF, (c) HF, and (e) LF/HF in study groups are shown. The LF, HF and the LF/HF ratio before and after the intervention are shown in (b), (d), and (f), respectively. Data presented as Mean±SEM. \*P<0.05, \*\*P<0.01 in comparison with Con, #P<0.05, ##P<0.01, and ###P<0.001 compared with pre-intervention. All LF and HF are displayed in normalized units (nu.). Con: Control group; Ex: Exercise training group; Ex+BFR: Exercise training+Blood flow restriction group, Pre: pre-intervention; Post: post- intervention

Both Ex and Ex+BFR groups showed significant HR reductions after intervention (P=0.018 and P=0.0006, respectively) (figure 7f). Exercise training with/without BFR had no significant effects on QTc and JT interval (figure 7g, h).

# **Discussion**

The results of the present study indicated that 10 weeks of low-intensity endurance exercise with and without BFR improved HRV and ECG parameters, reduced BP, shortened HRRT, and Ex with BFR showed greater improvement

in some indices. HRV parameters (SDSD and RMSSD) in the time domain increased, which implies an increase in the autonomic control and parasympathetic activity coupled with an increase in heart function and a decrease in cardiovascular risk. Studies on participants performing moderate-intensity exercise have confirmed a significant increase in RMSSD and SDSD, which aligns with our findings. Similarly, human studies suggest that walking exercises with BFR can enhance HRV and increase RMSSD, reflecting improved HR regulation. In contrast, high-intensity training in athletes

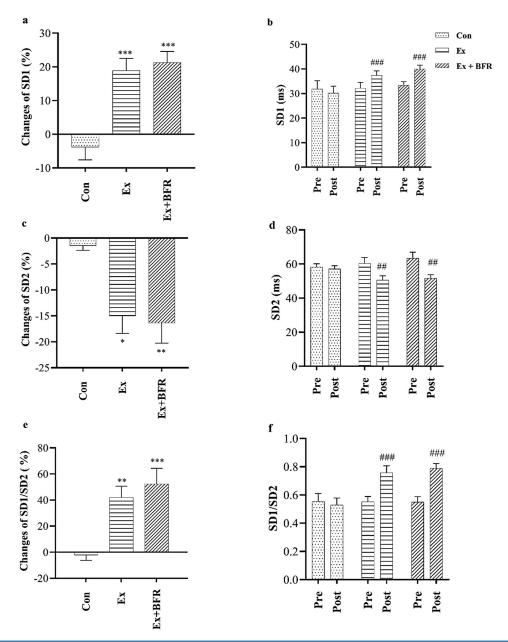


Figure 6: The effects of endurance exercise training with/without blood flow restriction on SD1, SD2 and SD1/SD2: The percentage changes in SD1 (a), SD2 (c), and the SD1/SD2 (e) among the study groups are shown. The values of SD1 (b), SD2 (d) and SD1/SD2 (f) before and after the exercise intervention are also presented. Data are expressed as mean±SEM. \*P<0.05, \*\*P<0.01, \*\*\*P<0.01 in comparison with Con, ##P<0.01, and ###P<0.001 in comparison with pre-intervention. The standard deviation of the Poincaré plot concerning (SD1) and along (SD2) the line of identity is denoted as SD1 and SD2, respectively. Short-term variability is captured by SD1, while long-term variability is captured by SD2. This is used as a measure of the balance and randomness of changes in the autonomic nervous system. Con: Control group; Ex: Exercise training group; Ex+BFR: Exercise training+Blood flow restriction group, Pre: pre-intervention; Post: post-intervention

reduced RMSSD and SDSD, likely due to the excessive stress of high-intensity exercise.<sup>17</sup> These findings highlight that exercise type and intensity should be carefully adjusted to optimize positive effects on HRV. Our study revealed that endurance exercise, with or without BFR, increases HF and decreases the LF/HF ratio, which indicates predominance of parasympathetic activity over sympathetic. Response to aerobic exercise in an animal model,<sup>18</sup> and BFR exercise in humans<sup>11</sup> also showed increased HF and

decreased LF/HF that were consistent with our findings. Despite this, high-intensity interval training increased LF/HF in animal models,<sup>19</sup> and resistance training increased LF/HF and decreased HF in humans,<sup>8</sup> unlike our findings. This may be due to differences in the type of exercise, intensity, and health of participants. Another significant finding of the present study was the increase in SD1, decrease in SD2, and increase in SD1/SD2 in both the Ex and Ex+BFR groups, with more pronounced changes in the Ex+BFR group.

