

Original Research

# A New Exercise Training Methods for Untrained Middle-Age Males: Comparison of Effectiveness Resistance Training with Blood Restriction Cuffs vs Traditional Resistance Training

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## ABSTRACT

The American College of Sports Medicine recommends moderate to high load resistance training to improve training adaptations. However, use of moderate to high loads are often not feasible in clinical populations. Blood flow restriction (BFR) training is a simple and practical way for older and middle-aged people to prevent the negative consequences of aging. Thus, this paper documents the design and implementation of a training program to improve adaptations of anabolic hormonal agents and muscle strength induced by resistance training with BFR in middle-aged individuals. In this semi-experimental study design, 20 (age  $48.55 \pm 2.11$  years) untrained middle-aged males were selected. Subjects were randomly divided into two groups: BFR and traditional resistance training (RES). Subjects in the 4-weeks BFR protocols performed knee extension and leg press at 20% 1-RM intensity, and the non-BFR training group performed the same movements at 80% 1-RM intensity. Blood samples were also taken to measure growth hormone and insulin-like growth factor-1. Levels of GH ( $P=0.001$ ) and IGF-I ( $P=0.001$ ) was significantly increased in all groups following the four weeks of resistance training with or without BFR. However, increase of GH concentrations in BFR group were significantly higher than RES group ( $P= 0.04$ ). Also, there was no different between groups for IGF-I ( $P=0.54$ ). It seems likely that performing resistance training with BFR during middle age is a good way to delay the adverse effects of aging on anabolic hormonal factors.

Keywords: Blood flow restriction, anabolic hormones, 1-mamximum repetition, middle-age males.

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## Introduction

The loss of body strength and muscle mass with age is a common detrimental issue leading to a decrease in functional capacity, mobility, and endurance in the elderly. In addition to strength and muscle mass, the decline of anabolic hormone concentrations is also a common physiological phenomenon during aging and middle-age periods. However, age-related decline of anabolic hormone concentrations may be restored by lifestyle modifications such as regular exercise training. Growth hormone (GH) is a pleiotropic peptide hormone that has primary roles in the regulation of metabolism, via stimulation of lipid mobilization and oxidation, and in the promotion of collagen synthesis within musculotendinous tissue (1). GH induces both direct and indirect effects on metabolism and protein synthesis, via GH receptor dimerization and/or stimulation of systemic and tissue-specific insulin-like growth factor (IGF)-I expression (2). GH and IGF-I concentrations peak during adolescence and undergo a precipitous decline throughout the age span, which is thought to partially elevation in visceral fat mass and reductions in musculotendinous quality that occur in the elderly (3). In this regard, exogenous GH administration does not promote accretion of skeletal muscle mass in adults, but instead reduces visceral and subcutaneous fat-mass in GH deficient populations and promotes collagen synthesis in musculotendinous tissue (3, 4). However, the side-effects associated with use of GH exogenous and its limited efficacy in promoting muscle function in older individuals exclude its recommendation as an anti-aging agent (5). Alternatively, exercise induces GH secretion in an intensity-dependent manner (6), which may at least partially underlie the influence of exercise on lipid oxidation and/or collagen synthesis within both muscle and tendon (1). Although, this remains to be determined. Traditional high-load resistance training performed more than 70% of one-repetition maximum (1RM) is the most established means of increasing both muscle and tendon cross-sectional area (CSA) and strength in young and older populations (7). High load resistance exercise (RE) results in a robust, yet transient, increase in circulating GH in young individuals, a result which is blunted in older populations (8). Also, some studies have reported that chronic resistance exercise training (RE) may increase central and peripheral arterial stiffness and sympathetic activity (9, 10, 11). Therefore, it is imperative to propose an alternative training protocol aimed at increasing muscular strength and mass, but without the detrimental effects on cardiovascular function in older adults. Recently, blood flow restriction (BFR) combined with low-intensity resistance exercise has been suggested as a useful exercise protocol to gain muscular strength and mass without an increase in blood pressure. BFR coupled with low-intensity resistance exercise is typically performed by placing a narrow compressive cuff around an appendicular limb and inflating it immediately before exercise. The pressure of the cuff is around super systolic (150-350 mmHg), and the exercise intensity is 25- 45% of maximum voluntary contraction (MVC). BFR coupled with low-intensity resistance exercise may be used for a variety of exercise modalities including both isometric and isotonic contractions including chest press, arm curl, leg extension, squat, etc. Improvements in muscular strength and mass in older people have been reported in many studies utilizing BFR coupled with low intensity resistance exercise (9, 10). Moreover, several studies reported that BFR coupled with low intensity resistance exercise training increased anabolic hormone concentrations along with improving muscular strength and hypertrophy (12, 13, 14). Additionally, it is suitable for special populations such as the elderly and diseased populations who cannot perform traditional resistance or high-intensity aerobic exercise training (15). Emerging evidence also indicates that low-load RE performed under conditions of local muscle blood flow restriction (BFR) produces comparable muscle hypertrophy to that observed with traditional high-load RE and that low-load RE alone stimulates intramuscular collagen synthesis (6). Interestingly, low-load RE coupled with BFR increases post-exercise GH concentrations to an equal or greater magnitude than that of high-load RE suggesting that low load RE with BFR may be an effective means of attenuating physiologic events that occur with aging (16). However, it remains unknown whether low-load RE with BFR is capable of increasing circulating GH in older populations who typically have low GH concentrations and who exhibit a blunted GH response to traditional high load RE (17).

