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The Effect of Low-Intensity Interval Exercise with Blood Flow Restriction on Plasma Cardiac Troponin: A Cross-Design Trial

ABSTRACT

Background: Low-intensity training with blood flow restriction (BFR) training could induce endurance adaptations, its impact on myocardial markers is still unclear compared to training without BFR. Consequently, the influence of low-intensity interval exercise with and without BFR and high-intensity interval exercise (HIIE) on cardiac troponin was determined in this study.

Methods: Twelve physically active males between 18 and 26 years volunteered as participants. The participants completed 3 exercise tests in random order, which included 40% VO_{2max} low-intensity cycling without BFR (group L), 40% VO_{2max} low-intensity cycling with BFR set at 60% limb occlusion pressure (LOP) (group B), and 80% VO_{2max} high-intensity cycling without BFR (group H). Participant muscle oxygen, blood flow, oxygen uptake, heart rate (HR), perceived exertion (RPE) rating, and pain levels were determined before and after exercise, after cuff inflation, and pre- and post-each exercise. Moreover, before each protocol, immediately after the exercises, and 3-4 hours after each exercise, elbow vein blood samples were collected to evaluate lactate (LA) and high-sensitivity cardiac troponin T (cTnT).

Results: Increased LA was recorded after exercise by the individuals in group H, which was more significant than in group B. Moreover, group B documented a more significant LA increment than group L ($P < .05$). The peak cTnT of groups B and H after exercise was significantly higher ($P < .05$). Furthermore, the increase was more significant than the values recorded by group L ($P < .05$).

Conclusion: The present study demonstrated that low-intensity interval exercise combined with BFR could cause cTnT elevations compared to training without BFR. The increase was similar to HIIE protocols.

Keywords: Blood flow restriction, low-Intensity interval exercise, cardiac troponin

INTRODUCTION

Acute intense physical activities could lead to slight and temporary cardiac-specific biomarker increments, including numerous cardiac troponin and myocardial infarction diagnostic indicators.[1,2] The intensity[3] and period[4] of exercises, an individual's training experience,[5] age,[6] and gender,[7] and hypoxic surrounding[8] affect cardiac troponin levels. Although enhanced transient myocardial membrane permeability could be the reason, the mechanism remains unknown.[9]

Oxidative stress is due to imbalances in the reactive oxygen species (ROS) production and clearance by the antioxidant defense system. The phenomenon is a crucial factor that leads to increased myocardial cell membrane permeability.[9] Richardson et al[10] also reported that cardiac troponin is linked to average and peak heart rates during workouts.

Blood flow restriction (BFR) exercise, also known as "KAATSU," is an emerging form of exercise that can increase metabolic pressure during exercise by limiting blood flow to the limbs, leading to an increase in anaerobic metabolism levels.[11] A study has shown that BFR can increase ROS levels and heart rate in the circulatory system after exercise.[12] Combining physical activities and BFR has gained interest

ORIGINAL INVESTIGATION

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as an effective training model to enhance muscle strength[13] and endurance improvements[11] without requiring significant external load.

Low-intensity BFR interval endurance training is correlated to enhanced blood lactate (LA) accumulation and maximal oxygen uptake (VO_{2max}),[14] similar to conventional high-intensity interval exercise (HIIE)[15,16] reported that combining low-intensity interval exercise with BFR could improve aerobic capacity and provide superior muscle hypoxia and metabolic strain with a smaller subjective perception than continuous BFR exercises. Although study[9] demonstrated that BFR training could induce endurance adaptations with low-intensity training, its impact on myocardial markers is still unclear compared to those without BFR. Consequently, the influence of low-intensity interval exercise with and without BFR and HIIE on cardiac troponin was determined in this study.