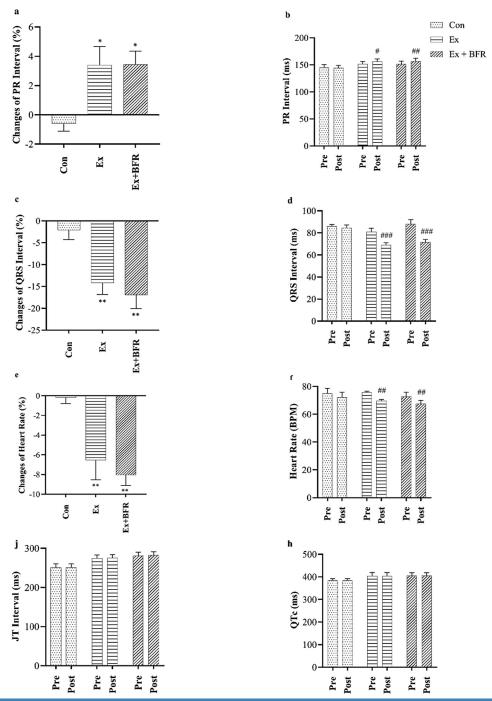


Figure 7: Percentage changes of PR interval, QRS interval, JT interval, QTc, and heart rate: The effect of endurance exercise training with/without blood flow restriction on electrocardiographic parameters (b, d, f, j and h) and absolute values of PR interval, QRS interval, JT interval, QTc, and heart rate before and after the intervention (a, c and e) is shown. Data presented as Mean±SEM. \*P<0.05, \*\*P<0.01 vs. Con group, #P<0.05, ##P<0.01, and ###P<0.001 in comparison with pre-intervention. PR interval is the time from the onset of the P to the start of the QRS, reflecting AV node conduction and atrial depolarization. The QRS interval is the time from the beginning of the Q wave to the end of the S wave and represents the time of ventricular depolarization. The JT interval is the time from the end of the QRS complex to the end of the T wave, ventricular repolarization. The corrected QT interval for heart rate (QTc) is the total time of ventricular depolarization and repolarization. heart rate is the number of heartbeats per minute. Con: Control group; Ex: Exercise training group; Ex+BFR: Exercise training+Blood flow restriction group, Pre: Pre-intervention; Post: Post- intervention

Increased SD1 indicates enhanced short-term HRV and reduced arrhythmic susceptibility, likely due to enhanced parasympathetic activity and stabilization of the autonomic system.<sup>20</sup> Decreased SD2 reflects diminished long-term HRV.<sup>20</sup> Increased SD1/SD2 suggests improved

sympathovagal balance and enhanced autonomic responsiveness.<sup>21</sup> The increase in SD1/SD2 in training groups of this study indicated improving balance between parasympathetic and sympathetic activities and a more favorable cardiovascular status.<sup>22</sup> Therefore, our study