In BFR training, a restrictive device is placed on the proximal end of a limb, reducing the amount of arterial blood flow, and occluding venous return, resulting in a reduced amount of oxygen supplied to the active muscle (18). These hypoxic conditions place the muscle under greater metabolite stress by increased lactate

and catecholamine concentrations (19) which may cause increases in anabolic hormones like GH (16), testosterone, and IGF-1 (20), although most studies have demonstrated non-significant findings (21, 22), but Madarame et al. (2010) reported lower body exercise with BFR can acutely increase total testosterone (12). Researchers have shown that BFR training induces rapid increase in plasma GH, because of the proposed association between lactate and GH release (21, 23, 24). Although GH may not be anabolic per se, it stimulates the release of IGF-1 and IGF-1 stimulates hypertrophic pathways (25). A study examining the response of IGF-1 to BFR resistance training on old men reported no change in plasma IGF-1 levels (24), but a study examining the chronic response on young men showed an increase in basal levels of circulating IGF-1 when compared to baseline (20). In contrast, 6 weeks of BFR training reported no changes in baseline levels of circulating IGF-1 (26). However, research has shown that there is no causal relationship between hormone production and training adaptation (27). Therefore, the purpose of this investigation is to determine the effects of blood flow restriction training on anabolic hormones and strength in untrained middle-aged males.

## **Material and Methods**

### **Subjects**

20 healthy sedentary middle-aged males (age:  $48.13 \pm 2.41$  years, BMI:  $26.15 \pm 2.04$  kg/m<sup>2</sup>) participated in this study. All participants were sedentary and not engaged in any sort of structured training program.

To be included, males (<60 minutes per week exercise participation and performing no resistance exercise in the past one year) between 40 and 60 years of age (14). Subjects were excluded if they had a body mass index (BMI) >30 kg/m<sup>2</sup>, diagnosed hypertension or use of anti-hypertensive medications, a resting blood pressure  $\geq 140/90$ , ankle-brachial index < 0.95, an orthopedic limitation that would preclude lower extremity RE, were currently undergoing active treatment for cancer, testosterone therapy, or anticoagulant therapy, or had a history of blood clotting disorders, peripheral vascular disease, valvular heart disease, rheumatoid arthritis, severe anemia, liver or renal disease, uncontrolled diabetes or hypertension, severe osteoarthritis, fracture in upper or lower extremity within the last 6 months, currently smoking, and alcohol or drug abuse in the past 6 months (14, 15). The three-day food record was used to make sure that the diet on the day before each test was similar in terms of meal and snack times, meal composition and sizes, and fluid intake (20, 21). The participants were instructed how to fill out a food record before each test day. A trained nutritionist gave recommendations on how to substitute certain foods in order to achieve a comparable nutrient intake. In addition, each participant consulted a trained nutritionist during a preliminary meeting before the study. The food intake before the tests was standardized to the extent that the subjects recorded their food intake on the day before the first test, and then were advised to reproduce their diet before each test day. Finally, the subjects were randomly assigned to two groups: BFR, and traditional resistance training (RES).