METHODS

Participants

In the current study, 12 physically active male university basketball players between 18 and 26 years volunteered as participants. The individuals reported performing moderate to high-intensity aerobic exercises for a minimum of 150 min/week per the American College of Sports Medicine (ACSM) guidelines.[17] A bioelectrical impedance analyzer (Inbody 770, South Korea) assessed the participants' body composition.

Participants who utilized nicotine products or suffered from diabetes, peripheral vascular disease, or any cardiopulmonary illnesses were excluded from the study. After the preliminary screening, the aims and risks of the study were explained to the participants.

Experimental Design

The crossover experiment in the present study required the participants to visit the laboratory 4 times at a minimum of 48 hour intervals. The individuals were asked not to perform vigorous physical activity for 24 hours before each meeting. A hot, neutral environment and approximately similar times were maintained throughout the data collection.

The participants familiarized themselves with the assessment protocols during initial laboratory visits. The individuals also completed a graded physical activity protocol to determine their VO_{2max}. During the subsequent visits, the participants completed 3 physical activity protocols in random order, which included 40% VO_{2max} low-intensity cycling without BFR (group L), 40% VO_{2max} low-intensity cycling with BFR set at 60% limb occlusion pressure (LOP) (group B), and 80% VO_{2max} high-intensity cycling without BFR (group H). (Figure 1).

The exercise plans utilized in the current study were chosen to represent current aerobic exercise guidelines that incorporated or did not incorporate BFR.[18] Participant muscle oxygen, blood flow, oxygen uptake (VO_2), HR, perceived exertion (RPE) rating, and pain levels were determined before and after exercise, after cuff inflation, and pre- and post-each exercise. Moreover, before each protocol, immediately after the exercises, and 3 and 4 hours after each exercise, elbow vein blood samples were collected to evaluate lactate (LA) and high-sensitivity cardiac troponin T (cTnT).

The VO_{2max}

A gradient cycling procedure that started at 60 W (pedal frequency = 60 rpm) was implemented to assess VO_{2max} values in the present study. The power output was increased by 40 W (male) and 20 W (female) every 2 minutes until the participants were exhausted. The HR and VO_2 of the participants were determined with an HR monitor (H12, Polar, Finland) and a gas metabolism analyzer (Quark-PFT, COSMED, Italy), respectively. The procured VO_{2max} denoted the most significant mean values in 30 seconds.

Exercise Protocol

Before the intermittent cycling protocol, the participants were asked to rest on the cycle ergometer for 5 minutes to obtain their baseline (Pre) responses. Subsequently, the cuffs were inflated to 60% LOP (only group B) during a 1 minute rest. The exercise protocols of groups L and H included a 1 minute rest. The individuals were required to complete 18 sets of 2 minute cycling intervals with a 1 minute rest between sets.

The intermittent cycling procedure in the present study was based on the hypothesis that work-rest intervals with inflated pressure cuffs are advantageous over continuous cycling when considering the incorporation of BFR.[16] For the cycling conditions that included BFR, the blood flow in each leg was restricted with a 7 cm wide nylon inflatable cuff (The Occlusion Cuff, Belfast, Britain). The cuff was positioned around the thigh at the most proximal location. The pressure in the cuff was sustained throughout the workout before being deflated immediately upon completion of the last cycling set.

Blood flow

This study determined blood flow in the superficial femoral artery, distal to the pressure cuff. Blood velocity (V_{mean}) and vessel diameter (V_d) were assessed with a Logiq E ultrasound system (General Electric Medical Systems, Milwaukee, United States). The ultrasound system had a linear array transducer operated at 12 MHz imaging and 5 MHz Doppler frequencies.

The Doppler pulse wave spectra and ultrasound images were documented throughout the experiment. The V_d values were obtained by averaging the perpendicular distance between the superficial and deep walls of the superficial femoral artery at 3 non-consecutive R waves during the final 15 seconds of each recording.

HIGHLIGHTS

- Blood flow restriction can cause an increase in cardiac troponin.
- Low-intensity exercise with blood flow restriction induces elevated cardiac troponin similar to high-intensity exercise.
- Blood flow restriction exercise causes higher levels of pain.