showed that combining low-intensity endurance training with BFR not only does not prevent the beneficial effects of exercise on HRV but may actually improve them. As mentioned, the difference in the results of our study with some previous studies,19, 8, 23 could be due to exercise type, intensity, duration, and participants' baseline health. Regarding ECG results, the increase in PR interval and reduction in QRS complex time in both exercise groups may indicate improved cardiac electrical conduction due to better autonomic balance and cardiac responses. The reduction in QRS interval may be related to enhanced ventricular conductivity, faster impulse propagation, and ventricular depolarization. The greater QRS reduction in Ex+BFR may reflect enhanced ventricular conduction velocity from BFR. Several human studies in relation to endurance exercise and ECG changes support our findings.<sup>24, 25</sup> Consistently, an animal study showed that regular endurance exercise can improve cardiac electrical function and reduce arrhythmias in rats with myocardial infarction.<sup>26</sup> However, some studies contradicting our results have shown that intense and prolonged endurance exercise may increase the risk of cardiac arrhythmias in certain individuals.27, 28 Additionally, prolonged intense endurance exercise in people with underlying heart disease may worsen their condition.29 These discrepancies may stem from variations in exercise intensity and participant characteristics. Another finding was the reduction in arterial pressure and improvement in HRRT in both the endurance exercise groups, with or without BFR, among participants. These results align with meta-analyses on exercise combined with BFR, which reported that this intervention reduces BP and improves HRRT.30, 31 Additionally, a metaanalysis identified endurance exercise as the most effective exercise type for reducing BP, aligning with our findings.<sup>32</sup> Conversely, our results differ from a study that reported the negative effects of high-intensity endurance training on the risk of atrial fibrillation (a type of cardiac arrhythmia),17 aggravation of hypertension by combining resistance training with BFR, which contrasts with our positive findings.33 These variations may be due to different exercise intensities and exercise types combined with BFR.

BFR is associated with increasing venous pressure and blood pooling, causing baroreceptor stimulation, which leads to decreased sympathetic activity and parasympathetic dominance.<sup>34, 35</sup> BFR also stimulates nitric oxide (NO) release, improving vascular function and reducing cardiovascular stress, both of which favor parasympathetic activity.<sup>36</sup> In addition,

it reduces oxidative stress and inflammation, improves mitochondrial function, and releases growth factors (such as VEGF and IGF-1).37 These adaptations likely result from local hypoxia, enhancing parasympathetic activity to restore homeostasis as the body attempts to return to balance.38 Based on the results of the present study, BFR with low-intensity endurance exercise is a practical, accessible intervention method for improving cardiovascular health in middle-aged individuals with mild hypertension. It seems to be a good approach for those who cannot do high-intensity exercise and could be used in cardiac rehabilitation programs or in community health centers under professional supervision. Some limitations of this study are participants' uncontrolled confounders (e.g., diet, sleep patterns), and also a limited sample size and brief intervention duration (10 weeks). Future studies in this field are recommended to address the aforementioned limitations.

#### Conclusion

This study demonstrated that Low-intensity endurance training, with or without BFR, significantly improved HRV, ECG parameters, and BP in middle-aged individuals with grade 1 hypertension. Combining exercise with BFR enhanced specific benefits without adverse effects, proposing a viable hypertension management strategy in middle-aged populations.

## Acknowledgment

The authors would like to thank Kerman University of Medical Sciences. Kerman, Iran, and also the Physiology Research Center, for their cooperation and support (grant number: 401000983).

#### **Authors' Contribution**

M.D.Z: Finding and screening study participants, briefing and training participants, obtaining informed consent, data collection, and drafting; S.J: Study concept, study design, supervision, and drafting; M.N: Data analysis, data interpretation, and drafting; S.A: Study design and drafting; M.K and Kh.M: Data gathering; All authors contributed to reviewing the manuscript. All authors read and agreed on the final manuscript and decided to be responsible for all features of the work in confirming that questions related to the integrity of any part of the work are appropriately explored and addressed.

Conflict of Interest: None declared.