### **Protocol**

Before any baseline testing, all subjects visited the laboratory for fasting blood samples and anthropometrical measurements. The following day, they participated in a familiarization session to adapt to the testing/training procedures, the laboratory environment. After the initial measurements and completion of 1-maximum repetitions tests, the middle-aged males began their four-week BFR or traditional resistance training program. Before the training periods, the middle-age males were matched according to their knee extension and leg press maximal strength (1RM), basal GH and IGF-1 concentrations and divided into two groups. At the end of the training period, the baseline tests were repeated in the same order. Standard environmental conditions) were ensured during the testing sessions (24).

### **Training intervention**

This project was designed to test hypotheses comparing response differences in exercise condition (low-load RE with BFR vs. high-load RE). Based on the results of previous studies, the main assumption of the present study was that traditional resistance training has a significant effect on the level of anabolic hormonal factors. Therefore, the control group was not considered and the main purpose was to compare a traditional training method with a new one. We choose leg press and knee extension exercise because it isolates the muscle group to specifically examine the effect of BFR on exercise-induced GH, and IGF-I

secretion without potential confounding effects of agonist muscles. Additionally, there is a large body of literature on GH, and IGF-I responses to leg press and knee extension exercise in middle-age and older adults with which to compare results. Prior to exercise and on a separate day, leg press and knee extension 1RM was performed according to a standard protocol (15). Exercise sessions were performed in a temperature controlled room under direct supervision of a trainers. During each exercise session, BFR group subjects performed three sets (one 30 repetition set and 2 sets of 15 repetitions) of leg press and knee extension exercise at 20% 1RM (low-load) with concurrent BFR. Also, traditional resistance training group subjects performed three sets (one 30 repetition set and 2 sets of 15 repetitions) of leg press and knee extension exercise at 80% 1RM (high-load RE) without BFR. Pneumatic cuffs (a 13 × 124 cm) were worn by the BFR group on the upper part of both thighs during the training sessions. Subjects sat down on a bench and inflated the cuff, when the target pressure. During low-load training, BFR was initiated 2 minutes prior to the start of exercise and the cuff remained inflated for the duration of the exercise and rest periods. Specifically, a 17 cm wide blood pressure cuff was inflated around the upper thigh according to published tourniquet safety guidelines (28). The degree of blood flow occlusion between individuals was standardized by inflating the cuff to 20-30% mmHg higher than the brachial systolic blood pressure of each subject (cuff inflation range: 140–195 mmHg) that was assessed in a sitting position prior to the start of the exercise. In addition, the GH response to RE is partially contingent on rest between sets and the volume of exercise performed (29), as such we standardized rest intervals between sets at 2 minutes and recorded training volume by calculating the number of repetitions performed multiplied by mass lifted in kilograms in each condition.

#### **Anthropometric measurements**

The anthropometric procedures and tests were conducted on all participants by the same researcher according to the Anthropometric Standardization Reference Manual (30). The BMI was calculated from height and body mass with the formula: body mass (kg)/height (m<sup>2</sup>). BF% was measured using the InBody devices and skinfold methods (15).

#### **Measurements**

Venous samples were collected for the determination of GH, and IGF-1. For GH and IGF-1 assessment, one venous blood sample was taken 18-24 h before (pre), and post-exercise training session. The blood (5 ml) was collected by the Vacutainer blood withdrawal system. After storage at 7 °C for ~30 min for deactivation of coagulation factors, the blood samples were centrifuged for 10 min. The serum was stored at -80 °C until the analysis. Serum concentrations of IGF-1, and GH were determined by human ELISA kits (Monobind Inc, L F, CA, United States). All samples for each parameter were analyzed in duplicate and mean values were used for statistical analysis. All results of the growth factor analysis were adjusted for changes in plasma volume (PV) (13).

#### **Data analysis**

Descriptive statistics are reported as mean ± SD. Levene’s test and Shapiro–Wilk test, respectively. The results showed that the data obtained met the assumptions of homogeneity of variance and normality. The baseline values of the dependent variables were compared between two groups using the independent sample T test. The level of statistical significance was set at  $p < 0.05$ . All statistical analyses were performed using SPSS 18 software (SPSS Inc., Chicago, IL, USA).

