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Chronic effectiveness of walking with blood flow restriction on the activation and strength in osteoporotic older women: A randomized clinical trial

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Abstract: *Background and Objectives:* Blood flow restriction (BFR) has been investigated as an alternative method combined with resistance training or AT to promote different health benefits for older people. Nevertheless, no study analyzed chronic effects of BFR on muscle activation in this population, and in some investigations, the application of BFR has been employed arbitrary pressures, which can be a serious methodological error, both from the results and of the risk to the health of the older. Thus, this study analyzed the effect of 24 weeks of walking with BFR on activation and muscle strength in elderly women with osteoporosis. *Materials and Methods:* Thirty older women (66.0±4.6 years) performed randomly to one of three training groups: WALK (moderate–intensity walking), WALK+BFR (low–intensity walking with BFR), or BFR (BFR alone). Muscle activation (sEMG) and strength of knee flexors and extensors were measured pre–intervention and after 12 and 24 weeks. *Results:* Only a trivial effect size (ES) for the WALK+BFR (ES= 0.16) was observed in sEMG of the knee flexors compared to WALK. A moderate effect was observed in sEMG of the knee extensors (ES= 0.65) for the WALK+BFR compared to the WALK. However, adverse effects were found in the strength of the knee flexors for the BFR (ES= −0.86) and WALK+BFR (ES= −0.69) compared to WALK. Adverse and null effects, respectively for the BFR (ES= −0.16) and WALK+BFR (ES= 0.06) groups, were also observed on the strength gain of the knee extensors. *Conclusions:* Low–intensity walk combined with BFR does not provide relevant chronic effects on strength gain or even limit muscle strength gain, however, due to greater activation of knee extensors over 24 weeks, it is possible to benefit from the use of similar strategies to obtain neuromuscular gains in the long-term for elderly women with osteopenia and osteoporosis.

Keywords: aging; aerobic exercise; vascular occlusion; electromyography

Article

Chronic effectiveness of walking with blood flow restriction on the activation and strength in osteoporotic older women: A randomized clinical trial

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1. Introduction

Associations between dynapenia and low functional performance or physical disability are present in 90% of studies with older adults (age ≥60 years), and only in 35% of them is there an association with sarcopenia [1]. Dynapenia is not associated with muscle or neurological diseases, but rather, a natural and multifactorial loss arises from the aging process [1,2], which increases the functional disability and risk of falls [3,4]. Moreover, it promotes a loss of muscle strength faster than the loss of muscle mass, and muscle mass gain does not minimize dynapenia due to aging [5]. For these reasons, traditional resistance training and aerobic training (AT) have been commonly recommended to improve health and mitigate physical disability related to aging [6–8].

To obtain substantial gains in muscle strength is necessary to apply loads greater than 65% of one–repetition maximum (1RM) [9] in resistance training, whereas, in AT, a minimum intensity greater than 45% VO_{2max} is recommended [10]. In general, a complete training program that includes both types of exercises would take 5 to 8 hours per week and these recommendations may be obstacles for most of the older and middle–aged populations. Furthermore, countless older people have contraindications to perform a traditional exercise program due to comorbidities or high mechanical stress to bones and joints [11–13].

In that perspective, blood flow restriction (BFR) has been investigated as an alternative method combined with resistance training or AT to promote different health benefits for older people [11–15]. For instance, low–load walk training with BFR has demonstrated improvements in isokinetic knee extension [16] and flexion [17,18], 1RM strength (leg press and leg curl) [16], muscle cross–sectional area [16,17,19], carotid arterial compliance [17], and physical function [18,20,21] in healthy older individuals. Nevertheless, no study analyzed chronic effects of BFR on muscle activation in this population, and in some investigations, the application of BFR is controversial [16,18,21], since arbitrary pressures (not individualized) were used, which can be a serious methodological error, both from the results and of the risk to the health of the older [22].

