Effect of blood flow restriction during low-intensity resistance training on bone markers and physical functions in postmenopausal women

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ABSTRACT

Background: The aim of this study was to investigate the effects of 12-week low intensity resistance training (RT) with blood flow restriction on bone mineral density (BMD), bone turnover markers (BTM), physical functions, and blood lactate concentration in postmenopausal women with osteoporosis or osteopenia.

Methods: 26 study participants (56 ± 1.8yrs, T-score: -2.5 ± 0.7) were randomly assigned into Moderate to High-Intensity RT (MHIRT, n = 7), BFR combined with Low-Intensity RT (LIBFR, n = 7), Low-Intensity RT (LIRT, n = 6), or Control group (CON, n = 6). Exercise group performed leg press, leg extension, biceps curl, and triceps extension 3 times a week for 12 weeks. Training intensity were set at 60% of 1-repetition maximum (1-RM) for MHIRT, and at 30% of 1-RM for LIBFR and LIRT, and reset every 4 weeks for increasing intensity.

Results: Lower, and upper limb 1-RM only increased in MHIRT (65%, $p < 0.001$), and LIBFR (40%, $p < 0.05$), while LIRT only showed increment on lower limb 1-RM (28%, $p < 0.05$). All exercise groups demonstrated significant increment on blood lactate concentration after training session ($p < 0.001$). However, LIBFR showed 2.7 folds higher increment than LIRT ($p < 0.001$). Although no changes were observed in MHIRT, LIBFR, and LIRT, CON showed significant decrease in BMD ($p < 0.05$). While, LIRT showed no responses on BTM, LIBFR significantly increased bone formation markers (P1NP) about 7.05 ng/ml ($p < 0.05$). Lastly, balance improvement was only found in MHIRT, and LIBFR ($p < 0.05$).

Conclusion: 12-week LIBFR can be implied as a safe, and effective method to improve muscle strength, P1NP, and balance similar to MHIRT in postmenopausal women with osteoporosis or osteopenia.

Introduction

Osteoporosis refers to deterioration in bone mass, and micro-architecture, with increase in bone fragility.[1] In 2010 fractures due to osteoporosis estimated approximately 158 million cases worldwide, and the numbers are predicted to be doubled by 2040.[2] Osteoporosis classified as a primary skeleton disorder due to not only imbalance in bone metabolism, but also disrupted whole body homeostasis. In normal bone metabolism, bone remodeling occurs towards tightly balance counteracting processes called bone resorption, and bone formation.[3] It can be treated or prevented with several methods, such as hormone therapy, medication, and exercise.[4] Hormone therapy is not considered as the first-line treatment due to the long-term side effects including higher risk of venous thromboembolism, gallbladder disease, breast cancer, and cardiovascular disease in older postmenopausal women.[5–7] Medication treatment has no effect to reduce fall risk, despite osteoporotic fracture is highly related with fall. On the other hand, exercise intervention positively influence both bone strength and balance to prevent falls.[8,9]

Resistance training (RT) seems to be a powerful stimulus to improve, and maintain bone mass while aerobic exercise proved to be less effective in osteoporosis prevention.[10] Progressive RT has further advantages in patients with osteoporosis due to the positive benefits in strength, muscle mass, and balance.[11] However, un-healthy population, such as sarcopenic, or osteoporotic patient

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might be contraindicate with high intensity resistance training (HIRT),[12,13] because, HIRT can elevate risk of injury in frail, and elderly population.[14,15] Whereas, low intensity resistance training (LIRT; 40% or lower 1-RM) showed to be insufficient maintain bone mineral density in elderly women.[16]

By Wolff's law, stress or mechanical load through exercise has a direct effect on bone formation, and remodeling.[17] Bone formation markers determine the activity of osteoblast, and bone mineralization, on the other hand bone resorption markers determine the activity of osteoclast, and bone degradation.[18] Bone formation markers are product of enzyme secreted by active osteoblast, or peptides which derived from cleavage of Procollagen Type 1 N-Terminal Peptide (P1NP).[18] On the other hand, bone resorption markers are product of the enzymes secreted by active osteoclast, and degradation product of type-1 collagen. International osteoporosis foundation also recommended serum C-telopeptide of collagen type 1 (CTx) as a reference of bone resorption marker.[18] P1NP, and CTx can be detected in serum or plasma.