#### **Results**

The results (mean ± standard deviation) of individual characteristics and hemodynamic parameters in both groups before the exercise protocol are shown in Table 1. There were no differences among groups in physical characteristics at the beginning of the study (Table 1) and hormonal factors associated growth (Table 2) ( $P > 0.05$ ). The anthropometric characteristics, and blood pressure, were similar between the two groups (Table 1).

Table 1. Demographic characteristics of the participants

Groups	Variables				
	n	Age (year)	Height (m)	Weight (kg)	Body mass index (kg/m <sup>2</sup> )
<b>BFR-UNTR AINED</b>	10	48.3±2.16	1.75±.5	80±6.03	26.03±2.83
<b>RESISTANCE-UNTR AINED</b>	10	48.8±2.14	1.74±.04	82.1±4.5	27.07±1.63

Values are indicated as mean ± standard deviation.

### Human growth hormone

Levels of serum GH was significantly increased in all groups following the four week of resistance training with or without BFR (Table 2). However, increase GH concentrations in BFR group were significantly higher than any groups (Table 2).

### Insulin like growth factor-1

Levels of serum IGF-I was significantly increased in all groups following the four week of resistance training with or without BFR (Table 2). Also, there was no different between groups.

### Knee extension and leg press strength

Knee extension and leg press strength were significantly increased in all groups following the four week of resistance training with or without BFR (Table 2). However, increase Knee extension and leg press strength in BFR group were significantly higher than RES group (Table 2).

### Lactate

Lactate concentration increased immediately following the first bout of both resistance exercise. Also, there was no different between groups.

Table 2. anabolic and catabolic hormones before and after resistance training with and without BFR in untrained middle-age males

	Group	Pretest	Posttest	Sig.
GH (ng/ml) <sup>a</sup>	BFR	0.81±0.3	1.28±0.39	0.001
	RES	0.83±0.35	1.08±0.4	0.004
IGF-1 (ng/ml) <sup>a</sup>	BFR	451.6±74.98	497±74.85	0.001
	RES	471.2±47.93	495.1±45.47	0.002
leg press strength (kg)	BFR	170.2±12.1	205.4±21.7	0.001
	RES	168.1±14.5	191.6±18.4	0.004
Knee extension (kg)	BFR	24.2±8.7	28.7±12.8	0.001
	RES	22.1±10.1	27.5±7.8	0.001
ΔLactate (mmol/L) <sup>b</sup>	BFR	8.23±1.74	6.28±1.49	0.001
	RES	8.47±1.46	9.69±1.16	0.001
Body fat percentage (%)	BFR	21.95±3.27	21.4±2.84	0.54
	RES	23.9±3.08	23.4±2.79	0.38

Values are indicated as mean ± standard deviation. GH: growth hormone; IGF-1: insulin-like growth factor-1.

<sup>a</sup> Compared to the pre-study protocol (day 1) and 24 hours after last training session (4 weeks).

<sup>b</sup> Compared to the first bout of both resistance exercise and immediately after first bout of both resistance exercise (mean difference).

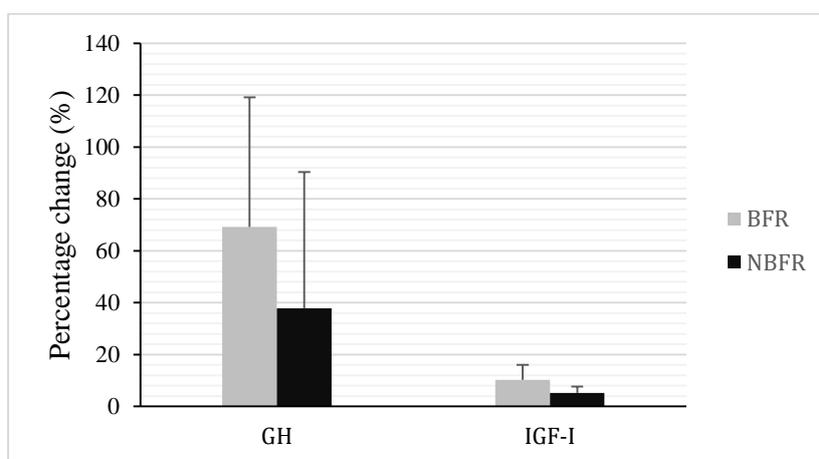


Figure 1. Percentage change of GH, and IGF-I concentrations in untrained middle-age males during pre and post resistance training with and without BFR. Values are means ± SE. \*Significant difference at  $P < 0.05$ . \*\*Significant difference at  $P < 0.01$ .