Although recent reviews have reported that AT with BFR increases muscle strength, muscular hypertrophy, and physical function [11,12], and with promises of positive effects on bone metabolism [14,15] in this population, the quality of studies has only been rated as moderate and most of this evidence demonstrated a high heterogeneity [11–13]. The main differences occurred in sample sizes, randomization techniques, training protocols (e.g. training duration, load progression, or BFR pressure application), trained limbs (e.g. lower vs upper extremity), strength assessments (dynamic 1RM, isometric or isokinetic testing), and health status (e.g. comorbidities, level of physical activity) [11–13]. Therefore, to fully understand the clinical utility of BFR for promoting the benefits mentioned above, its relationships must be further analyzed, especially in older people with comorbidities.

To address some knowledge gaps, the present study aimed to apply AT combined with BFR (using individualized pressures) and to analyze the chronic effects on muscle activation and strength of the knee flexors and extensors in older women with osteopenia or osteoporosis. We hypothesized that AT with BFR promotes an increase in strength and muscle activation similar to AT of moderate intensity. The individualized BFR method may assist different therapeutics to design more effective and tolerable training sessions and improve the fastest neuromuscular adaptation in older women with osteopenia or osteoporosis. Furthermore, the variables of muscle activation and muscle strength are important for the prevention of falls and possible fractures [23].

2. Materials and Methods

2.1 Participants

Older women were selected by the following criteria: age ≥60 years; postmenopausal; with osteopenia (T–score [standard deviation] = −1.0 to −2.5) or osteoporosis (T–score [standard deviation] ≤ −2.5) in at least one of the areas analyzed by DXA (Table 1): lumbar spine, femoral neck, and total femur; no hormone therapy in the last 3 months before the study; no AT and resistance training in the last 3 months before the study; irregularly active according to the International Physical Activity Questionnaire (walking frequently ≤ 3 times a week and duration ≤ 30 minutes or walking 4 times a week lasting ≤ 20 minutes and moderate physical activity 1 time a week lasting ≤ 30 minutes); ABI between 0.91 and 1.30; without musculoskeletal and cardiorespiratory diseases; and nonusers of medications that could interfere the bone metabolism (e.g., corticosteroids). Older women with musculoskeletal pain or osteomyoarticular dysfunction during the inter-

vention period, who attended fewer than 85% of the session, or who dropped out were excluded.

A total of 60 women volunteered for the current study, however, five participants did not meet all the inclusion criteria, nine were not able to fit the study into their schedule, three requested to be withdrawn from the study before initiating the training, and 13 during training for reasons unrelated to the study procedures (Figure 1). Thus, 30 older women (age: 66.0 ± 5.0 years; body mass: 66.2 ± 10.7 kg; height: 1.52 ± 0.04 m; BMI: 28.7 ± 4.5 kg/m^2) with overweight and osteopenia or osteoporosis were enrolled in the trial (Table 1). The older women were asked to maintain their usual diet and activities of daily living during the intervention, so no nutritional and lifestyle monitoring was performed. They were recruited from a physiotherapy clinic and an association of retirees of the local university. The project was conducted in the municipality of João Pessoa–PB, in northeast Brazil.

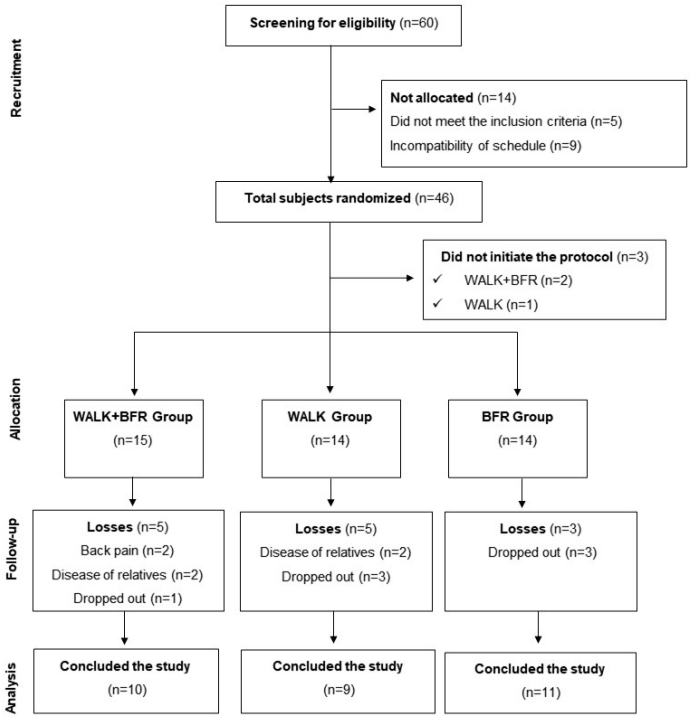

Figure 1. Sample recruitment flowchart. WALK+BFR, low–intensity walk with blood flow restriction intervention; WALK, moderate–intensity walking intervention; BFR, blood flow restriction intervention.