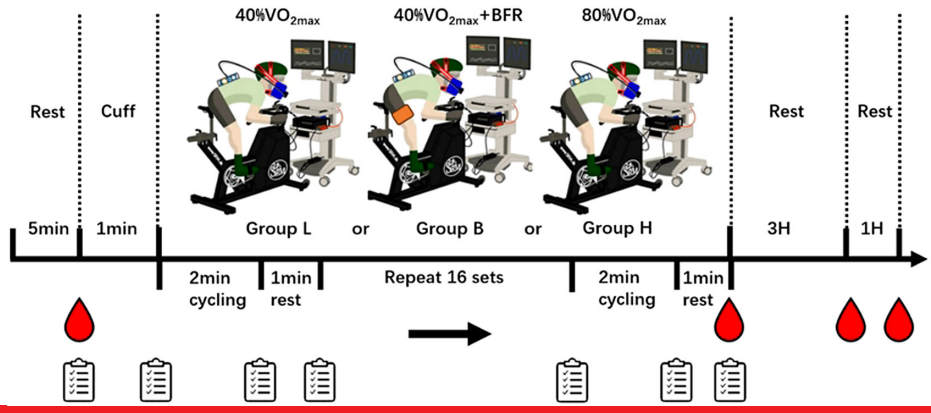

Figure 1. Cycling test flow chart. The blood droplet diagram represents the time of blood collection; the recording chart represents blood flow, oxygen uptake, heart rate, and scale testing.

The V_{mean} was established by positioning the probe to maintain a ≤60° insonation angle. The mean V_{mean} was averaged across 15 second intervals during the recording. Blood velocity data obtained with Doppler ultrasound are reliable,[19] which is critical due to its complexity during dynamic muscle contractions. Blood flow was calculated utilizing the V_d and V_{mean} according to Equation 1.[20] The mean blood flow was also procured during the 1 minute rest intervals.

$$\text{Blood flow} = V_{mean} \times \pi \times V_d / 2 \times 60 \quad (1)$$

The Limb Occlusion Pressure

The present study employed an ultrasonic pocket Doppler (Edan, Northampton, Britain) to determine the participants' leg arterial occlusive pressure (mmHg). Each individual sat on the cycle ergometer with Doppler probes placed on their tibial artery to record auscultation pulses.[21] Subsequently, the cuff was positioned within the thigh–groin region before being inflated slowly. When auscultation pulse interruptions were detected, the cuff pressure was recorded as the LOP.

Tissue Oxygenation

A continuous-wave near-infrared spectroscope (PortaLite; Artinis Medical Systems BV, Netherlands) was utilized to detect oxygenated and deoxygenated hemoglobin concentration alterations of the participants in the present study. The LEDs of the device emitted 760 and 850 nm wavelengths with a 3.5 cm inter-optode distance. The data were collected at 10 Hz. A 4.0 differential path length factor was also employed to correct photon scattering within the evaluated tissues.

The sensor on the spectroscope was positioned parallel to the muscle fibers between the anterior superior iliac spine and the proximal patella. A double-sided tape was attached to the sensor before wrapping it in an opaque bandage to prevent ambient light from reaching it. The oxy- and deoxy-hemoglobin tissue saturation indexes (TSI) were calculated with integrated software (Oxysoft; Artinis Medical Systems BV, Netherlands). The average TSI was recorded over the last 10 seconds of each exercise protocol.