Blood flow restriction (BFR) training works by occluding venous flow yet allowing partial arterial inflow with manual or pneumatically inflated cuff on the most proximal site of limb during exercise.[19,20] A number of studies reported low-intensity resistance training with BFR (LIBFR) increased both muscle size, and strength in healthy adult.[21–23] In elderly, LIBFR also has beneficial in muscle strength,[24–26] bone markers,[27,28] and hormonal responses.[29,30] Several studies showed positive effects of LIBFR on bone metabolism, formation, and resorption in adult healthy men.[31] Moreover, study with middle age women reported LIBFR effectively increased growth hormone (GH), and insulin like growth factor-1 (IGF-1).[32] Also, study in elderly women with osteoporosis showed similar increase in muscle strength on LIBFR, and HIRT group.[33] However, the advance understanding in the role of LIBFR on Bone mineral density (BMD), Bone turnover markers (BTMs), physical function, etc in postmenopausal women with osteoporosis or osteopenia has shown to be still unclear. Most of the postmenopausal osteoporotic women studies focus on BMD or BTMs without investigate the other related variables, such as muscle strength, balance, and lactate concentration comprehensively, despite the lactic acidosis is the primary factor influencing GH release.[34] Therefore, the aim of this study was to investigate the effects of blood flow restriction during low-intensity RT on BMD, BTMs, blood lactate concentration, and physical functions in postmenopausal women with osteoporosis or osteopenia. We hypothesized that LIBFR would elicit similar response with MHIRT, and more positive response than LIRT and control group.

Methods

Participants

We screened 37 postmenopausal women aged from 50 to 60 years old. 11 of them did not meet the criteria, thus only 26 participated in this study. Among 26 participants, 12 had osteopenia, and 14 had osteoporosis, which were diagnosed by physician through T-score. T-score ≥ -1 indicates normal bone mass, T-score between -1 and -2.5 indicates low bone mass or osteopenia, and T-score below -2.5 indicates osteoporosis.[35] Exclusion criteria included participants who were in medication which affect bone, estrogen level, and glucocorticoids other than calcium and vitamin D within a year before study. Participants who had been attending strength training during the last year before study also excluded. Before the study, all participants signed informed consent form, and explanation regarding the purposes and risk of the study. 26 study participants were randomly assigned into Moderate to High-Intensity RT (MHIRT, n = 7), BFR combined with Low-Intensity RT (LIBFR, n = 7), Low-Intensity RT (LIRT, n = 6), or Control group (CON, n = 6). Ethics Research Committee of Kyungsung University, Busan, South Korea (KSU-19-02-001-0408), approved this study.

Blood flow restriction

BFR cuffs were applied on the most proximal site of the upper and lower limbs using BFR cuffs (The EDGE mobility system, USA). BFR pressure should be adjusted to each individual characteristic to elicit best result, and reduce common concerns, such as the risk of developing a blood clot, and muscle damage, as well as negative effect on cardiovascular system.[36] Moreover, fixed pressure of BFR may not always stimulate across participants under vary conditions due to neglecting the important factors affect limb occlusion pressure (LOP), such as limb circumference and cuff width.[36] Thus, the circumference(c) of arm, and thigh were measured at the most proximal site to calculate the LOP with cuff width (W).[37–39] Cuff size for arm is 38.1 cm length x 5.5 cm width, and for leg is 68.58 cm length x 7.5 cm width. Personalized pressure were applied during whole training program including resting time based on following formula; LOP = 67 + c/0.06 W mmHg.[37–39] However, lower limb cuffs did not apply while performing upper body workout, and vice versa. LIBFR group mean occlusion pressure for upper limbs and lower limbs were 152 ± 6 mmHg and 188 ± 9 mmHg respectively.

Resistance training protocol

Training program held 3 times a week for 12 weeks with a 48-h interval between each session. All participants were randomly assigned into 4 groups, moderate to high-intensity resistance training (MHIRT), low-intensity RT with blood flow restriction (LIBFR), low-intensity RT (LIRT), and control (CON) group.

