

# Effects of Blood Flow Restriction During Rest From High-intensity Training on Muscle Hypertrophy and Muscle Strength

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## Research article

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# Abstract

**Background:** The present study investigated the effects of different timings of BFR during HIT on muscle hypertrophy, muscle strength, and pain during exercise.

**Methods:** The study included 14 limbs from seven healthy males. Participants were divided into three groups: BFR during exercise (EX); BFR during rest (RE), and training only (CON). Participants performed elbow flexion exercises by BIODEx, two days / week for eight weeks. BFR was set at 120 mmHg pressure. Elbow flexor peak torque, and muscle cross-sectional area were measured, before and after the training period. The pain during exercise were measured during training.

**Results:** The peak torque was significantly increased the RE and CON ( $p < 0.05$ ), but no increase was observed in the EX. Exercise repetitions the RE (set 1,  $26.5 \pm 8.7$  reps; set 2,  $15.2 \pm 8.0$  reps; set 3,  $13.1 \pm 4.7$  reps; set 4,  $13.8 \pm 6.3$  reps) decreased two sets earlier than the CON (set 1,  $28.0 \pm 8.6$  reps; set 2,  $25.6 \pm 7.5$  reps; set 3,  $24.4 \pm 8.2$  reps; and set 4,  $23.8 \pm 7.2$  reps) ( $p < 0.01$ ). The numerical rating scale was higher in the EX during exercise and in the RE during rest compared with the CON. However, the RE did not show exacerbated pain during exercise ( $p < 0.01$ ).

**Conclusions:** This present study showed that BFR during rest can lead to muscle hypertrophy and muscle strength with fewer exercise repetitions than training only. BFR during rest showed the greatest decreases in peak torque during exercise and did not exacerbate pain during exercise.

## Background

The American College Sports Medicine suggested that training for muscle hypertrophy and muscle strength should be performed at  $> 70\%$  of one-rep max (1RM) [1]. However, low-mechanical stress training (e.g., low-intensity training, walking) with blood flow restriction (BFR) or fatigue increased muscle hypertrophy and muscle strength [2–5]. Mechanical and metabolic stress affects muscle hypertrophy and muscle strength in response to exercise [6–8], and the contribution of both stresses affects muscle hypertrophy. Therefore, increasing metabolic stress is thought to compensate for low-mechanical stress and lead to muscle hypertrophy [9].

Studies into the effect of different training intensities on muscle hypertrophy and muscle strength have shown that equal volumes of training performed at different intensities (20%, 40%, 60%, and 80% 1RM) led to muscle hypertrophy at 80% 1RM, increased muscle strength with 60% 1RM, and 80% 1RM showed a greater effect than 20% 1RM (Lasevicius et al. 2018). Another study compared high-intensity training (HIT;  $>60\%$  1RM) with low-intensity training (LIT;  $<60\%$  1RM) and showed that while muscle hypertrophy was induced equally with both HIT and LIT, muscle strength increased to a greater extent with HIT (Schoenfeld et al. 2017). Therefore, high-mechanical stress should induce higher muscle hypertrophy and muscle strength, and training that increases both stresses is expected to induce greater muscle hypertrophy and muscle strength. However, HIT with BFR revealed that BFR does not affect peak torque,

muscle activity, muscle hypertrophy, and muscle strength after exercise [10–14]. Therefore, while HIT with BFR is not considered useful, these results show the effect of performing BFR during or after exercise.

It was recently reported that HIT with BFR during rest increases metabolic stress and decreases muscle activation to a greater extent than under conditions of natural blood flow or BFR during exercise [15]. Furthermore, BFR affects muscle function without combined exercise because BFR only prevents muscle atrophy [16, 17] and BFR alone affect muscle function and shape. We hypothesized that BFR during rest in HIT would increase both stresses, and that the effect of BFR would increase muscle hypertrophy and muscle strength. Previous studies into BFR during rest have only shown acute effects, and it is not obvious whether muscle hypertrophy and muscle strength are affected. It is thought that versatility can be improved by solving issues such as discomfort and pain during exercise [18] as well as restriction of movement. The present study investigated the effects of different timings of BFR during HIT on muscle hypertrophy, muscle strength, and pain during exercise.

## Methods

### Participants

The present study included 14 arms from seven healthy males (age,  $23.6 \pm 1.0$  years; height,  $173.5 \pm 5.5$  cm; weight,  $66.4 \pm 4.7$  kg) with no history of injury to the upper arm muscle and not habitually training. Participants were instructed not to perform upper arm training until completion of this study. The purpose, methods, procedures, risks, and compensation for this study were explained to the participants verbally and in writing, and all participants gave informed consent. The study was conducted according to the guidelines of the Declaration of Helsinki and was approved by the Ethics Committee for Human Experiments of Juntendo University, Japan (No. 30–28).

### Design

Participants visited the laboratory three to five times for premeasurements before starting training. The cross-sectional area (CSA) of the biceps was measured first, followed by the elbow flexor strength, which was measured two times. The muscle endurance of the elbow flexor was then measured, followed by peak torque, and magnetic resonance imaging (MRI) of the elbow flexors was performed either on the same day or another day. If the measurements were made on the same day, MRI was performed first. Participants were divided into three groups: BFR during exercise (EX); BFR during rest (RE); and training only (CON). Training involved elbow flexor exercises using an isokinetic strength training device (BIODEX system3; BIODEX Medical Systems, Shirley, NY, USA) two days per week for eight weeks (for a total of 16 sessions). Brachial biceps CSA, peak torque, and muscle endurance of elbow flexor were measured after training for eight weeks (Experiment 1). Afterwards, all participants performed training under three conditions (EX, RE, and CON) for an eight-week training period (Experiment 2).