Cardiorespiratory and Perceptual Responses

Oxygen utilization and HR of the participants in the present study were obtained with the metabolic assessment system previously mentioned. The data over the final 30 seconds of the training and recovery procedures were averaged. Perceptual responses, which included RPE and pain, were obtained during the last 30 seconds of each exercise protocol and recovery period. The complete body RPE was evaluated utilizing a Borg 6-20 scale, while the pain was determined with an 11-point numeric rating scale.[22]

Blood Collection

Each sample in the current study consisted of 5 mL of venous blood procured from the antecubital vein. Venipunctures were conducted while the participants were in a seated position. Subsequently, LA levels were assessed with a portable lactate analyzer (EKF, Lactate Scout 4, Germany) calibrated per the instructions outlined by the manufacturer before each evaluation.

The blood specimens were centrifuged at 3500 g for 20 minutes. The plasma components were drawn and stored at −80℃ before further cTnT assessments. The cTnT data procured were quantitatively determined with a novel elect rochemiluminescence technology-based high-sensitivity immunoassay. The Cobas E 601 analyzer (Roche Diagnostics, Penzberg, Germany) utilized could assess between 3 and 10 000 ng/L samples with a 3 ng/L lower detection limit.

This study documented serum cTnT concentrations under the detection limit of 1.5 ng/L.[7] The 13.5 ng/L documented a 5.2% variation coefficient mean cTnT concentration. The upper reference limit (URL) for cTnT, the 99th percentile of healthy participants, was 14 ng/L.[23]

Statistical Analysis

The current study employed the Kolmogorov–Smirnov assessment to evaluate data normality. The cTnT at Pre and across Post, 3 and 4 hours post-exercise time points and 3 intensities, were compared with the post-hoc tests for Friedman due to the skewed data distribution. Groups L, B, and H cTnT values were compared via the post-hoc tests for Kruskal–Wallis. Fisher's exact test compared the percentages of subjects with cTnT over the 3 ng/L limit of detection and the 14 ng/L URL in each assessment.

A 3 × 6 repeated measures analysis of variance (ANOVA) on time was employed to determine blood flow alterations

across the 3 groups from baseline to post-exercise. A 3 × 10 2-way repeated measures ANOVA was also conducted to determine HR, VO_2, TSI, RPE, and pain differences during exercise between the groups and 10 time points (pre, cuff, E1, R1, E6, R6, E12, R12, E18, and R18). The present study also conducted post hoc evaluations with the Newman–Keuls test when the primary effects were notable. Statistical significance was assumed at $P < .05$. A statistical software package, SPSS 22.0 (IBM Corp., Armonk, New York, United States of America), was employed for data analysis. We did not use any artificial intelligence-assisted technology in the production of the submitted work.

RESULTS

Participants' Physical Characteristics

Table 1 summarizes the physical attributes of the participants in this study. All 12 individuals completed all the assessments and exercise protocols without adverse events. Cuff pressures for group B during cycling were 120.8 ± 5.7 mm Hg.

Table 1. The Physical Characteristics of the Participants

Items	
Age (years)	20.6 ± 1.6
Weight (kg)	89.4 ± 7.3
Height (cm)	194.5 ± 9.4
BMI (kg/m^2)	23.9 ± 3.5
Fat (%)	21.6 ± 1.8
LOP (mm Hg)	201.3 ± 9.5
VO_{2max} (mL/min/kg)	52.3 ± 4.9

BMI, body mass index; VO_{2max}, maximal oxygen uptake.

The mean power outputs for groups L and B were 95.6 ± 6.8 W, while group H recorded 238.6 ± 15.8 W under the cycling condition.

Blood Flow and Tissue Saturation Index

Figures 2a and b demonstrate blood flow and TSI alterations before and after each exercise. The repeated ANOVA