A priori sample size was estimated by the G*Power 3.1.9 software (Franz Faul, University Kiel, Germany) for an RM–ANOVA (within–between interaction), given α= 0.05, power (1−β)= 0.8, and effect size (ES)= 0.7 (large) [24,25]. Therefore, a minimum of 27 participants was required. A similar effect size has been observed in previous clinical trials involving the BFR approach with older women [17,18,20]. Since some volunteers denied or were unable to carry out the evaluations, the analyzes were performed by protocol.

Table 1. Demographic, anthropometric, and osteopenic data of the study participants

Variables	Total (n=30)	WALK Group (n=9)	WALK+BFR Group (n=10)	BFR Group (n=11)
Ethnicity				
White	9 (30.0)	2 (22.2)	5 (50.0)	2 (18.2)
Black	10 (33.3)	2 (22.2)	5 (50.0)	3 (27.3)
Mixed	11 (36.7)	5 (55.6)	0 (0.0)	6 (54.5)
Bone Mineral Density				
T–LS				
Normal	5 (16.7)	2 (22.2)	1 (10.0)	2 (18.2)
Osteopenia	16 (53.3)	5 (55.6)	6 (60.0)	5 (45.5)
Osteoporosis	9 (30.0)	2 (22.2)	3 (30.0)	4 (36.4)
T–FN				
Normal	6 (20.0)	2 (22.2)	2 (20.0)	2 (18.2)
Osteopenia	22 (73.3)	7 (77.8)	8 (80.0)	7 (63.6)
Osteoporosis	2 (6.7)	0 (0.0)	0 (0.0)	2 (18.2)
T–TF				
Normal	14 (46.7)	6 (66.7)	4 (40.0)	4 (36.4)
Osteopenia	14 (46.7)	3 (33.3)	5 (50.0)	6 (54.5)
Osteoporosis	2 (6.7)	0 (0.0)	1 (10.0)	1 (9.1)

Note: Data presented as mean and (standard deviation) or absolute and (relative, %) frequency. Abbreviations: WALK+BFR, low–intensity walk with blood flow restriction intervention; WALK, moderate–intensity walking intervention; BFR, blood flow restriction intervention; T–LS, total score lumbar spine; T–FN, total score femoral neck; T–TF, total score femur; BMI, body mass index.

This study was approved by the Ethics Committee of the Health Science Center of the Federal University of Paraíba following (CAAE: 67125317.1.0000.5188) the Declaration of Helsinki and registered on the Brazilian Clinical Trials Registration Platform (RBR–3d957w). All volunteers signed an informed consent form.

2.2 Experimental design and procedures

A 3 (training group: WALK, WALK+BFR or BFR) × 3 (time: baseline, 12, and 24 weeks) factorial randomized clinical trial was performed (Figure 2). On the first day, the older women performed ankle–brachial index (ABI), body composition by dual–emission X–ray absorptiometry – DXA (Lunar Prodigy Advance®, GE Healthcare, USA), BFR pressure, and maximum oxygen uptake (VO_{2max}) measures. On the second day, 48 hours after the first session, muscle activation and muscle strength were recorded concomitantly, by electromyography and dynamometry, and from the third to the fifth day, three familiarization sessions were performed followed by the intervention. Outcomes were assessed at baseline, 12 weeks, and 24 weeks (Figure 2). Participants were randomized (www.randomization.com) among the training groups to start data collection. One of the authors was blinded for the statistical analyses, in which he did not know the groups tested.