### Experiment 1

# Training protocol

Training included performing elbow flexor exercises using a BIODEX device. Participants performed an elbow flexion exercise at 60 degrees/s under concentric contraction at 60 degrees/s (CC60) with a range of motion (ROM) of 120 degrees (full extension = 0 degrees). The standard for the end of training was based on a previous study [15], and was performed until the participant could not complete torque > 50% of peak torque of the CC60 premeasurement two times consecutively (one set). Training was performed with a 3-min rest between each set and was performed as four sets per day, two days per week for eight weeks.

## BFR

BFR to the proximal upper arm was restricted using a cuff (width, 77 mm; length, 770 mm, MIZUHO, Tokyo, Japan) using a pressure of 120 mmHg (almost 100% of systolic blood pressure) as described previously [19]. The RE underwent BFR only training during rest, whereas the EX underwent BFR only during training.

## Peak torque

Before and after (pre and post) training, changes in peak torque of the elbow flexor were measured by isotonic and isometric contraction with BIODEX. Measurements were made with participants in a sitting position, with two belts fixed on the shoulder and one on the abdomen. Measurements were made at CC60, CC120, and CC240, eccentric contraction at 60 and 120 degrees/s (EC60, 120), and isometric contraction (IM) at 90 degrees/s flexion positions with an elbow flexion ROM of 120 degrees.

Muscle strength test–retest reliability was made using an intraclass correlation coefficient (ICC) at EC120 (0.588), EC60 (0.902), IM (0.959), CC60 (0.942), CC120 (0.960), and CC240 (0.942). The peak torque was recorded during exercise for each set to evaluate training.

## Muscle endurance

Before and after training, changes in muscle endurance of the elbow flexor under isotonic contraction were measured using a BIODEX device. Participants performed elbow flexion exercises at CC120 for 30 reps and the decrease in rate of total work over this time was used as an index of muscle endurance. The rate of decline was calculated from the work volume of the first (1–10 reps) and last (21–30 reps) thirds of the exercise.

## Muscle CSA

Before and after, training changes in the muscle CSA of brachial biceps were measured using MRI (E-scan XQ; 0.2T, ESAOTE, Genoa, Italy). Measurements were made at 50% and 60% distal between the lateral epicondyle to the acromial process using T1-weighted MRI using the spin-echo method (TR, 740 msec; TE, 18 msec; NEX, 2; MATRIX, 192 × 192; FOV, 170 × 170 mm, slice number, 28; slice width, 5 mm). Osirix open-software (Pixmeo SARL, version: 10.0.0, Switzerland) was used to calculate muscle CSA.

Measurements were made twice before the study and the coefficient of variation was confirmed to be within 2%. Measurements made after the study were performed three days after completion of the training. The participants rested in a supine position for 30 min before the measurements were made. CSA test–retest reliability was assessed using ICC at the 50% (0.999) and 60% (1.000) sections.

## **Muscle thickness**

During training, changes were measured in the brachial biceps thickness using a Noblus diagnostic ultrasound imaging system (Hitachi Aloka Medical Ltd, Mitaka, Tokyo, Japan). Measurements were taken before and after training and each rest at 50%, 60%, and 70% distal between the lateral epicondyle to the acromial process at elbow extension position. The perpendicular distance from subcutaneous fat to muscle tissue was taken as muscle thickness, and BFR was performed after measurement of the muscle thickness in the RE.

## **Pain during exercise and rest**

NRS was evaluated as an assessment of arm pain using a scale of 0–10, where 0 indicated no pain and 10 indicated extreme pain. NRS was evaluated immediately after each set and rest session. The pain during exercise was evaluated acutely after the end of each set, and pain during rest was evaluated 20 s before the start of each set.

## **Experiment 2**

The participants used in Experiment 2 were the same as those used in Experiment 1, except for one participant who dropped out and one limb that was excluded due to difficulties evaluating due to wrist joint injury was. A final total of 11 participants (age,  $23.5 \pm 1.0$  years; height,  $172.9 \pm 5.7$  cm; weight,  $66.1 \pm 5.0$  kg) were included. Measurement items included peak torque during exercise and subjective pain during exercise and rest. Peak torque, which was used as a reference for terminating exercise, was determined using the value at the time of the post measurement.

## **Statistical analysis**

All data are shown as mean  $\pm$  standard deviation. Analysis of peak torque, muscle endurance, and muscle CSA before and after training was performed using Wilcoxon signed-rank test for each time (pre and post), and Kruskal–Wallis test was performed for between-group analysis (Experiment 1). Friedman's test was performed for training evaluation for each test (MT, exercise repetition, peak torque during exercise, NRS) and Kruskal–Wallis test was performed for between-group analysis (Experiment 2). For Experiment 1, the effect size (ES) was calculated based on a previous study  $[(\text{post mean} - \text{pre mean})/\text{pre standard deviation}]$ , where  $< 0.50$  indicated trivial ED,  $0.50 - 1.25$  indicated small ED,  $1.25 - 1.9$  indicated moderate ES, and  $> 2.0$  indicated large ES. Statistical analyses were performed using IBM software package (IBM SPSS Statistics, version 22.0, Armonk, NY, USA), and the significance level was set to  $p < 0.05$ .

## **Results**

There were no significant differences at baseline between the groups for each measurement item. Table 1 shows the exercise repetition, peak torque, and pain during each set during the training period (Experiment 1).