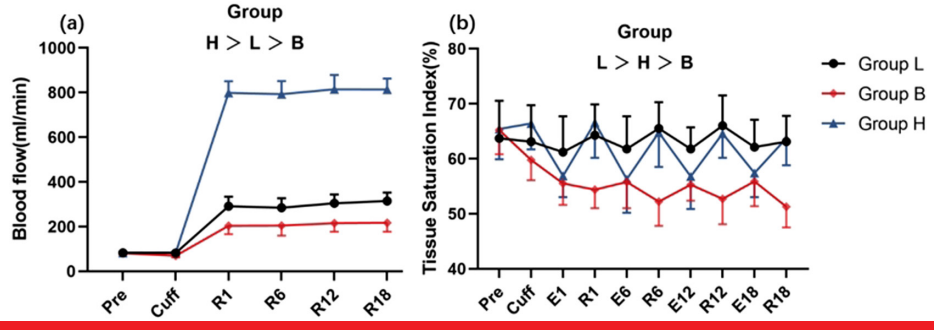

Figure 2. Fluctuations in blood flow and TSI pre- and post-exercise protocols according to group.

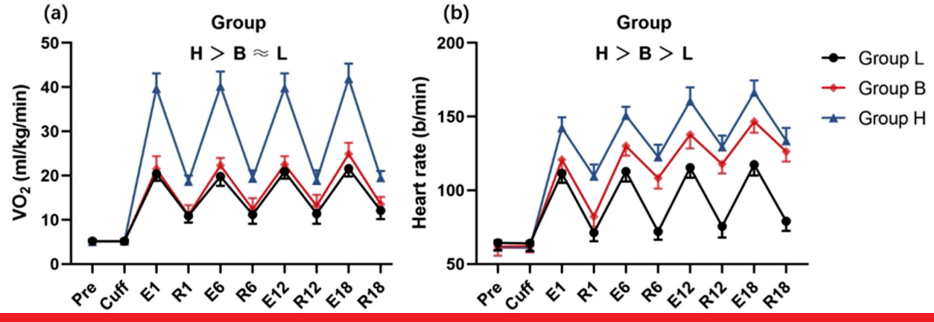

Figure 3. Changes in VO_2 and HR levels before and after exercise in each group.

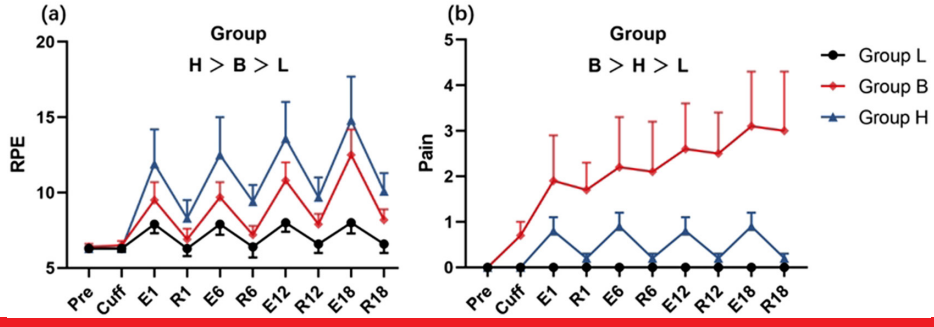

Figure 4. Comparisons of RPE and pain levels before and after training in each group.

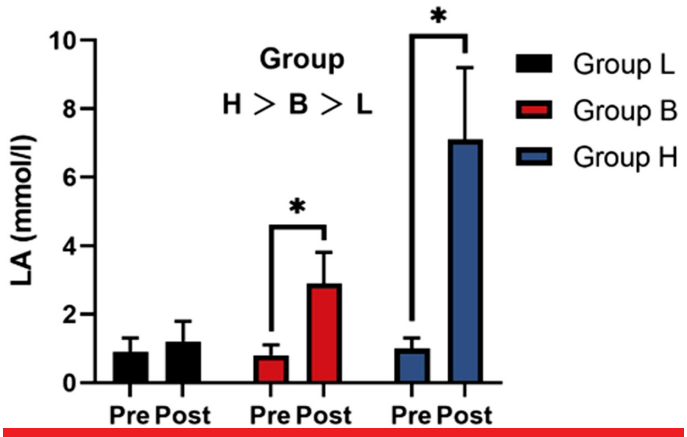

Figure 5. The LA alterations before and after exercise in each group. LA, lactate; *significantly different from the corresponding baseline (pre).

measures revealed significant primary effects in each group ($P < .05$) and time ($P < .05$) and group × time interaction ($P < .05$) on blood flow and TSI. Generally, group B exercise protocol participants recorded lower blood flow than group L. Moreover, the blood flow of group H was notably higher than groups L and B ($P < .05$). On the other hand, TSI was higher in groups L and H than in group B ($P < .05$).