Each group performed 10 min warm-up exercise using treadmill with speed of 3 km/h followed by basic stretching. As a RT all participants performed bilateral leg press, leg extension, dumbbell biceps curl, and triceps extension. Training intensity for MHIRT were set from 60% to 80% of 1-RM (60%1-RM at 1st & 2 nd week, 70%1-RM at 3rd & 4th week, 80%1-RM at 5th-12th week). MHIRT group performed 10 repetitions of 3 sets for each workout with 60 s of rest between sets (Table 1). LIBFR, and LIRT group training intensity were set at 30% of 1-RM, and each workout was performed for 20 repetitions of 3 sets with 30 s rest between sets. All group had 90 s rest between each workout.

One repetition maximum (1-RM)

One repetition maximum (1-RM) was measured to determine change in muscle strength based on ACSM procedure.[40] Bilateral leg press machine, and bilateral leg extension machine (Infinity, South Korea) were used to test 1-RM leg press and 1-RM leg extension.

Table 1
Resistance training program.

Workout	MHIRT	LIBFR	LIRT
Warming-Up	10min		
Basic stretching	5 min		
Leg press	60–80% 1 R M	30% 1 R M	30% 1 R M
Leg extension	10 reps	20 reps	20 reps
Biceps curl	3 sets	3 sets	3 sets
Triceps extension	60 s rest	30 s rest	30 s rest

Note. MHIRT (Moderate to High-Intensity Resistance Training group), LIBFR (Low-Intensity resistance with Blood Flow Restriction group), LIRT (Low-Intensity Resistance Training group).

For 1-RM biceps curl test, unilateral dumbbell biceps curl with dominant arm were tested, and for 1-RM triceps extension, we used cable cross-over machine (Infinity, South Korea). To maintain the intensity during training program, 1-RM retested every 4 weeks, and no training session held on the day of 1-RM test.

Bone mineral density (BMD)

BMD was measured before and after intervention by using dual-energy X-ray absorptiometry (DEXA; BMtech, South Korea). In lumbar spine, scanning started at L5, and lower border of T12. Patient were lying in supine position with spine flatten against the scanning table. BMD measure for lumbar is typically for total of L1-L4 in the posterior-anterior projection (x-ray behind patient's back and detectors above the abdomen).[41]

Bone turnover markers (BTMs)

Serum concentration of P1NP, and CTx assessed as markers for bone formation and resorption respectively. Pre and post intervention blood sample were collected at 9:00 a.m. in the morning after a 12-h fast, and stored in Serum Separating Tube (SST) with clot activator. It was centrifuged at 3,000 rpm for 10—15 min to separate plasma with the serum blood. The concentration of P1NP and CTx were analyzed using COBAS 8000 e801 (Roche, Germany) with ECLIA (Electrochemiluminescence Immunoassay). We used Elecsys total P1NP (Roche, Germany) for P1NP reagent, and Elecsys β-CrossLaps (Roche, Germany) for CTx reagent.

Blood lactate concentration

Blood lactate level was assessed before and after the training at week 4th, 8th, and 12th. Accutrend (Roche Diagnostics, USA) was used to evaluate capillary blood lactate level. Because peak level of blood lactate was reached at 2 min after training,[42] we took blood sample 2 min after the training ended. For LIBFR group, after all work out done, cuff was immediately removed, and the same process were proceeded for post-training lactate test.

Balance assessment

Static balance was assessed by using modified timed single leg stance with eyes open, and closed. Participants were instructed to do a tandem stance, and asked to place the dominant foot in front. With arms across, and vision forward, participants were instructed to lift their dominant leg from the posterior foot as high as the knee. Participants should hold the position, and timing stopped if foot moved, foot touched ground, or hands moved from starting position. Static balance eyes closed test performed using same protocol, but with eyes closed.

Dynamic balance was assessed by using timed backward tandem walk test over a 6-m course. Participants with barefoot were instructed to walk backward with toe of one foot placed exactly behind the heel of the other guided with a straight line. Participants

conducted to walk as fast as they could without falling down or stepping out of the line. Each participant performed two attempts for all balance tests, and the mean score was collected for analysis.