## Peak torque

Table 2 shows changes in peak torque before and after training under each condition. Significant increases were observed for CC60 (ES, 1.27), IM (ES, 1.78), EC120 (ES, 0.74) in the RE ( $p < 0.05$ ) and IM (ES, 2.91) in the CON group ( $p < 0.05$ ), but no increases were observed in the EX. A tendency toward an increase was observed for CC60 (ES, 1.21), EC60 (ES, 0.77), and EC120 (ES, 0.96) in the CON ( $p < 0.10$ ). The rate of change was as follows: CC60,  $-2.9\% \pm 5.9\%$ ; CC120,  $4.8\% \pm 6.2\%$ ; CC240,  $3.2\% \pm 11.9\%$ ; IM,  $5.8\% \pm 5.7\%$ ; EC60,  $4.9\% \pm 10.1\%$ ; and EC120,  $5.3\% \pm 8.6\%$  in the EX; CC60,  $18.9\% \pm 18.6\%$ ; CC120,  $15.9\% \pm 21.6\%$ ; CC240,  $23.2\% \pm 40.2\%$ ; IM,  $15.0\% \pm 12.1\%$ ; EC60,  $7.9\% \pm 9.6\%$ ; and EC120,  $11.0\% \pm 5.5\%$  in the RE; and CC60,  $18.1\% \pm 13.4\%$ ; CC120,  $8.0\% \pm 9.4\%$ ; CC240,  $4.5\% \pm 8.5\%$ ; IM,  $19.3\% \pm 10.2\%$ ; EC60,  $7.9\% \pm 7.9\%$ ; and EC120,  $13.6\% \pm 10.9\%$  in the CON.

## Muscle endurance

Table 2 shows the changes in muscle endurance before and after training under each condition. The rate of decreases tended to decrease in the RE (ES, 1.55;  $p < 0.10$ ), and there was an increase in total work in the CON (ES, 0.82;  $p < 0.10$ ). The rate of change was as follows:  $6.4\% \pm 7.1\%$  in the EX;  $16.2\% \pm 25.0\%$  in the RE; and  $15.0\% \pm 12.1\%$  in the CON, and there was a significant decrease in the rate in the CON (ES, 1.23;  $p < 0.05$ ).

## Muscle CSA

Table 2 shows changes in CSA before and after training under each condition. A significant increase was observed in the 50% (ES, 0.64) and 60% (ES, 1.00) sections in the RE ( $p < 0.05$ ) and the 50% (ES, 1.51) and 60% (ES, 1.43) sections in the CON ( $p < 0.05$ ). A tendency toward an increase was observed in the 50% and 60% sections in the EX ( $p < 0.10$ ).

## Muscle thickness

Table 3 shows the changes in muscle thickness during exercise and training. Muscle thickness was significantly higher than that in the preconditions for all conditions after each set in all sections ( $p < 0.01$ ). In addition, muscle thickness was significantly higher at sets 3–4 compared with that at set 2 ( $p < 0.05$ ).

## Exercise repetition

Figure 1 shows changes in exercise repetition under each condition. The exercise repetitions were as follows: set 1,  $11.8 \pm 3.3$  reps; set 2,  $11.1 \pm 3.0$  reps; set 3,  $10.1 \pm 3.1$  reps; and set 4,  $9.7 \pm 3.4$  reps in the EX; set 1,  $26.5 \pm 8.7$  reps; set 2,  $15.2 \pm 8.0$  reps; set 3,  $13.1 \pm 4.7$  reps; and set 4,  $13.8 \pm 6.3$  reps in the RE group; and set 1,  $28.0 \pm 8.6$  reps; set 2,  $25.6 \pm 7.5$  reps; set 3,  $24.4 \pm 8.2$  reps; and set 4,  $23.8 \pm 7.2$  reps in the CON group. The RE showed a significant decrease after set 2 compared with set 1 (set 1–4,  $p < 0.001$ ),

and sets 3–4 in the CON (set 3,  $p < 0.05$ , set 4,  $p < 0.01$ ). The EX showed a significant decrease for all sets (sets 1–4,  $p < 0.001$ ) and the RE showed a greater decreased than the CON for two sets (set 2–4,  $p < 0.01$ ; set 3,  $p < 0.001$ ).

## Peak torque during exercise

Figure 2 shows the changes in peak torque during exercise under each condition. The peak torque during exercise was as follows: set 1,  $33.7 \pm 3.9$  N·m; set 2,  $32.4 \pm 4.1$  N·m; set 3,  $31.4 \pm 4.9$  N·m; and set 4,  $31.5 \pm 5.4$  N·m in the EX; set 1,  $36.4 \pm 3.5$  N·m; set 2,  $27.0 \pm 4.0$  N·m; set 3,  $26.8 \pm 3.2$  N·m; and set 4,  $26.1 \pm 2.9$  N·m in the RE; and set 1,  $36.5 \pm 4.2$  N·m; set 2,  $32.8 \pm 3.6$  N·m; set 3,  $31.0 \pm 3.4$  N·m; and set 4,  $30.7 \pm 3.1$  N·m in the CON. The RE and CON showed significantly lower peak torque values after set 2 compared with that of set 1 (RE: set 1–4,  $p < 0.001$  and CON: set 2,  $p < 0.05$ , set 3–4,  $p < 0.001$ ). The RE showed significantly lower values than the EX after set 2, and was significantly lower in sets 2 and 4 than the CON (set 2–4,  $p < 0.05$ ), and set 2 compared with set 4 in the CON (set 2,  $p < 0.01$ , set 4,  $p < 0.05$ ).