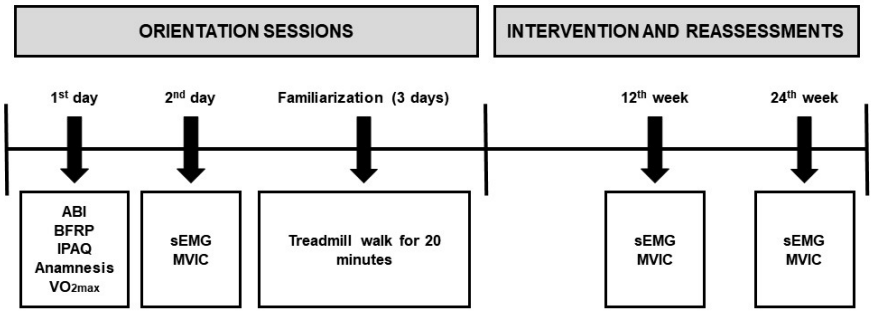

Figure 2. Study design. ABI, ankle–brachial index; BFRP, blood flow restriction pressure; IPAQ, international physical activity questionnaire; VO_{2max}, maximum oxygen uptake; sEMG, surface electromyography; MVIC, maximum voluntary isometric contractions.

Maximal oxygen uptake. To estimate VO_{2max} (mL/kg/min) and ensure the speed progression on the treadmill (820EX, Embreex, Brazil) for the AT, a submaximal test proposed by Sousa et al. [26] was performed. Evaluations were performed at baseline, 1, 3, 5, and 6 months postintervention, and heart rate was monitored during all training sessions.

Blood flow restriction (evaluation and intervention). Arterial occlusion pressure was obtained using a portable vascular doppler (DV – 2001, MedPej®, Brazil) and a pneumatic cuff for obese people (width 180 mm; length 900 mm; Custom Built – no manufacturer) according to the study by Laurentino et al. [27]. For women in the WALK+BFR and BFR groups, pneumatic tourniquet cuffs were used on the proximal portions of the thighs and remained inflated throughout the session [27]. The BFR pressure protocol (cuff pressure) was applied as follows: familiarization and 1st month (20% BFR= 35.2 ± 5.3 mmHg); 2nd month (30% BFR= 52.5 ± 8,1 mmHg); 3th month (40% BFR= 65.6 ± 12.4 mmHg); and 4th to 6th month (50% BFR= 82.4 ± 13.8 mmHg).

Dynamometry. The maximum isometric strength of the knee was measured using a digital dynamometer (DD–300, Instrutherm Ltd., Brazil) with the woman sitting in an adapted Bonett chair, keeping the knee at a 60° angle for the extensors and a 30° angle for the flexors, measured by a fleximeter (Instituto Code de Pesquisa, Brazil), with the trunk supported on the backrest and stabilized by restraining belts on the trunk, pelvis, and thigh of the lower limb to be evaluated. During all the test procedures, the participants were instructed to firmly hold the lateral supports of the seat to stabilize all body segments. The test consisted of a series of three maximum voluntary isometric contractions for 5 seconds, with an interval of 1 minute between each; the mean of the 3 strength peaks was recorded.

Electromyography. Surface electromyography (sEMG) of the flexor muscles (semitendinosus – ST and biceps femoris – BF) and extensor muscles (vastus medialis – VM and vastus lateralis – VL) of the knee were recorded using an electromyograph (W4X8, Biometrics Ltd., UK) with eight channels, Bluetooth, and the following technical specifications: hardware with a 12–bit analog–to–digital conversion card; amplifier with a gain of 1000x; 20 to 500 Hz bandpass filter (second order–Butterworth); common–mode rejection ratio > 100 dB; signal noise ratio< 3 μV root mean square; 10^9 Ohm impedance; superficial, bipolar, active, differential simple electrodes, with preamplification of 20x; and a sampling frequency of 1000 Hz. After shaving, cleaning the skin, and marking the points with henna dye, the electrodes were fixed on the ST, BF, VL, and VM muscles, according to Surface Electromyography for the Non–Invasive Assessment of Muscles – SENIAM [28], while the reference electrode was fixed on the lateral malleolus of the contralateral limb, always by the same examiner. The mean square root was used to process the signal from the central 3 seconds of the signal window during the 5 seconds of maximum voluntary isometric contraction. The reference value for normalization of

the sEMG signal was the maximum voluntary isometric contraction peak of each muscle, and to ensure the comparison between subjects and groups, the VL+VM and BF+ST values were summed. Both for recording the strength and for sEMG, randomization was performed between the lower limbs (www.randomization.com).