# References

- Sessa F, Anna V, Messina G, Cibelli G, Monda V, Marsala G, et al. Heart rate variability as predictive factor for sudden cardiac death. Aging (Albany NY). 2018;10:166-77. doi: 10.18632/aging.101386. PubMed PMID: 29476045; PubMed Central PMCID: PMCPMC5842851.
- 2 Fajemiroye JO, da Cunha LC, Saavedra-Rodriguez R, Rodrigues KL, Naves LM, Mourao AA, et al. Aging-Induced Biological Changes and Cardiovascular Diseases. Biomed Res Int. 2018;2018:7156435. doi: 10.1155/2018/7156435. PubMed PMID: 29984246; PubMed Central PMCID: PMCPMC6015721.
- 3 Garavaglia L, Gulich D, Defeo MM, Thomas Mailland J, Irurzun IM. The effect of age on the heart rate variability of healthy subjects. PLoS One. 2021;16:e0255894. doi: 10.1371/journal.pone.0255894. PubMed PMID: 34624048; PubMed Central PMCID: PMCPMC8500436.
- 4 Jadhav UM, Kadam SA. Heart rate variability, blood pressure variability: what is their significance in hypertension. Hypertension and Cardiovascular Disease in Asia. Cham: Springer; 2022. p. 139-47. doi: 10.1007/978-3-030-95734-6 10.
- 5 Grassler B, Thielmann B, Bockelmann I, Hokelmann A. Effects of different exercise interventions on heart rate variability and cardiovascular health factors in older adults: a systematic review. Eur Rev Aging Phys Act. 2021;18:24. doi: 10.1186/s11556-021-00278-6. PubMed PMID: 34789148; PubMed Central PMCID: PMCPMC8597177.
- 6 Gibala MJ, Rakobowchuk M. Physiological Adaptations to Training. In: Olympic Textbook of Science in Sport. New Jersey: Wiley; 2008. p. 56-69. doi: 10.1002/9781444303315.ch4.
- 7 McArdle WD, Katch FI, Katch VL. Exercise physiology: nutrition, energy, and human performance. Philadelphia: Lippincott Williams & Wilkins; 2010.
- 8 Lin LL, Chen YJ, Lin TY, Weng TC. Effects of Resistance Training Intensity on Heart Rate Variability at Rest and in Response to Orthostasis in Middle-Aged and Older Adults. Int J Environ Res Public Health. 2022;19. doi: 10.3390/ijerph191710579. PubMed PMID: 36078296; PubMed Central PMCID: PMCPMC9517804.
- 9 Cognetti DJ, Sheean AJ, Owens JG. Blood Flow Restriction Therapy and Its Use for Rehabilitation and Return to Sport: Physiology, Application, and Guidelines

- for Implementation. Arthrosc Sports Med Rehabil. 2022;4:e71-e6. doi: 10.1016/j. asmr.2021.09.025. PubMed PMID: 35141538; PubMed Central PMCID: PMCPMC8811521.
- 10 Lopes KG, Farinatti P, Bottino DA, MDGC DES, Maranhao PA, Bouskela E, et al. Does Resistance Training with Blood Flow Restriction Affect Blood Pressure and Cardiac Autonomic Modulation in Older Adults? Int J Exerc Sci. 2021;14:410-22. doi: 10.70252/OXXF4710. PubMed PMID: 34055161; PubMed Central PMCID: PMCPMC8136558.
- 11 Junior AF, Schamne JC, Perandini LAB, Chimin P, Okuno NM. Effects of Walking Training with Restricted Blood Flow on HR and HRV Kinetics and HRV Recovery. Int J Sports Med. 2019;40:585-91. doi: 10.1055/a-0942-7479. PubMed PMID: 31272111.
- 12 Ferreira Junior A, Schamne JC, Altimari LR, Okano AH, Okuno NM. Effect of walk training combined with blood flow restriction on resting heart rate variability and resting blood pressure in middle-aged men. Motriz: Revista de Educação Física. 2019;25:e101945. doi: 10.1590/s1980-6574201900020005.
- 13 Carey RM, Whelton PK, Committee AAHGW. Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: Synopsis of the 2017 American College of Cardiology/American Heart Association Hypertension Guideline. Ann Intern Med. 2018;168:351-8. doi: 10.7326/M17-3203. PubMed PMID: 29357392.
- 14 Bayles MP. ACSM's exercise testing and prescription. Philadelphia: Lippincott Williams & Wilkins; 2023.
- 15 Pescatello LS. ACSM's guidelines for exercise testing and prescription. Philadelphia: Lippincott Williams & Wilkins; 2014.
- 16 Goit RK, Pant BN, Shrewastwa MK. Moderate intensity exercise improves heart rate variability in obese adults with type 2 diabetes. Indian Heart J. 2018;70:486-91. doi: 10.1016/j.ihj.2017.10.003. PubMed PMID: 30170641; PubMed Central PMCID: PMCPMC6116720.
- 17 Opondo MA, Aiad N, Cain MA, Sarma S, Howden E, Stoller DA, et al. Does High-Intensity Endurance Training Increase the Risk of Atrial Fibrillation? A Longitudinal Study of Left Atrial Structure and Function. Circ Arrhythm Electrophysiol. 2018;11:e005598. doi: 10.1161/CIRCEP.117.005598. PubMed PMID: 29748195; PubMed Central PMCID: PMCPMC5951393.
- 18 Pagan LU, Damatto RL, Gomes MJ, Lima ARR, Cezar MDM, Damatto FC, et al.