## NRS

Figure 3 shows changes in pain during exercise under each condition. The NRS values were as follows: set 1,  $6.1 \pm 1.8$ ; rest 1,  $2.2 \pm 1.3$ ; set 2,  $6.9 \pm 2.1$ ; rest 2,  $2.7 \pm 1.7$ ; set 3,  $7.3 \pm 2.5$ ; rest 3,  $2.7 \pm 1.7$ ; set 4,  $6.8 \pm 2.5$ ; and after,  $3.7 \pm 1.9$  in the EX; set 1,  $3.2 \pm 1.6$ ; rest 1,  $6.6 \pm 2.6$ ; set 2,  $3.3 \pm 1.3$ ; rest 2,  $6.9 \pm 2.5$ ; set 3,  $3.5 \pm 1.7$ ; rest 3;  $6.6 \pm 3.3$ ; set 4,  $3.6 \pm 1.8$ ; and after,  $2.3 \pm 1.5$  in the RE; and set 1,  $3.0 \pm 0.9$ ; rest 1,  $1.5 \pm 1.1$ ; set 2,  $3.4 \pm 1.1$ ; rest 2,  $1.8 \pm 1.5$ ; set 3,  $3.1 \pm 1.7$ ; rest 3,  $1.9 \pm 1.7$ ; set 4,  $3.4 \pm 1.9$ ; and after,  $1.9 \pm 2.2$  in the CON. The EX showed significantly higher values during each set than in each rest, and each set of the RE and CON ( $p < 0.01$ ). The RE showed significantly lower values in each set than in each rest ( $p < 0.01$ ) and showed significantly higher values in each rest than those of the EX and CON ( $p < 0.01$ ).

## Discussion

The present study investigated three different conditions, BFR during exercise (EX), BFR during rest (RE), and training only (CON), in males and examined muscle strength, muscle CSA, and pain during exercise and at rest. HIT with BFR during exercise was shown to prevent muscle hypertrophy and muscle strengthening. Other hand, HIT with BFR during rest increased muscle hypertrophy and muscle strength with fewer exercise repetitions under natural blood flow. Furthermore, BFR during rest did not exacerbate pain during exercise.

In the present study, HIT with BFR during exercise prevented training effects. Training volume was previously shown to be important for muscle hypertrophy due to training [20, 21]. It was recently reported that muscle hypertrophy could be obtained even when LIT was performed to fatigue (Sampson and Groeller 2016), and training volume was shown to be important for muscle hypertrophy regardless of the exercise intensity.

There for, muscle hypertrophy necessary a training volume regardless of exercise intensity. However, HIT with BFR during exercise did not decrease peak torque during exercise, which is considered that no fatigue to training. It is considered that the cuff pressure prevented the muscle strength. Therefore, it is presumed that necessary training volume was not secured in the BFR during exercise, it is not desirable to perform BFR during HIT. On the other hand, BFR during rest led to increased blood flow efficiency and induced muscle hypertrophy and muscle strengthening. In a previous study, training with BFR decreased repetition to fatigue [22] and similar results were obtained in the present study. It was reported that conventional LIT with BFR can lead to muscle hypertrophy and muscle strengthening more than LIT under natural blood flow conditions [19, 23–25]. These studies were performed using a protocol with certain exercise repetition (step 1, 30 reps; steps 2–4, 15 reps). However, muscle hypertrophy was equivalent when training to fatigue with BFR [26]. HIT with BFR was shown to have no effect on muscle hypertrophy and muscle strength [12, 13], and led to fatigue with few reps due to high-mechanical stress. Therefore, training to fatigue with BFR is thought to contribute greatly to training efficiency (e.g., exercise repetition, time). The training protocol used the present study indicates that it is optimal to perform BFR during rest. Furthermore, peak torque during exercise decreased BFR during rest, suggesting that BFR during rest may be useful when training to fatigue.

Muscle swelling (or cell swelling) is evaluated as the increase muscle thickness acute after exercise and is an important factor for muscle hypertrophy because it promotes muscle protein synthesis [3, 27]. In a previous study, LIT with BFR led to an increase in leg circumference after training to a greater extent than with LIT under natural blood flow conditions [23]. Training with BFR using CC or EC was performed, and CC training with BFR showed greater muscle swelling, muscle hypertrophy, and muscle strength [24]. Therefore, muscle swelling is an important factor for muscle hypertrophy, but it is unclear how important it is to induce muscle swelling. Muscle swelling is a useful index of muscle hypertrophy, but training protocols need to be evaluated in more detail.

Pain during exercise increased with BFR. In a previous study, LIT with high-pressure BFR led to greater pain during exercise than HIT [28]. It is predicted that because pain differed with BFR and exercise, ischemia–reperfusion numbness was caused by stimulation of the sensitization of transient receptor potential ankyrin 1 with active oxygen generated by reperfusion [29]. Pain during exercise is caused by the combination of many factors (e.g., oxygen, ion, protein) as well as muscle damage (Miles and Clarkson 1994). This present study found that pain was greater with BFR than pain during exercise because it was increased with BFR regardless of exercise or rest conditions. Pain was greatest during BFR with HIT to near fatigue, rather than exercise failure due to muscle fatigue; therefore, intense pain may make exercising more difficult, which makes the necessary training volume unachievable. However, BFR during rest was the same as pain during exercise, but increased muscle hypertrophy and muscle strength with decreased exercise repetitions and peak torque during exercise. Although exercise pain was the same as HIT without BFR, BFR during rest decreased the exercise repetition and peak torque required to result in muscle hypertrophy and muscle strength. Therefore, BFR during rest could be a useful method to examine the effects of BFR without inducing excessive pain.