Before each training session, the women stretched the upper limbs for 10 minutes with an emphasis on the antero–internal chain, the posterior chain, the extensor muscles of the shoulders and trunk. Then, a stretch was performed for the lower limbs for the knee extensor and flexor muscles. Finally, the participants performed to one of three training groups – speed progression for the AT was prescribed according to the VO_{2max} test: (1) WALK: The women performed 20 minutes of moderate–intensity walking on an ergometric treadmill at 60% VO_{2max} 3 times per week (Monday, Wednesday, and Friday) for 6 months; (2) WALK+BFR: The women performed 20 minutes of low–intensity walk on an ergometric treadmill at 40% VO_{2max} combined to BFR 3 times per week (Monday, Wednesday, and Friday) for 6 months; (3) BFR: The women, lying in the supine position, performed 20 minutes of BRF 3 times per week (Monday, Wednesday, and Friday) for 6 months.

2.3 Statistical Analysis

Simple imputation analysis was performed for sEMG variables with missing values in the 12 weeks evaluations [29]. Data were analyzed using two–way repeated–measures ANOVA (3 training conditions × 3 times). If a significant group, time, or interaction effect was observed, post hoc analyses were performed by the Sidak *post hoc.* Levene's test confirmed that the error variance of the dependent variables was equal across groups. Mauchly's test was used to test the assumption of sphericity, and when it was violated, the Greenhouse–Geisser corrected values were used. Moreover, effect size (ES) was estimated by the Cohen's *d* (pretest–posttest designs and pre–post–control design) [30] using the Psychometrica calculator and interpreted as: $d< 0.20$ trivial, $d= 0.20–0.59$ small, $d= 0.60–1.19$ moderate, $d= 1.20–1.99$ large, $d= 2.00–3.99$ very large and $d\geq 4.0$ almost perfect [31]. To assess the correlation between muscle activation and strength of the knee flexors and extensors at baseline, 12, and 24 weeks of intervention, Pearson's correlation test was used. Data were analyzed using the IBM Statistical Package for the Social Sciences, version 25.0 (IBM Corp., Armonk, USA), and the results at $P<0.05$ were considered statistically significant.

3. Results

3.1 Surface electromyography of the knee flexors and extensors muscles

At baseline, no difference was found in the sEMG of the knee flexors ($P= 0.720$) and extensors ($P= 0.313$), or for the strength of the knee flexors ($P= 0.751$) and extensors ($P= 0.995$). For the sEMG of the knee flexors, a significant main effect was only found for time, in which the WALK and WALK+BFR groups improved the activation after 24 weeks (Table 2). Although a greater intragroup ES has been observed for the WALK+BFR group at the 24 weeks, a trivial ES was only verified in comparison to the WALK group. About the sEMG of the knee extensors, a significant main effect was found for time and training condition × time interaction. BFR and WALK+BFR groups at the 24 weeks presented a very large intragroup effect (Table 2) and a moderate ES has estimated in favor of the WALK+BFR group compared to the WALK group.

3.2 Strength of the knee flexors and extensors muscles

Regarding the strength of the knee flexors, a significant main effect was found for time and training condition × time interaction. All groups increased the strength of the knee flexors after 24 weeks; however, the WALK group presented a very large effect (Table 2). For the strength of the knee extensors, a significant main effect was only found for time, in which the WALK+BFR group increased the muscle strength after 12 (moder-

ate effect) and 24 weeks (very large effect). In the other groups, the strength gain was observed only after 24 weeks.