- Low-intensity aerobic exercise improves cardiac remodelling of adult spontaneously hypertensive rats. J Cell Mol Med. 2019;23:6504-7. doi: 10.1111/jcmm.14530. PubMed PMID: 31317657; PubMed Central PMCID: PMCPMC6714166.
- 19 Engel LE, de Souza FLA, Giometti IC, Okoshi K, Mariano TB, Ferreira NZ, et al. The high-intensity interval training mitigates the cardiac remodeling in spontaneously hypertensive rats. Life Sci. 2022;308:120959. doi: 10.1016/j.lfs.2022.120959. PubMed PMID: 36108768.
- 20 Davidson BL, Byrne KA, Rood BL, Edwards ES, Akers JD, Wenos DL, et al. Impact of Moderate Exercise Training on Heart Rate Variability in Obese Adults. Journal of Clinical Exercise Physiology. 2021;10:12-9.
- 21 Castello V, Simoes RP, Bassi D, Catai AM, Arena R, Borghi-Silva A. Impact of aerobic exercise training on heart rate variability and functional capacity in obese women after gastric bypass surgery. Obes Surg. 2011;21:1739-49. doi: 10.1007/s11695-010-0319-4. PubMed PMID: 21104041.
- Yılmaz M, Kayançiçek H, Çekici Y. Heart rate variability: Highlights from hidden signals. J Integr Cardiol. 2018;4:1-8.
- 23 Deng Y, Zeng X, Tang C, Hou X, Zhang Y, Shi L. The effect of exercise training on heart rate variability in patients with hypertension: A systematic review and meta-analysis. J Sports Sci. 2024;42:1272-87. doi: 10.1080/02640414.2024.2388984. PubMed PMID: 39115012.
- 24 Dorey TW, O'Brien MW, Kimmerly DS. The influence of aerobic fitness on electrocardiographic and heart rate variability parameters in young and older adults. Auton Neurosci. 2019;217:66-70. doi: 10.1016/j. autneu.2019.01.004. PubMed PMID: 30744904.
- 25 de Andrade PE, Zangirolami-Raimundo J, Morais TC, De Abreu LC, Siqueira CE, Sorpreso ICE, et al. Cardiac Behavior and Heart Rate Variability in Elderly Hypertensive Individuals during Aerobic Exercise: A Non-Randomized Controlled Study. Int J Environ Res Public Health. 2023;20. doi: 10.3390/ijerph20021292. PubMed PMID: 36674046; PubMed Central PMCID: PMCPMC9859152.
- 26 Dor-Haim H, Lotan C, Horowitz M, Swissa M. Intensive Exercise Training Improves Cardiac Electrical Stability in Myocardial-Infarcted Rats. J Am Heart Assoc. 2017;6. doi: 10.1161/JAHA.117.005989. PubMed PMID: 28733433; PubMed Central PMCID: PMCPMC5586305.