Statistical analysis

All analyses were performed using SigmaPlot 12.0 (Systat Software, San Jose, CA). As repeated measurements were made within subject, a mixed effects model was used to analyze the data. Variables were analyzed with one-way ANOVA (baseline difference) or two-way repeated-measures ANOVA (main effects of treatment and time, treatment × time interaction). In the event of a significant treatment × time interaction, the Holm-Sidak post hoc procedure was used to identify differences between specific means. If the interaction term was not significant (leg press, femur neck T-score, CTX, P1NP, and P1NP/CTX ratio), it was removed, and only the main effects of group and time were included in the model. Since BTMs showed wide variance, we used Welch's T-test. The type I error rate was <0.05.

Results

General characteristics of participants

All participants (n = 26) completed 12 weeks training program with each group compliance of 99%, 100%, and 99% for MHIRT, LIBFR, and LIRT respectively. As shown by Table 2, the menopausal periods (5.84 ± 0.32 yrs) were not different between all groups, 46% had osteopenia, and 54% had osteoporosis based on total lumbar T-score. Total lumbar T-score, height, body mass, muscle mass, and % body fat also showed no difference. Likewise, no differences were observed after 12 weeks of intervention in each interest site (all $p > 0.05$).

One repetition maximum

Lower limb: 1-RM leg press, and leg extension showed no difference between all groups at baseline (Table 3). As shown by Fig. 1A, all training groups resulted in a significant strength increment on 1-RM leg press, and leg extension (MHIRT & LIBFR $p < 0.001$; LIRT $p < 0.05$), while CON showed no changes on all lower limb strength. In detail, MHIRT showed noticeable differences compare to LIBFR (41.4 kg; $p < 0.05$), LIRT (47.3 kg; $p < 0.05$), and CON (81.5 kg; $p < 0.001$) at post 1-RM leg press. Interestingly, LIBFR indicated greater 1-RM increment compare to CON with difference of 40.1 kg ($p < 0.05$). In a matter of 1-RM leg extension, difference between groups only was found between MHIRT and CON with value of 13.4 kg ($p < 0.001$) (Fig. 1B).

Upper limb: At baseline mean value of 1-RM biceps curl, and triceps extension there was no differences between all groups ($p > 0.05$; Table 4). LIRT, and CON did not show any change of strength over time on 1-RM upper limb at all sites of interest. While MHIRT, and LIBFR gained 1.14 kg (18.3%), and 0.86 kg (16.4%) of strength respectively in 1-RM biceps curl compare to pre value

Table 2
Characteristics of Study participants.

	MHIRT (n = 7)	LIBFR (n = 7)	LIRT (n = 6)	CON (n = 6)
Age (yrs)	56.43 ± 0.72	55.71 ± 0.52	56.50 ± 0.99	56.83 ± 0.70
Post-menopause periods (yrs)	6.57 ± 1.00	5.29 ± 0.68	5.67 ± 1.09	6.50 ± 0.92
Height (cm)	157.60 ± 0.94	157.69 ± 1.02	155.33 ± 0.97	158.60 ± 2.23
Body mass (kg)	61.99 ± 3.45	56.06 ± 2.34	56.13 ± 3.22	56.42 ± 2.28
Muscle mass (kg)	21.99 ± 0.76	20.36 ± 0.54	20.57 ± 1.00	20.55 ± 0.81
Body fat (%)	33.90 ± 2.40	32.36 ± 1.26	29.97 ± 2.56	31.85 ± 1.94

Table 3
Lower Limb 1 repetition maximum (1-RM).

		MHIRT (n = 7)	LIBFR (n = 7)	LIRT (n = 6)	CON (n = 6)
Leg Press (kg)	pre	97.43 ± 8.45	82.86 ± 3.76	94.17 ± 9.61	91.67 ± 10.78
	post	165.71 ± 18.50*†‡§	124.29 ± 4.93*†	118.33 ± 10.14*	84.17 ± 10.83
Leg Extension (kg)	pre	24.29 ± 2.00	26.00 ± 1.27	25.67 ± 1.23	26.67 ± 2.58
	post	39.43 ± 3.24*†	33.71 ± 1.21*	32.83 ± 1.33*	26.00 ± 2.58