Cardiorespiratory and Perceptual Responses

Figures 3a and 3b and 4a and 4b illustrate the changes in VO_2, HR, RPE, and pain pre- and post-training. The repeated measures analysis of variance (ANOVA) results revealed considerable effects of group ($P < .05$) and time ($P < .05$) and group × time interactions ($P < .05$). All groups also documented a general VO_2 "sawtooth" pattern, while group H ($P < .05$) recorded the highest value due to the intermittent nature of the cycling protocol.

The HR and RPE levels recorded by group H were notably higher than those of groups B and L. The participants reported lower pain levels during groups L and H exercises than in group B ($P < .05$). Furthermore, pain levels reported by individuals performing exercise protocols in group B rose steadily and were almost at maximum values at the end of the final interval.

The Lactate Levels

Comparisons of LA before and after exercise in each group are demonstrated in Figure 5. No statistically significant difference in Pre values was observed among the groups before exercise. Nevertheless, the LA concentrations documented by participants during groups B and H exercises significantly increased ($P < .05$) after the physical activities. Repeated ANOVA measures indicated notable group interaction effects ($P < .05$). Increased LA was also recorded after exercise by the individuals in group H, which was more significant than in group B. Moreover, group B documented a more significant LA increment than group L ($P < .05$).

High-sensitivity cardiac troponin T

The cTnT data for each group at Pre and after-cycling (Post, 3, and 4 hours) are presented in Table 2, while Figure 6 exhibits the individual data points. The plasma cTnT concentrations of individuals 3 and 4 hours after performing groups B and H protocols were significantly higher than before exercise ($P < .05$) and group L at similar time points ($P < .05$). A 1 cTnT positive rate documented by the participants in groups B and H at 3 and 4 hours post each training protocol was considerably higher than before exercise ($P < .05$). Similarly, a cTnT positive rate in groups B and H was notably higher than in group L after 3 hours of exercise ($P < .05$). In Figure 6, the peak cTnT of groups B and H after exercise was significantly higher ($P < .05$). Furthermore, the increase was more significant than the values recorded by group L ($P < .05$).

DISCUSSION

The current study assessed low-intensity interval exercise with BFR effects on cardiac troponin in active adult men. Nonetheless, a relatively moderate cuff pressure was applied to prevent dizziness or severe pain in the cuff area due to excessive BFR pressure.[24] Primarily, the findings indicated that BFR exercises led to increased cTnT levels compared to without BFR. Even in low-intensity interval exercise, when used in combination with BFR, cTnT elevation exceeding the threshold can be observed in clinical diagnosis. Although cTnT increments during BFR training were similar to HIIE at identical periods, BFR caused higher body pain than HIIE.

In the present study, the resting cTnT prevalence over the 3 ng/L assay detection limit was 25% (9 of 36). The value demonstrated similarity to the data reported by de Lemos et al.[25] The BFR protocols also resulted in higher HR and RPE, consistent with the findings noted by Chen et al[26] and Li et al.[27] Most participants (86.1%, 31 of 36) demonstrated enhanced cTnT after