Table 2. Comparison of the activation and muscle strength for knee flexors and extensors over the 24 weeks of intervention in older women with osteopenia or osteoporosis

Variable	Time	Training group			ANOVA Effects	F	*P*	Cohen's *d*
		WALK	WALK+BFR	BFR				
Activation of the knee flexors[a]	Baseline	0.50 (0.02)	0.49 (0.02)	0.52 (0.02)	Group	0.3	0.720	
	12 weeks	0.54 (0.02)	0.53 (0.02)	0.52 (0.02)	Time	14.7	0.001	
	24 weeks	0.56 (0.02)*	0.56 (0.01)*	0.53 (0.01)	Group × Time	2.2	0.083	
	ES Baseline vs. 12 weeks	0.51 [−0.4; 1.4]	0.59 [−0.3; 1.4]	0.00 [−0.8; 0.8]	**ES WALK+BFR vs. WALK**			**0.16**
	ES Baseline vs. 24 weeks	0.85 [−0.1; 1.7]	1.23 [0.3; 2.2]	0.52 [−0.3; 1.3]	**ES BFR vs. WALK**			**−0.75**
Activation of the knee extensors[b]	Baseline	0.51 (0.02)	0.46 (0.02)	0.52 (0.02)	Group	1.2	0.313	
	12 weeks	0.55 (0.03)	0.49 (0.02)	0.54 (0.02)	Time	50.2	0.001	
	24 weeks	0.56 (0.02)*	0.55 (0.02)*	0.56 (0.02)*	Group × Time	4.2	0.005	
	ES Baseline vs. 12 weeks	1.24 [0.2; 2.2]	1.26 [0.3; 2.2]	0.77 [−0.1; 1.6]	**ES WALK+BFR vs. WALK**			**0.65**
	ES Baseline vs. 24 weeks	0.89 [−0.1; 1.8]	2.8 [1.6; 4.1]	2.00 [0.9; 3.0]	**ES BFR vs. WALK**			**−0.02**
Strength of the knee flexors (kgf)	Baseline	122.6 (12.1)	128.7 (11.5)	121.4 (10.9)	Group	0.1	0.751	
	12 weeks	134.6 (13.7)	137.4 (13.0)	131.1 (12.4)	Time	52.5	0.001	
	24 weeks	180.3 (13.9)*	161.5 (13.2)*	148.1 (12.6)*	Group × Time	3.4	0.027	
	ES Baseline vs. 12 weeks	1.49 [0.4; 2.4]	0.95 [0.0; 1.8]	0.59 [−0.3; 1.5]	**ES WALK+BFR vs. WALK**			**−0.69**
	ES Baseline vs. 24 weeks	2.30 [1.2; 3.4]	1.15 [0.2; 2.0]	1.71 [0.7; 2.7]	**ES BFR vs. WALK**			**−0.86**
Strength of the knee extensors (kgf)	Baseline	233.6 (20.6)	229.8 (19.6)	239.8 (18.7)	Group	0.1	0.995	
	12 weeks	249.5 (23.6)	249.9 (22.3)*	253.1 (21.3)	Time	44.4	0.001	
	24 weeks	289.8 (24.9)*	290.1 (23.6)*	285.4 (22.5)*	Group × Time	0.3	0.741	
	ES Baseline vs. 12 weeks	0.85 [−0.1; 1.7]	1.12 [0.2; 2.0]	0.60 [−0.3; 1.5]	**ES WALK+BFR vs. WALK**			**0.06**
	ES Baseline vs. 24 weeks	1.70 [0.6; 2.8]	2.19 [1.1; 3.3]	1.34 [0.4; 2.2]	**ES BFR vs. WALK**			**−0.16**

Note: Data presented by mean (standard error).

Abbreviations: ES, effect size [95%CI]; WALK+BFR, low–intensity walk with blood flow restriction intervention; WALK, moderate–intensity walking intervention; BFR, blood flow restriction intervention.

[a]Sum of activation from the semitendinosus and biceps femoris.

[b]Sum of activation from vastus medialis and vastus lateralis.

*Intragroup difference to baseline (P<0.05).

3.3 Correlations between the strength and surface electromyography

The correlations between the strength and sEMG of the knee flexors and extensors are summarized in table 3. The relationship pattern was different for muscle and training groups.