## Discussion

The study aimed to identify the effects of blood flow restriction training on anabolic and catabolic hormones in untrained middle-age males. Levels of GH and IGF-I was significantly increased in all groups following the four weeks of resistance training with or without BFR. However, increase of GH concentrations in BFR group were significantly higher than RES group. Also, there was no different between groups for IGF-I. Also, knee extension and leg press strength were significantly increased in all groups following the four weeks of resistance training with or without BFR. However, increase of knee extension and leg press strength in BFR group were significantly higher than RES group.

As such, GH may exert direct systemic effects via receptor dimerization or indirect effects via the stimulation of systemic or local IGF-I expression (1). GH stimulates increase of skeletal muscle mass in adults, considering that GH does not induce myofibrillar protein synthesis (4) and that exogenous GH administration does not improve muscle performance in healthy young individuals, GH deficient individuals, or older men. In addition, GH influences musculotendinous tissue via stimulation of collagen protein synthesis either directly or indirectly, through effects on IGF-I (1). The GH response to RE has been well characterized (32) and is traditionally known to be influenced by chronological age, amount of muscle mass recruited, type of muscle action (concentric or eccentric), exercise load, training status (an athlete versus a sedentary individual), volume of exercise, and the amount of rest given between sets of exercise.

In middle-age males, we observed that low-load RE with BFR produces a similar increase in GH to that of high-load RE, which corroborates the findings of several previous studies (12, 33). The accumulation of metabolic byproducts produced by exercising muscle is involved in the hypothalamic-stimulated release of GH. Specifically, metabolic acidosis in the form of lactate accumulation is involved in GH release, as evidenced by Luger and colleagues who infused lactate to produce the same serum concentrations observed during an exercise bout and observed roughly half the GH response resulting from exercise (34). In our study, while we observed that lactate concentration was related with GH concentrations, we found no clear differences between the conditions or age groups that could explain the elevated peak GH response. Alternatively, exercise volume is known to influence the GH response to exercise. However, we find it unlikely that the observed differences in exercise volume influenced the GH response in older individuals because the amount of mechanical work performed was not related to the GH response in our study. As such, exercise volume and lactate concentration may play a lesser role in GH secretion following low-load RE with BFR than others have suggested (16, 35).

In agreement with the findings of several previous studies, we report that basal GH concentrations were significantly different between trained and untrained older men (36, 37). However, our results appear to at least partially conflict with a number of studies, which have reported that both the maximal and integrated GH responses to high-load RE are blunted in old individuals (36).

In older men, we observed that the GH response to high-load RE was blunted compared with that following low-load RE with BFR. In particular, it remains unknown whether these deficits result from central or peripheral mechanisms; however, both metaboreceptor activation and central command influence GH secretion (38, 39). Additionally, the relative importance of the maximal GH response to stimuli versus that of the total GH response remains somewhat controversial. The fact that GH is typically secreted in a pulsatile manner, as opposed to continuously, suggests that the maximal or peak GH response may be of some importance when evaluating the physiological effects of this hormone; although, this remains to be determined (1). Pain receptors are activated to a greater extent during BFR RE than high load RE. While the mechanism is not completely clear, it is plausible that decreased venous outflow during BFR reduces clearance of metabolic acidosis resulting in activation of proton-activated nociceptors. Importantly, acute pain is known to regulate GH secretion through stimulation of opioid receptors (40). The researchers speculated that high acute pain perceived during the stimulated contractions contributed to the elevated GH response. It would appear that the higher levels of pain induced by low-load BFR contributed to the GH release compared to the relatively painless high-load RE

bout (41). From a more applied perspective, elevated pain levels seen during BFR RE reduce its potential utility as a viable modality for the public.