Note. *: represents significant difference between pre and post within group (p < 0.05). †: represents significant group difference with CON (p < 0.05). ‡: represents significant group difference with LIRT (p < 0.05). §: represents significant group difference with LIBFR (p < 0.05).
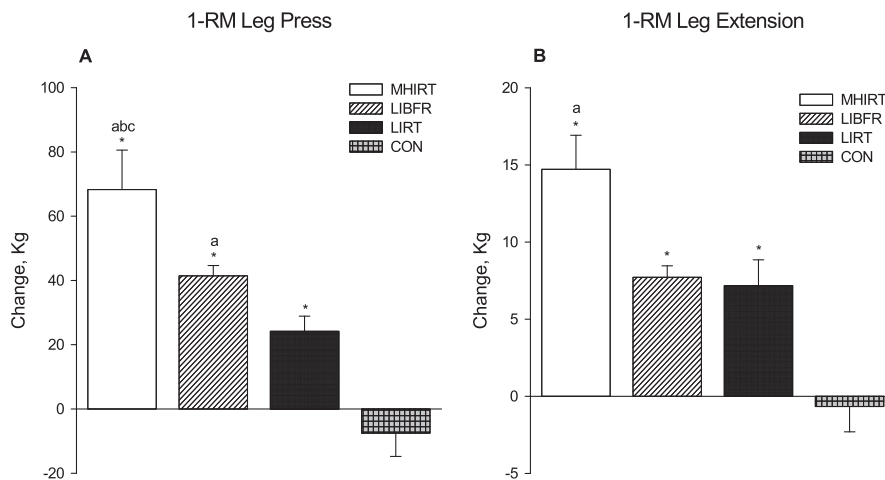
Fig. 1. *Lower limb* 1-RM *change from pre to post.*
Note. *: represents significant difference between pre and post within group (p < 0.05). a: represents significant group difference with CON (p < 0.05). b: represents significant group difference with LIRT (p < 0.05). c: represents significant group difference with LIBFR (p < 0.05).

Table 4
Upper Limb 1 repetition maximum (1-RM).

		MHIRT (n = 7)	LIBFR (n = 7)	LIRT (n = 6)	CON (n = 6)
Unilateral Biceps Curl (kg)	pre	6.29 ± 0.18	6.00 ± 0.44	6.50 ± 0.43	5.83 ± 0.40
	post	7.43 ± 0.20*†	6.86 ± 0.34*	6.83 ± 0.40	5.67 ± 0.42
Triceps Extension (kg)	pre	26.86 ± 1.28	24.43 ± 1.02	24.67 ± 1.26	22.83 ± 0.98
	post	32.00 ± 1.57*†‡§	27.71 ± 0.81*†	26.00 ± 1.59	23.33 ± 0.49

Note. *: represents significant difference between pre and post within group (p < 0.05). †: represents significant group difference with CON (p < 0.05). ‡: represents significant group difference with LIRT (p < 0.05). §: represents significant group difference with LIBFR (p < 0.05).

(p < 0.001, p < 0.05, respectively; Table 4).

On 1-RM triceps extension, greater increment of strength was detected in MHIRT, and LIBFR (p < 0.001, p < 0.05, respectively), with expectantly highest absolute change of strength was in MHIRT (5.14 kg), followed by LIBFR (3.29 kg). A group difference at post 1-RM biceps curl was only occurred between MHIRT, and CON (1.76 kg; p < 0.05). Even though there was no statistical difference, LIBFR showed 0.53 kg (≒2.6 times) greater gains in strength (LIBFR: 0.86 vs LIRT: 0.33 kg) compare to LIRT (Fig. 2A) despite of identical training intensity and exercise volume. As shown by Fig. 2B, MHIRT showed noticeable increment on 1-RM triceps extension at post than LIBFR (4.2 kg; p < 0.05), LIRT (6 kg; p < 0.05), and CON (8.6 kg; p < 0.001). LIBFR also demonstrated greater difference compared to CON (2.6 kg; p < 0.05).

Bone mineral density

Table 5 represents bone mineral density, and T-score at lumbar, and femur neck. The equal variance on total lumbar BMD, and femur neck BMD was ensured among all groups at the baseline (p > 0.05). There was no statistical difference between pre and post

intervention on total lumbar, and femur neck BMD in MHIRT, LIBFR, and LIRT. However, total lumbar BMD and T-score in CON decreased 0.04 g/cm^2 (3.5%) and 0.3 significantly after 12 weeks (p < 0.05).