Table 3. Pearson's correlation (r) between muscle activation and strength for knee flexors and extensors of the older women with osteopenia or osteoporosis

Variable	Time	Training group		
		WALK	WALK+BFR	BFR
Knee flexors	Baseline	0.76 [0.19; 0.94]	−0.22 [−0.75; 0.47]	0.20 [−0.46; 0.71]
	12 weeks	0.74 [0.15; 0.94]	0.28 [−0.42; 0.77]	0.36 [−0.31; 0.79]
	24 weeks	0.48 [−0.27; 0.86]	0.67 [0.10; 0.91]	0.19 [−0.46; 0.71]
Knee extensors	Baseline	0.31 [−0.44; 0.80]	−0.14 [−0.71; 0.53]	−0.71 [−0.92; −0.20]
	12 weeks	0.54 [−0.18; 0.88]	−0.25 [−0.76; 0.45]	−0.70 [−0.91; −0.18]
	24 weeks	0.46 [−0.29; 0.86]	−0.28 [−0.77; 0.42]	−0.63 [−0.89; −0.04]

Note: Data reported by r and [95%CI].

Abbreviations: WALK+BFR, low–intensity walk with blood flow restriction intervention; WALK, moderate–intensity walking intervention; BFR, blood flow restriction intervention.

4. Discussion

This randomized clinical trial applied AT combined with BFR using individualized pressures and analyzed the chronic effects on muscle activation and strength of the knee flexors and extensors in older women. Our novel observation is that low–intensity AT combined with BFR over 24 weeks elicited a greater activation of the knee extensors in comparison with AT exclusively. However, AT with BFR presented an adverse or trivial chronic effect for the strength gain of knee flexors and extensors, respectively, in comparison to AT alone. Moreover, the individualized BFR method applied alone induced null or adverse effects on activation and strength of knee flexors and extensors when compared to moderate–intensity AT. Therefore, our hypothesis that AT with BFR should promote an increase in strength and muscle activation in older women similar to moderate–intensity AT was partially rejected.

The present investigation reinforces the use of BFR as an effective, tolerable and potential clinical rehabilitation approach [11–13] since only using individualized pressures enhances the activation and strength of the knee flexors (sEMG: +2%; Strength: +22%) and extensors (sEMG: +8%; Strength: +19%) after 24 weeks. Thus, older women, for whom a conventional exercise program might be contraindicated due to comorbidities or high mechanical stress to bones and joints, can perform this alternative BFR method [12]. Moreover, the activation of the selected muscles seemed to be more susceptible to improvement than the strength gain in older women with overweight and osteopenia or osteoporosis.

For activation of knee extensors, a moderate effect in favor of AT with BFR was found, while the BFR alone promoted adverse and null effects for activation of knee flexors and extensors, respectively, compared to low–intensity walking. Although the BFR method induces more intense acute activation of the muscle [32–34], the evidence is

sparse on the long–term effects of an AT with BFR program on muscle activation in older people. One of the factors that explain such differences is based on the low BFR pressure, since a higher percentage of estimated arterial occlusion pressure seems to provide the most robust muscular response (e.g., muscle activation, torque) [17,18,21,35]. However, some of these studies that applied low–intensity walking did not individualize the BFR pressures for the older participants [17,18].

In general, under conditions with BFR, the reduction in oxygen supply and the accumulation of metabolites might be responsible for the participation of higher threshold motor units even at low intensities [32,36,37]. Additionally, the BRF method induces a significant increase in the recruitment of fast–twitch fibers for maintenance and preservation of strength production during the performance of the exercise [32,37]. Nevertheless, a higher EMG amplitude might not necessarily represent a higher motor unit recruitment and hence our results must be interpreted with caution. Several intrinsic and extrinsic factors also affect the EMG signal. For example, if the motor unit newly recruited with the training is located close to the electrode, the EMG signal will be greater than the corresponding strength increase. Therefore, the non–linear relationship causes the amplitude of the EMG signal to increase more than muscle strength [38].

Regarding the strength of the knee extensors, the presented investigation is supported by similar works [17,18]. With analogous training protocols, Ozaki et al. [17] and Ozaki et al. [18] did not observe a statistically significant increase in isokinetic and isometric knee extension of healthy older individuals, respectively. Other training protocols have also shown no advantage to exercise combined with BFR for muscle strength in older adults with osteoarthritis [39,40]. To our knowledge, this is the first chronic study involving older women with these comorbidities and there is no convincing evidence demonstrating strength gains employing AT with BFR [11–13].