- 27 Eijsvogels TM, Thompson PD. Exercise Is Medicine: At Any Dose? JAMA. 2015;314:1915-6. doi: 10.1001/jama.2015.10858. PubMed PMID: 26547459.
- 28 Sharma S, Merghani A, Mont L. Exercise and the heart: the good, the bad, and the ugly. Eur Heart J. 2015;36:1445-53. doi: 10.1093/eurheartj/ehv090. PubMed PMID: 25839670.
- 29 Lavie CJ, Arena R, Swift DL, Johannsen NM, Sui X, Lee DC, et al. Exercise and the cardiovascular system: clinical science and cardiovascular outcomes. Circ Res. 2015;117:207-19. doi: 10.1161/CIRCRESAHA.117.305205. PubMed PMID: 26139859; PubMed Central PMCID: PMCPMC4493772.
- 30 Wong V, Song JS, Bell ZW, Yamada Y, Spitz RW, Abe T, et al. Blood flow restriction training on resting blood pressure and heart rate: a meta-analysis of the available literature. J Hum Hypertens. 2022;36:738-43. doi: 10.1038/s41371-021-00561-0. PubMed PMID: 34140637.
- 31 Zhang T, Tian G, Wang X. Effects of Low-Load Blood Flow Restriction Training on Hemodynamic Responses and Vascular Function in Older Adults: A Meta-Analysis. Int J Environ Res Public Health. 2022;19. doi: 10.3390/ijerph19116750. PubMed PMID: 35682336; PubMed Central PMCID: PMCPMC9180641.
- 32 Saco-Ledo G, Valenzuela PL, Ruiz-Hurtado G, Ruilope LM, Lucia A. Exercise Reduces Ambulatory Blood Pressure in Patients With Hypertension: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. J Am Heart Assoc. 2020;9:e018487. doi: 10.1161/JAHA.120.018487. PubMed PMID: 33280503; PubMed Central PMCID: PMCPMC7955398.
- 33 Domingos E, Polito MD. Blood pressure response between resistance exercise with and without blood flow restriction: A systematic review and meta-analysis. Life Sci. 2018;209:122-31. doi: 10.1016/j. lfs.2018.08.006. PubMed PMID: 30086274.
- 34 Pope ZK, Willardson JM, Schoenfeld BJ. Exercise and blood flow restriction. J Strength Cond Res. 2013;27:2914-26. doi: 10.1519/JSC.0b013e3182874721. PubMed PMID: 23364292.
- 35 Su Y, Wang F, Wang M, He S, Yang X, Luan Z. Effects of blood flow restriction training on muscle fitness and cardiovascular risk of obese college students. Front Physiol. 2023;14:1252052. doi: 10.3389/fphys.2023.1252052. PubMed PMID: 38235388; PubMed Central PMCID: PMCPMC10791898.

- 36 Laurence P, Hanney WJ, Purita J, Graham A, Kolber M. Blood flow restriction training: a potential adjunct to orthobiologic procedures. Biologic Orthopedics Journal. 2022;4:e142-e63.
- 37 Lopes KG, Farinatti P, Bottino DA, de Souza M, Maranhao P, Bouskela E, et al. Exercise with blood flow restriction improves muscle strength and mass while preserving the vascular and microvascular function and structure of older adults. Clin Hemorheol
- Microcirc. 2022;82:13-26. doi: 10.3233/ CH-221395. PubMed PMID: 35599474.
- 38 Bane A, Wilson L, Jumper J, Spindler L, Wyatt P, Willoughby D. Effects of Blood Flow Restriction Resistance Training on Autonomic and Endothelial Function in Persons with Parkinson's Disease. J Parkinsons Dis. 2024;14:761-75. doi: 10.3233/JPD-230259. PubMed PMID: 38701159; PubMed Central PMCID: PMCPMC11191514.