There are some limitations to the present study. First, the time and duration of BFR differed in the EX and RE groups, which may have led to different effects. Training intensity may be changed by increasing the number, time, and pressure of BFR. However, it was reported that training effects of BFR are equal regardless of whether high or low pressure is used [18, 30]. Therefore, the present study most focused on the timing of BFR. However, it is necessary to investigate the number and duration of BFR in the future. Second, the training in this experiment involved isokinetic resistance training using a BIODEX device, and each repetition was performed at the maximum output, representing HIT. In previous study, BFR was not shown to be useful during HIT combined with BFR. However, studies in athletes have shown the effect of BFR, which may be more effective in athletes, even at high intensity. Also, there are many items to the training effect, and it is easy to only evaluate the effect on muscle hypertrophy or muscle strengthening. Therefore, a study that focuses on items and/or training intensity may be useful for BFR other than during exercise. Third, this study evaluated fatigue during exercise on peak torque, and it did not investigate torque at each repetition. However, previous studies that investigated muscle fatigue with BFR investigated muscle activation and subjective fatigue during exercise as well as and maximum voluntary contraction. Few studies have investigated peak torque during exercise. Therefore, measuring the peak torque of each repetition will allow us to investigate the effects of BFR on the body in more detail.

## Conclusions

In conclusion, this present study showed that BFR during rest can lead to muscle hypertrophy and muscle strength with fewer exercise repetitions than training only. BFR during rest showed the greatest decreases in peak torque during exercise and did not exacerbate pain during exercise.

## Abbreviations

BFR: Blood flow restriction, CSA: Cross sectional area, ES: Effect size, HIT: High-intensity training, ICC: Intraclass correlation coefficient, LIT: Low-intensity training, MRI: Magnetic resonance imaging, NRS: Numerical Rating Scale, 1RM: One-repetition maximum.

## Declarations

### *Ethics approval and Consent to participate*

The study was conducted according to the guidelines of the Declaration of Helsinki and was approved by the Ethics Committee for Human Experiments of Juntendo University, Japan (No. 30–28). The purpose, methods, procedures, risks, and compensation for this study were explained to the participants verbally and in writing, and all participants gave informed consent.

### *Consent for publication*

Not applicable

### ***Availability of data and material***

The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

### ***Conflicts of Interest / Competing interests***

The authors declare that they have no conflict of interest.

### ***Funding***

Not applicable

### ***Authors' contributions***

TT, AK, and HO conceived and designed research. TT conducted experiments, and drafted the first manuscript. AK, HO, HN and YT manuscript revisions and contributed to interpretation, and all authors approval of the version to be published.

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Not applicable

## **References**

1. American College of Sports M: American College of Sports Medicine position stand. Progression models in resistance training for healthy adults. *Med Sci Sports Exerc* 2009, 41(3):687-708.
2. Sampson JA, Groeller H: Is repetition failure critical for the development of muscle hypertrophy and strength? *Scand J Med Sci Sports* 2016, 26(4):375-383.
3. Loenneke JP, Fabs CA, Rossow LM, Abe T, Bemben MG: The anabolic benefits of venous blood flow restriction training may be induced by muscle cell swelling. *Med Hypotheses* 2012, 78(1):151-154.
4. Ozaki H, Sakamaki M, Yasuda T, Fujita S, Ogasawara R, Sugaya M, Nakajima T, Abe T: Increases in thigh muscle volume and strength by walk training with leg blood flow reduction in older participants. *J Gerontol A Biol Sci Med Sci* 2011, 66(3):257-263.
5. Takarada Y, Takazawa H, Sato Y, Takebayashi S, Tanaka Y, Ishii N: Effects of resistance exercise combined with moderate vascular occlusion on muscular function in humans. *J Appl Physiol (1985)* 2000, 88(6):2097-2106.
6. Campos GE, Luecke TJ, Wendeln HK, Toma K, Hagerman FC, Murray TF, Ragg KE, Ratamess NA, Kraemer WJ, Staron RS: Muscular adaptations in response to three different resistance-training regimens: specificity of repetition maximum training zones. *Eur J Appl Physiol* 2002, 88(1-2):50-60.
7. McDonagh MJ, Davies CT: Adaptive response of mammalian skeletal muscle to exercise with high loads. *Eur J Appl Physiol Occup Physiol* 1984, 52(2):139-155.