Bone turnover markers

CTX: CTx value at the baseline showed homogeneity of variance across all groups (p > 0.05). Only MHIRT showed substantial increment approximately of 0.098 ng/ml (21%) on CTx compare to the baseline (p < 0.05). No changes were noticed in LIRT and CON, however LIBFR tended towards decrement about 0.062 ± 0.02 ng/ml (11%) from baseline (p = 0.098).

P1NP: There were no difference at baseline on P1NP between all groups. Greater increases on P1NP were founded in MHIRT (9.2 ng/ml; p < 0.05), LIBFR (7.05 ng/ml; p < 0.05), and CON (10.28 ng/ml; p < 0.05) compare to the baseline. No statistical interaction was determined between groups on the post P1NP value.

P1NP/CTx ratio: We calculated the ratio of bone remodeling by dividing bone formation marker (P1NP) with bone resorption marker (CTx). P1NP/CTx ratio were statistically identical at baseline. We found LIBFR had tendency to increase on P1NP/CTx ratio
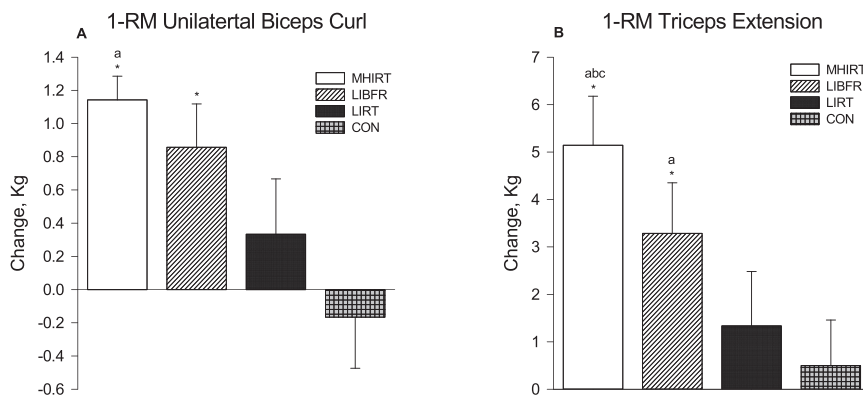
Fig. 2. *Upper limb 1-RM change from pre to post.*
Note. *: represents significant difference between pre and post within group (p < 0.05). a: represents significant group difference with CON (p < 0.05). b: represents significant group difference with LIRT (p < 0.05). c: represents significant group difference with LIBFR (p < 0.05).

Table 5
Total lumbar bone mineral density and T-score.

		MHIRT (n = 7)	LIBFR (n = 7)	LIRT (n = 6)	CON (n = 6)
Total Lumbar BMD (g/cm^2)	pre	0.89 ± 0.04	0.88 ± 0.01	0.86 ± 0.03	0.94 ± 0.04
	post	0.88 ± 0.04	0.86 ± 0.02	0.85 ± 0.02	0.90 ± 0.03*
Total Lumbar T-score	pre	−2.51 ± 0.34	−2.66 ± 0.11	−2.80 ± 0.27	−2.15 ± 0.36
	post	−2.61 ± 0.36	−2.83 ± 0.18	−2.82 ± 0.18	−2.45 ± 0.28*
Femur neck BMD (g/cm^2)	pre	0.87 ± 0.04	0.84 ± 0.06	0.78 ± 0.03	0.90 ± 0.06
	post	0.88 ± 0.03	0.84 ± 0.03	0.78 ± 0.04	0.93 ± 0.08
Femur neck T-score	pre	−0.84 ± 0.32	−1.04 ± 0.49	−1.58 ± 0.28	−0.54 ± 0.53
	post	−0.74 ± 0.24	−1.04 ± 0.27	−1.58 ± 0.34	0.04 ± 0.70

Note. *: represents significant difference between pre and post within group (p < 0.05).

for about 23.37 (18%; p = 0.09). While all groups did not show any change compare to baseline.