Table 2. Plasma cTnT Levels During the Exercises in Each Group

Median (Range)	Pre	Post	3H	4H
Group L (ng/L)	1.5 (1.5-4.1)	1.5 (1.5-4.2)	3.3 (1.5-6.5)	3.1 (1.5-5.4)
Group B (ng/L)	1.5 (1.5-4.7)	3.3 (1.5-6.8)	5.5 (3.0-15.7)*#	5.0 (1.5-12.6)*#
Group H (ng/L)	1.5 (1.5-3.6)	3.4 (1.5-6.6)	7.0 (3.5-18.9)*#	7.3 (3.1-23.9)*#
Positive rate 1 / 2				
Group L (%)	25.0/0	41.7/0	41.7/0	66.7/0
Group B (%)	33.3/0	58.3/0	100*#/8.3	83.3*/0
Group H (%)	16.7/0	66.7/0	100*#/8.3	100*/16.6

H, hours, positive rate; 1, percentage of participants with serum high-sensitivity cTnT over the 3 ng/L limit of detection; positive rate 2 percentage of subjects with serum high-sensitivity cTnT exceeding the 14 ng/L URL. *remarkably different from corresponding Pre, #significantly different from the corresponding group L.

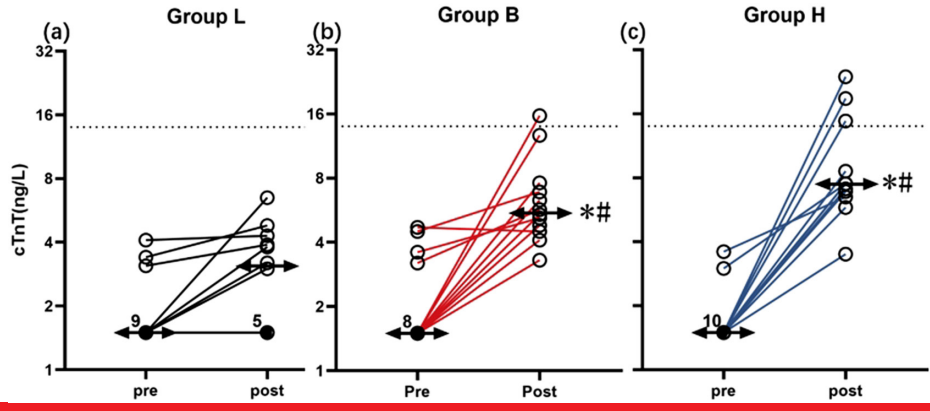

Figure 6. Pre- and peak post-exercise (Post) cTnT levels after cycling in each group. Individual data points are presented as circles with values for each condition documented by a participant and are connected by lines; a logarithmic scale was employed due to data spread, the horizontal dotted line is the 99th percentile value, the double-headed arrow denotes the cTnT median values of each exercise, *notably varied from corresponding Pre; #substantially different from the corresponding group L.

exercise. Nonetheless, only 11.1% (4 of 36) exceeded the URL (14 ng/L), which was lower than the results (83%) of a meta-analysis that employed similar high-sensitivity assays.[28]

A higher cardiac load could increase cTnT levels.[29] Consequently, the findings in this study were expected as the total myocardial work was low relative to previous reports that involved endurance tasks lasting several hours, days, and weeks.[30] Some studies[31,32] also applied similar HIIE (28 and 18 minute durations, respectively) and reported identical cTnT increments. The findings suggested that exercise-induced increased cTnT might occur even after a standard exercise recommended by public health guidelines[33] and not exclusive to high-intensity and ultra-endurance efforts.

In this study, almost all participants showed an increase in cTnT after exercise, but most cTnT data were below the population reference limit of 14 ng/L. These findings suggest that the exercise-induced increase in cTnT may be mandatory, representing a reversible non-pathological increase in cTnT after exercise.[5] In addition, there are still individual participants in groups B and H whose cTnT levels have increased to above 14 ng/L, which is of practical significance for clinical diagnosis. When making a diagnosis, clinical doctors should be aware that BFR exercise, like high-intensity exercise, is common in causing an increase in cTnT. Understanding the patterns of cTnT release after exercise can help clinicians interpret these data in the clinical environment after exercise and avoid misdiagnosis.