8. Pearson SJ, Hussain SR: A review on the mechanisms of blood-flow restriction resistance training-induced muscle hypertrophy. *Sports Med* 2015, 45(2):187-200.
9. Ozaki H, Loenneke JP, Buckner SL, Abe T: Muscle growth across a variety of exercise modalities and intensities: Contributions of mechanical and metabolic stimuli. *Med Hypotheses* 2016, 88:22-26.
10. Dankel SJ, Buckner SL, Jessee MB, Mattocks KT, Mouser JG, Counts BR, Laurentino GC, Loenneke JP: Can blood flow restriction augment muscle activation during high-load training? *Clin Physiol Funct Imaging* 2018, 38(2):291-295.
11. Neto GR, Santos HH, Sousa JB, Junior AT, Araujo JP, Aniceto RR, Sousa MS: Effects of high-intensity blood flow restriction exercise on muscle fatigue. *J Hum Kinet* 2014, 41:163-172.
12. Laurentino G, Ugrinowitsch C, Aihara AY, Fernandes AR, Parcell AC, Ricard M, Tricoli V: Effects of strength training and vascular occlusion. *Int J Sports Med* 2008, 29(8):664-667.
13. Biazon T, Ugrinowitsch C, Soligon SD, Oliveira RM, Bergamasco JG, Borghi-Silva A, Libardi CA: The Association Between Muscle Deoxygenation and Muscle Hypertrophy to Blood Flow Restricted Training Performed at High and Low Loads. *Front Physiol* 2019, 10:446.
14. Dankel SJ, Buckner SL, Jessee MB, Mattocks KT, Mouser JG, Counts BR, Laurentino GC, Abe T, Loenneke JP: Post-exercise blood flow restriction attenuates muscle hypertrophy. *Eur J Appl Physiol* 2016, 116(10):1955-1963.
15. Husmann F, Mittlmeier T, Bruhn S, Zschorlich V, Behrens M: Impact of Blood Flow Restriction Exercise on Muscle Fatigue Development and Recovery. *Med Sci Sports Exerc* 2018, 50(3):436-446.
16. Kubota A, Sakuraba K, Sawaki K, Sumide T, Tamura Y: Prevention of disuse muscular weakness by restriction of blood flow. *Med Sci Sports Exerc* 2008, 40(3):529-534.
17. Kubota A, Sakuraba K, Koh S, Ogura Y, Tamura Y: Blood flow restriction by low compressive force prevents disuse muscular weakness. *J Sci Med Sport* 2011, 14(2):95-99.
18. Sumide T, Sakuraba K, Sawaki K, Ohmura H, Tamura Y: Effect of resistance exercise training combined with relatively low vascular occlusion. *J Sci Med Sport* 2009, 12(1):107-112.
19. Yasuda T, Brechue WF, Fujita T, Sato Y, Abe T: Muscle activation during low-intensity muscle contractions with varying levels of external limb compression. *J Sports Sci Med* 2008, 7(4):467-474.
20. Krieger JW: Single vs. multiple sets of resistance exercise for muscle hypertrophy: a meta-analysis. *J Strength Cond Res* 2010, 24(4):1150-1159.
21. Wolfe BL, LeMura LM, Cole PJ: Quantitative analysis of single- vs. multiple-set programs in resistance training. *J Strength Cond Res* 2004, 18(1):35-47.
22. Yasuda T, Fukumura K, Iida H, Nakajima T: Effect of low-load resistance exercise with and without blood flow restriction to volitional fatigue on muscle swelling. *Eur J Appl Physiol* 2015, 115(5):919-926.
23. Fry CS, Glynn EL, Drummond MJ, Timmerman KL, Fujita S, Abe T, Dhanani S, Volpi E, Rasmussen BB: Blood flow restriction exercise stimulates mTORC1 signaling and muscle protein synthesis in older men. *J Appl Physiol (1985)* 2010, 108(5):1199-1209.

24. Yasuda T, Loenneke JP, Thiebaud RS, Abe T: Effects of blood flow restricted low-intensity concentric or eccentric training on muscle size and strength. *PLoS One* 2012, 7(12):e52843.
25. Fujita S, Abe T, Drummond MJ, Cadenas JG, Dreyer HC, Sato Y, Volpi E, Rasmussen BB: Blood flow restriction during low-intensity resistance exercise increases S6K1 phosphorylation and muscle protein synthesis. *J Appl Physiol (1985)* 2007, 103(3):903-910.
26. Farup J, de Paoli F, Bjerg K, Riis S, Ringgard S, Vissing K: Blood flow restricted and traditional resistance training performed to fatigue produce equal muscle hypertrophy. *Scand J Med Sci Sports* 2015, 25(6):754-763.
27. Grant AC, Gow IF, Zammit VA, Shennan DB: Regulation of protein synthesis in lactating rat mammary tissue by cell volume. *Biochim Biophys Acta* 2000, 1475(1):39-46.
28. Soligon SD, Lixandrao ME, Biazon T, Angleri V, Roschel H, Libardi CA: Lower occlusion pressure during resistance exercise with blood-flow restriction promotes lower pain and perception of exercise compared to higher occlusion pressure when the total training volume is equalized. *Physiol Int* 2018, 105(3):276-284.
29. So K, Tei Y, Zhao M, Miyake T, Hiyama H, Shirakawa H, Imai S, Mori Y, Nakagawa T, Matsubara K *et al*: Hypoxia-induced sensitisation of TRPA1 in painful dysesthesia evoked by transient hindlimb ischemia/reperfusion in mice. *Sci Rep* 2016, 6:23261.
30. Singer TJ, Stavres J, Elmer SJ, Kilgas MA, Pollock BS, Kearney SG, McDaniel J: Knee extension with blood flow restriction: Impact of cuff pressure on hemodynamics. *Eur J Appl Physiol* 2020, 120(1):79-90.

## Tables

Due to technical limitations, tables 1 to 3 PDF are only available as a download in the Supplemental Files section.