Balance

At baseline, no statistical differences were found in all aspects of balance test between all groups. Static eye open (EO) balance test showed significance increase in MHIRT (28.2sec; p < 0.05), and LIBFR (46.3sec; p < 0.001) compared to baseline. On eye closed (EC) static balance, only LIBFR result in longer time (5.34sec) compare to the baseline (p < 0.05). While MHIRT, LIRT, and CON showed no changes over time. For dynamic balance test, significant improvement was only indicated in MHIRT (7.02sec; p < 0.05), while other groups did not present any significant changes. Taken together, MHIRT, and LIBFR showed greater improvement only on static balance with eyes open.

Blood lactate concentration

Fig. 3 represents results of changes in blood lactate concentration before and after training session at week 4th, 8th, and 12th. At week 4th, all training groups showed significant increase on blood lactate level compare to baseline, with almost 2 times higher in MHIRT (Δ:4.57 mmol/L, p < 0.001), followed by LIBFR with increment of 4.52 mmol/L (p < 0.001), and lastly LIRT with increment of 1.48 mmol/L (p < 0.05). After assigned exercise session no difference was found between MHIRT, and LIBFR, however MHIRT, and LIBFR showed significant group differences when compared to LIRT (MHIRT:3.12 mmol/L, p < 0.001; LIBFR:2.66 mmol/L, p < 0.05). Similar results were observed at week 8th & 12th with all training group. At the 12th week, we found significant increase of blood

lactate level after training session in MHIRT (6.97 mmol/L; p < 0.001), LIBFR (6.87 mmol/L; p < 0.001), and LIRT (2.48 mmol/L; p < 0.001), and both MHIRT and LIBFR showed almost 2 times higher concentration compare to LIRT on post training session (LIBFR:8.8 vs LIRT: 4.57 mmol/L; p < 0.001).
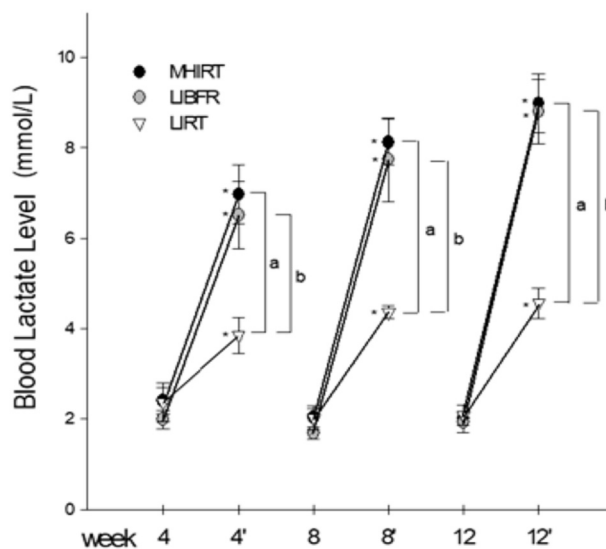
Fig. 3. *Blood lactate concentration.*
Note. *: represents significant difference between pre and post within group (p < 0.05). a: represents significant group difference with CON (p < 0.05). b: represents significant group difference with LIRT (p < 0.05). c: represents significant group difference with LIBFR (p < 0.05).

Table 7
Balance.

		MHIRT (n = 7)	LIBFR (n = 7)	LIRT (n = 6)	CON (n = 6)
Static eyes open (sec)	pre	93.21 ± 27.76	83.88 ± 14.60	80.68 ± 20.49	86.01 ± 26.92
	post	121.46 ± 35.84*	130.25 ± 22.50*	107.91 ± 21.13	83.45 ± 31.89
Static eyes closed (sec)	pre	10.55 ± 4.21	5.95 ± 1.29	15.61 ± 7.00	9.05 ± 3.37
	post	10.03 ± 2.05	11.30 ± 2.86*	16.36 ± 8.16	7.44 ± 3.81
Dynamic (sec)	pre	34.19 ± 5.95	32.34 ± 5.87	30.12 ± 1.96	33.32 ± 2.60
	post	27.15 ± 2.39*	29.05 ± 5.99	31.28 ± 2.14	33.64 ± 3.01

Note. *: represents significant difference between pre and post within group ($p < 0.05$).

related with increase in osteoclast number by enhance osteoclast formation, reduce osteoclast apoptosis, and increased osteoclast activity. Increased osteoclast activity promotes more bone resorption, and lead to loss of bone mass.[58] Therefore, the menopause women with osteoporosis or osteopenia highly related with unbalance bone metabilosm and high risk of bone related injuries.