A modification of the BFR exercise protocol that minimizes pain levels by releasing cuff pressure between sets of exercise might improve tolerability, but it is unknown how this will impact the physiological responses. Additional research is needed to ensure low-load BFR RE is tolerable while providing the physiological signals that are associated with muscle adaptation. GH circulates in multiple molecular forms, only some of which are biologically active (42). It is thought cell swelling and metabolites accumulation may increase the anabolic response by releasing GH (43, 44). GH has shown to be stimulated by an acidic intramuscular environment and also evidence points out that a low pH stimulates sympathetic nerve activity through group III and IV afferent fibers which plays an important role in the regulation of hypophyseal secretion of GH (45). In the present study, quadriceps strength of untrained subjects increased significantly in both groups, but the magnitude of the observed strength gain in the BFR group was greater than the non-BFR group. The strength changes in response to BFR training thought to depend on both muscle hypertrophy and non-hypertrophy mechanisms. The two major mechanisms thought to be responsible for provoking skeletal muscle adaptation following BFR are cell swelling and metabolite accumulation which inhibit protein breakdown or increase protein synthesis (44). The accumulation of metabolites during BFR may indirectly stimulate anabolic hormonal pathways (44), by stimulating the group III and IV afferent fibers which in turn leads to further recruitment of fast twitch fibers, resulting in a hypertrophic mechanical stimulus as well as strength increment (18).

### **Conclusion**

In conclusion, our findings suggest that the addition of BFR resistance training can provide greater physical enhancements specifically at the muscle activation and endocrine level. Fitness coaches could apply the BFR to impose more physical stress on players in order to gain increased training benefits.

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## چکیده فارسی

یک روش تمرینی جدید برای مردان میانسال تمرین نکرده: مقایسه اثربخشی تمرین مقاومتی با کاف محدودیت جریان خون در مقابل تمرین مقاومتی سنتی

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به منظور بهبود سازگاری‌های تمرینی کالج آمریکایی طب ورزشی استفاده از بارهای تمرین مقاومتی با شدت متوسط تا بالا را توصیه کرده است. با این حال، اغلب استفاده از بارهای تمرینی با شدت متوسط تا بالا در جمعیت‌های میانسال و بیمار امکانپذیر نیست. تمرین با محدودیت جریان خون (BFR) یک روش ساده و کاربردی برای پیشگیری از پیامدهای منفی ناشی سالمندی برای افراد میانسال و سالمند است. بنابراین، این مقاله به منظور طراحی و پیاده‌سازی یک برنامه تمرینی برای بهبود عوامل هورمونی آنابولیک و قدرت عضلانی توسط تمرین مقاومتی با BFR در مردان میانسال انجام شده است. در یک طرح تحقیق نیمه تجربی، ۲۰ (سن ۴۸/۵۵±۲/۱۱) مرد میانسال تمرین نکرده انتخاب شدند. آزمودنی‌ها به صورت تصادفی در دو گروه قرار گرفتند: تمرین با BFR و تمرین مقاومتی سنتی. چهار هفته تمرین BFR شامل اجرای حرکات باز کردن زانو و پرس پا در ۲۰ درصد بود و گروه تمرین مقاومتی سنتی همان حرکات را با شدت ۸۰ درصد یک تکرار بیشینه انجام دادند. نمونه‌های خونی به منظور اندازه‌گیری هورمون رشد و عامل رشد شبه انسولینی-۱ اخذ شدند. سطوح GH و IGF-I به طور معنی داری در هر دو گروه افزایش یافت. با این حال، افزایش غلظت GH در گروه تمرین با BFR به طور معنی داری بیشتر از گروه تمرین سنتی بود. همچنین، غلظت IGF-I بین دو گروه تفاوت معنی داری نداشت. به نظر می‌رسد که اجرای تمرین مقاومتی با BFR طی دوران میانسالی روش مناسبی برای به تاخیر انداختن تاثیر سالمندی بر عوامل هورمونی آنابولیک و قدرت عضلانی است.

واژه‌های کلیدی: محدودیت جریان خون، هورمون‌های آنابولیک، یک تکرار بیشینه، مردان میانسال