## Figures

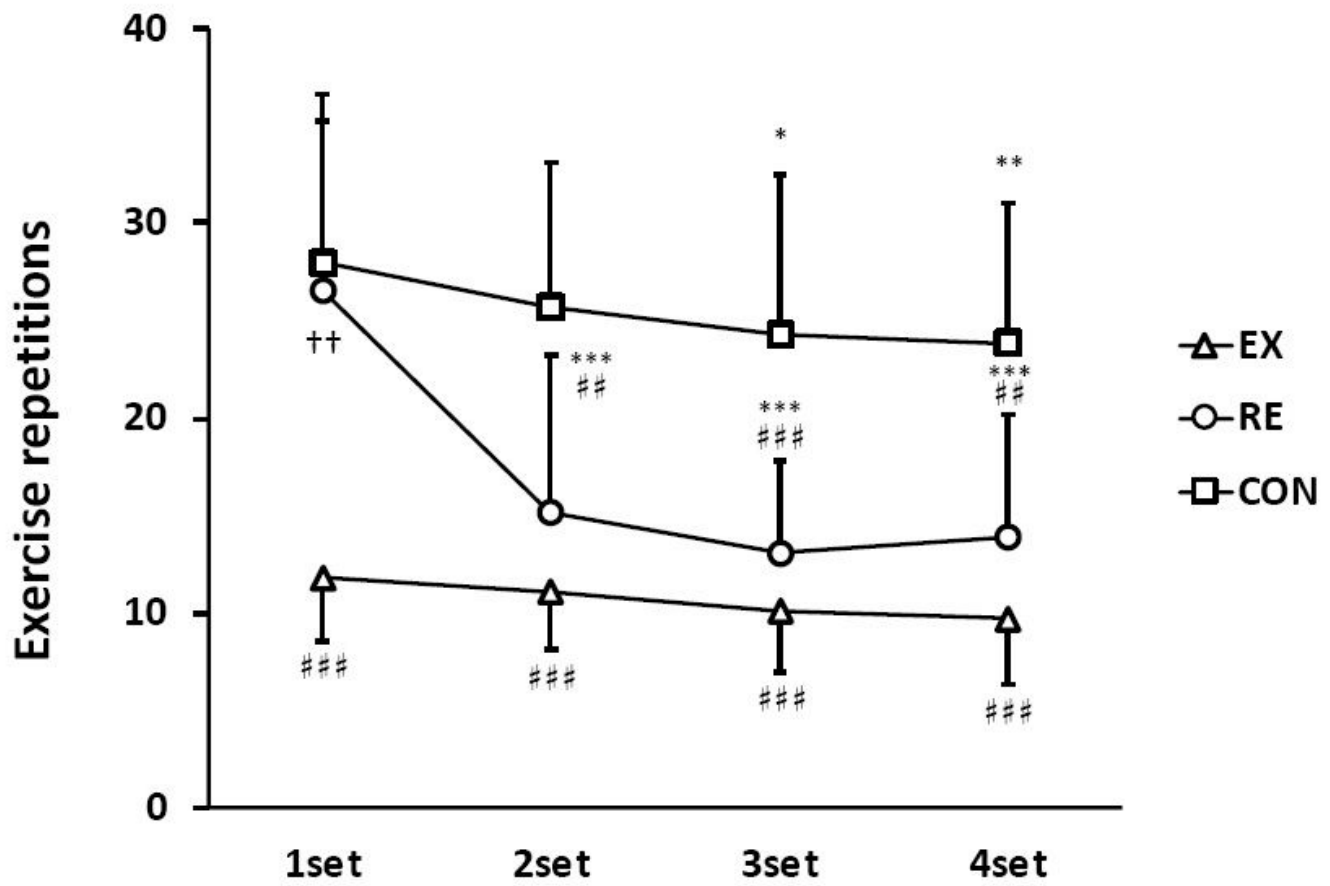
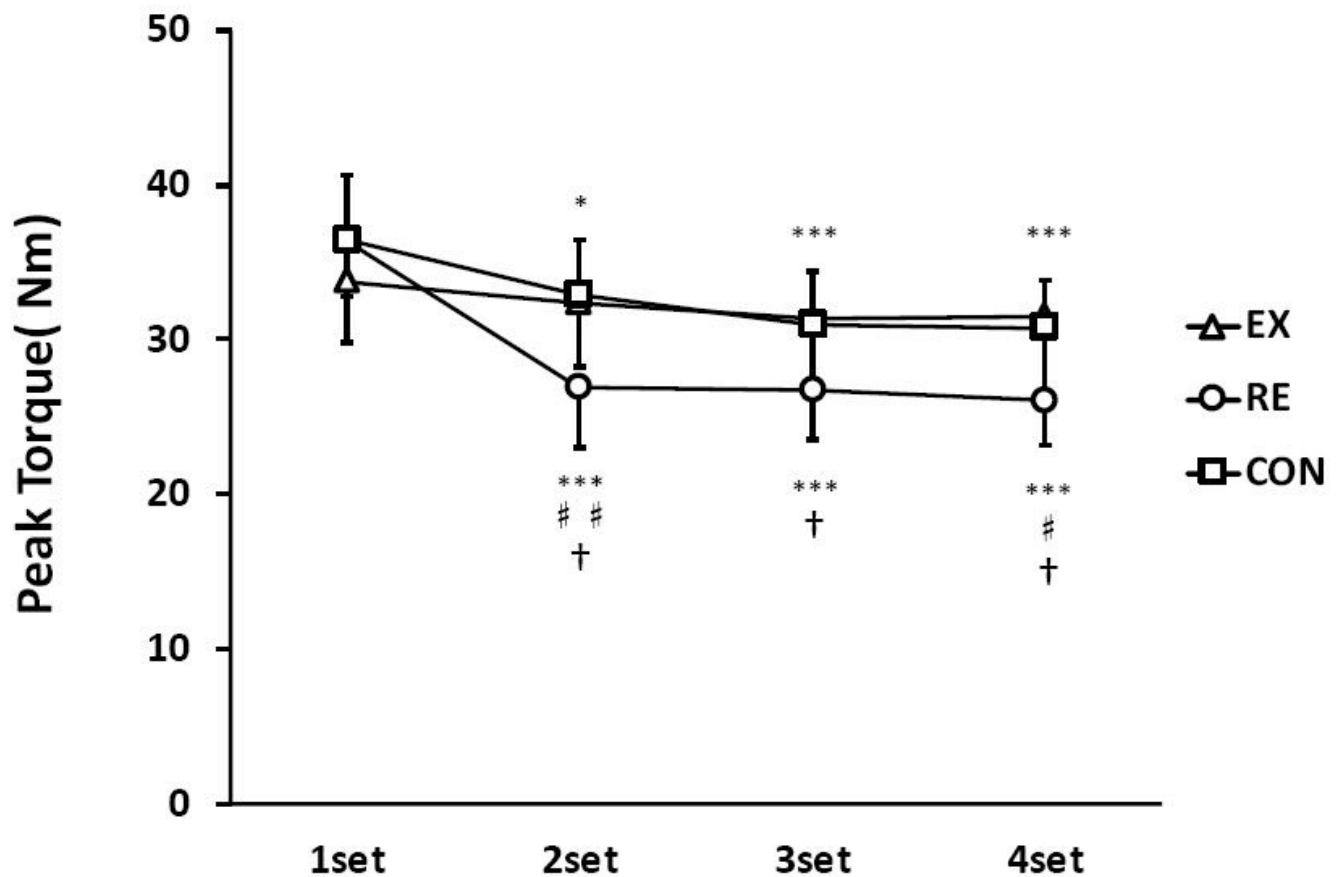