In fact, BMD results from the prior studies showed wide variant following resistance training. Mostly a 12-months training with 70–80% 1-RM of high-intensity RT, performed at least 2 sets of 8–10 repetitions for 3 times a week resulted in increase on BMD.[59–62] However, 6 months interval training revealed that high-intensity RT only appeared to maintain BMD, while CON group showed significant decrease (Hartard et al., 1996; Bemben et al., 2000). In contrast, Vincent & Braith (2002)[63] showed 6 months of high-intensity RT in older male, and female (68 ± 6 yr) increased BMD at the femoral neck. However, the maintained BMD in our study with 12-week intervention is also clinically significant due to the rate of BMD loss with advancing age.

BTM and BFR: For BTM we only analyzed 6 participants out of 7 from LIBFR due to medication (Tylenol), and 5 out of 6 participants from CON due to protein supplement.

Biochemical markers of bone remodeling may be useful for providing information about mechanisms of bone loss, and for monitoring the efficacy of treatments on bone.[64] An advantage of these markers in bone turnover cycle is their rapid response to treatments, as shown by increases in bone formation markers in the first month of a 4-month resistance-training program in young men.[65] Thus, we measured serum P1NP as an indicator of bone formation and serum CTx as a marker of bone resorption. In our study, after 12 weeks MHIRT showed significantly increase both in serum CTx (0.098 ng/ml; $p < 0.05$), and P1NP (9.2 ng/ml; $p < 0.05$). While LIRT showed no response on both BTMs, LIBFR showed a significant increase in P1NP bone formation markers (Δ: 7.05 ng/ml; $p < 0.05$; Table 6). Therefore, chemical stimulus induced in LIBFR may be adequate to stimulate bone formation resemble with MHIRT. However, we assumed that mechanical load from LIBFR were inadequate to produce micro-cracks which induce bone resorption.

Balance and BFR: Balance is an ability to maintain the center of body mass within the base support with minimal postural sway.[66] Maintaining balance requires coordination of input from multiple sensory systems including the vestibular, somatosensory, and visual systems.[67] In detail, vestibular system senses organs that regulate equilibrium, somatosensory system senses of proprioception, and kinesthesia of joints, information from skin and joints (pressure and vibratory senses); spatial position of different body parts relative to each other. In addition, visual system refer to verticality of body, and head motion; spatial location relative to objects. Since balance has complex factors, it is difficult to determine which factors were stimulated in this study. However, we observed that low mechanical load had no effect in balance, while high mechanical load improved static and dynamic balance

(Table 7). Of particular interest, LIBFR showed improvement in static balance, both open and closed eyes ($p < 0.05$), but not on dynamic balance. It appears to be the strengthening of the major muscle groups, such as knee flexor and knee extensor for postural stability, because muscle mass and muscle strength were positively correlated to balance.[68] We assume that dynamic balance has more relation with muscle strength, and/or speed, while static balance seems have more relation with neuromuscular connection, since no movement but only maintaining the equilibrium. In the further study, comprehensive assessment of balance in people with osteoporosis or osteopenia include a muscle strength of lower limb and abdominal, and the many other subsystems underlying balance control mechanism.

Conclusions

Blood flow restriction during low-intensity resistance training (LIBFR) revealed to be more effective to increase muscle strength, lactate concentration, bone formation markers, and balance in low bone density postmenopausal women compared to traditional low-intensity resistance training (LIRT). Even though moderate to high-intensity resistance training (MHIRT) showed greatest improvement in muscle strength, and bone turnover markers (BMT), however, the higher risk in injury also can not be neglected.

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Author statement

Linero Christian: Conceptualization, Methodology, Validation, Formal analysis, Writing original draft, Visualization.

Choi Seung-Jun: Conceptualization, Methodology, Validation, Formal analysis, Writing original draft, Writing review & editing, Resources, Supervision.

Declaration of competing interest

The authors have no conflicts of interest relevant to this article.

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