The mechanisms contributing to exercise-induced enhanced cTnT levels remain unclear, considering no direct human evidence is available. Nevertheless, the animal study[34] aligned with the hypothesis that an increased ROS could lead to a reversible membrane "insult," resulting in transient cytoplasmic cTnT leakages from cardiomyocytes. Cocking et al[35] provided the first indirect evidence of myocardial ischemia roles in exercise-induced cTnT elevations in a study employing a remote ischemic preconditioning model in healthy individuals. Nevertheless, the study also noted that other potential mechanisms could not be ruled out.

Although ROS are involved in harmful biological events, a moderate concentration might be essential for optimal cell functions and signal transductions.[36] In this study, the BFR protocol led to significantly increased cTnT, possibly due to elevated ROS.[12] found that combining low load resistance with a 50% LOP BFR considerably improved systemic ROS in healthy adult males compared to those without BFR. Nonetheless, some studies reported opposing observations, where BFR did not increase ROS.[37]

Fluctuations in LA levels could improve cTnT levels following BFR exercises. The training protocol could induce local hypoxia and increase lactate accumulation, while intermittent exercise could restore LA accumulated during exercise.[27] Consequently, intermittent BFR might result in LA fluctuations. Periodic LA concentration alterations could also reflect systemic acid-base and electrolytic balance changes.[38,39] Furthermore, inflammatory reactions might arise from an acute-phase response to muscle damage mediated by LA elevations.[39,40]

Acid-base or electrolyte changes and inflammatory reactions could improve cardiomyocyte cell membrane permeability, which could cause cTnT leakages from the cytosol to the blood and mild cTnT increments, which was observed immediately after a race.[41] The average and peak HR during exercise are also closely linked to cTnT secretion.[10] Elevated HR during BFR might contribute to enhanced cTnT levels.

The present study had numerous limitations. Firstly, only physically active males were employed as participants due to the high intensity of exercises involved, excluding other populations. The cTnT samples were only obtained at 3 and 4 hours after each exercise due to individual peak value differences; thus, they might not accurately reflect actual data. Moreover, the present study only assessed one of multiple subtypes of cardiac troponin. Consequently, the limit for detecting high-sensitivity cTnT was set at 1.5 ng/L. This study did not determine cTnT release mechanisms induced by BFR exercises and was only inferred from previous reports. Future investigations should consider further increasing the sample population, evaluating multiple time points and

indicators, and verifying BFR mechanisms that enhanced cTnT levels.

CONCLUSION

The present study demonstrated that low-intensity interval exercise combined with BFR could cause cTnT elevations compared to training without BFR. The increase was similar to HIIE protocols. Therefore, for athletes who are unable to engage in high-intensity sports due to injuries or other reasons, low-intensity exercises with BFR can be considered a potential alternative solution.

Data Availability Statement: The data underlying this paper, which includes the privacy of the individuals involved, cannot be made public for the following reasons. These data will be shared with the respective authors upon reasonable request. If you need the data, you can contact me via my email: gks191108@gmail.com.

Ethics Committee Approval: The study was conducted in accordance with the Declaration of Helsinki and approved by the Ocean University of China Ethical Committee (Approval ID: OUC-HM-2021016, Date: 21-07-2021), China. This study has completed clinical trial registration at ISRCTN on 24 January 2024 (Number: ISRCTN59736069).

Informed Consent: All subjects were informed about the study protocol and signed an informed consent form before participating in the study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – L.G., W.Y.; Design – L.G., W.Y.; Supervision – L.G.; Resources – J.M.; Materials – Z.C.; Data Collection and/or Processing – J.Z., R.G.; Analysis and/or Interpretation – J.Z., R.G.; Literature Search – J.Z., J.M.; Writing – J.Z., R.G.; Critical Review – L.G., W.Y.

Declaration of Interests: The authors have no conflict of interest to declare.

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