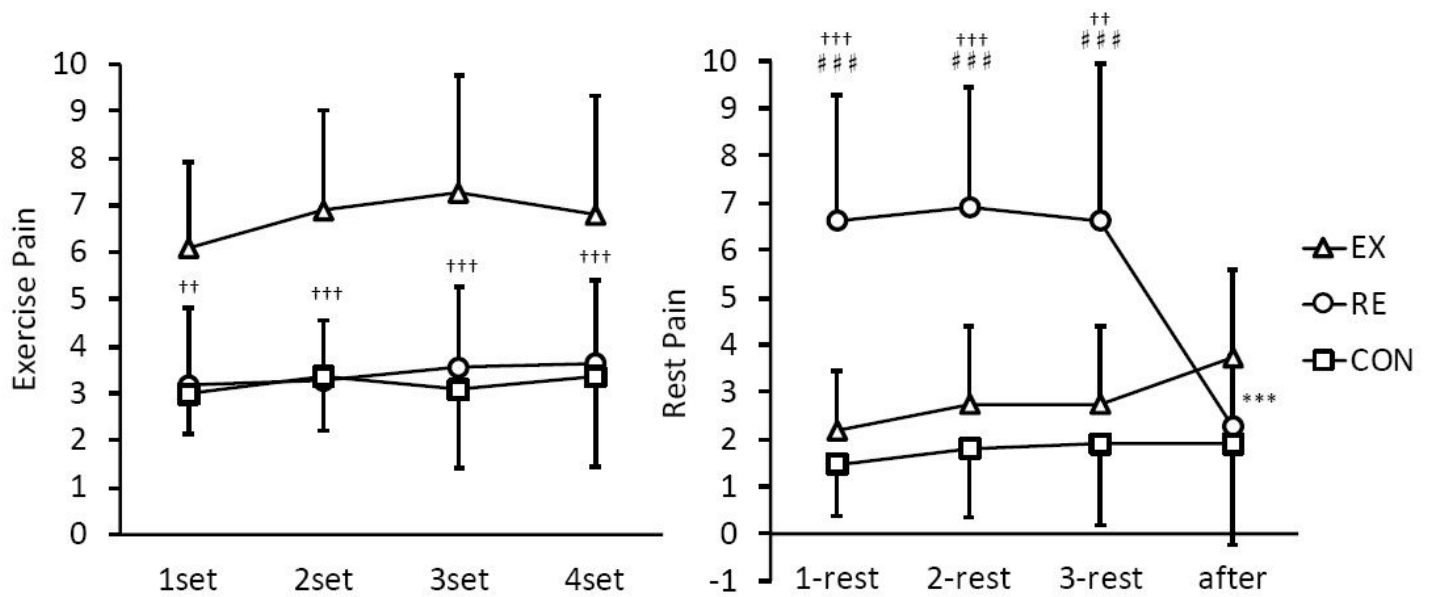
Figure 1

Exercise repetition during each set (after the training period). Data were mean  $\pm$  SD. Blood flow restriction during exercise (EX), Blood flow restriction during rest (RE), Training only (CON) (all condition, n=11). Exercise repetition of BFR-RE and CON were significantly decrease. \*: p<0.05, \*\*: p<0.01, \*\*\*: p<0.001 (vs. 1set). ##: p<0.01, ###: p<0.001 (vs. CON). ††: p<0.01 (vs. EX).



**Figure 2**

Peak Torque during each set (after the training period). Data were mean  $\pm$  SD. Blood flow restriction during exercise (EX), Blood flow restriction during rest (RE), Training only (CON) (all condition, n=11). Peak Torque of BFR-RE and CON were significantly decrease. \*:  $p<0.05$ , \*\*\*:  $p<0.001$  (vs. 1set). #:  $p<0.05$ , ##:  $p<0.01$  (vs. CON). † † †:  $p<0.001$  (vs. EX).



**Figure 3**

Muscle pain during training (after the training period). Data were mean  $\pm$  SD. Blood flow restriction during exercise (EX), Blood flow restriction during rest (RE), Training only (CON) (all condition, n=11). \*\*\*:  $p < 0.001$  (vs. 1-3set). ###:  $p < 0.001$  (vs. CON). ++:  $p < 0.01$ , +:  $p < 0.001$  (vs. EX).

## Supplementary Files

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