Our finding of a lack of strength gain for the knee flexors by the low–load walk training with BFR is in contrast to previous high–quality randomized clinical trials [17,18]. For instance, Ozaki et al. [17] and Ozaki et al. [18] verified that a treadmill walking with BFR training for 10 weeks (20 min × 4 days/week) increased the knee flexors strength about 15% for older adults and 22% for health older women, respectively. Besides, Clarkson et al. [20] observed a greater strength by the sit–to–stand test in older adults who performed walking with BFR (10 min × 4 days/week) for 6 weeks. From a practical standpoint, our results indicate that low–intensity AT with BFR does not seem to have a relevant chronic effect on strength gain or even limit muscle strength gain for older women with osteopenia or osteoporosis, however, there is insufficient evidence focusing on these mechanisms.

Osteoporosis disease is characterized by chronic inflammation associated with the immune system. According to Cornish et al., [41] M1–type macrophages, being pro–inflammatory phenotypes, are prevalent in diseases with chronic inflammation, such as osteoporosis. So, in the face of high–intensity exercise, M1 macrophages are stimulated to secrete large amounts of interleukin (IL) 1 beta, tumor necrosis factors, IL–12, IL–18, and IL–23 [42], and hence maintenance or increased inflammation and possible losses occur in strength and muscle mass [41]. This supports the adverse effects on the strength of the population with osteopenia or osteoporosis in our study. Since the exercise strategy with BFR aims to stimulate effects and promote physiological adaptations similar to high–intensity exercises [12,16–18,21], perhaps this population needs more training time from low to moderate intensity without BFR to occur a transition from M1 macrophages to M2, which has an anti–inflammatory action and is involved in the regeneration of muscle damage [41]. As a result, an environment of type M2 macrophages is more suitable for high–intensity exercise routines for older women with osteopenia or osteoporosis.

The correlation pattern between muscle activation and strength was different among groups but inconsistent for most of them. In the WALK + BRF group, the magnitude of this relationship increased over time for knee extensors. However, despite the moderate correlation at 24 weeks, this was not reversed in greater strength gains when compared to the group without BFR. Based on the resistance training and BFR approach, BFR pressure

does not influence the magnitude of strength gains [43]. Thus, the increase in strength for both groups seems to have a greater influence on the walking speed progression over the intervention.

Interestingly, the increase in cuff pressures in the WALK+BFR group every month, added to the increase in the exercise intensity, may have provided an effect of chronic fatigue. Fatigue accumulation over the weeks, which results in central fatigue [44,45], is usually associated with inhibition of the excitability of alpha motoneurons, providing low production of maximum strength [46]. A recent systematic review proposed a positive relationship between metabolic accumulation and myoelectric activity following BFR exercise, however, it is not possible to affirm that there is a long–term cause and effect relationship. [12]. Therefore, the WALK+BFR group might have recruited more muscle fibers to perform a similar amount of strength to the WALK group. Considering the importance of applying interventions longer than 12 weeks when involving older people [47], an increase in the walking speed instead of the cuff pressures seems to be a better training strategy.

This study provides the first reference for chronic effects longer than 16 weeks, applying individualized BFR pressure and continuous load progression in older people with comorbidities. Our data, obtained from older women with osteopenia or osteoporosis, demonstrate the relevant role of the BFR method to promote long–term muscle activation, however, there was a limitation to provide strength gains in comparison to moderate–intensity AT in this population. Although some evidence supports the positive effects of exercise with BFR on bone metabolism [14,15], the presence of chronic disease, sedentary behavior, and/or insufficient physical activity in older women are factors that need further investigation in the areas of BFR and physical exercise.

It can be listed as limitations of the study, the sample loss (13 subjects), and the lack of an experimental group that performed the walk at low intensity without the BFR, which reduced the possibility of finding a more significant effect for the variables studied.

5. Conclusions

Low–intensity walk combined with BFR does not provide relevant chronic effects on strength gain or even limit muscle strength gain, however, due to greater activation of knee extensors over 24 weeks, it is possible to benefit from the use of similar strategies to obtain neuromuscular gains in the long-term for elderly women with osteopenia and osteoporosis. Furthermore, the isolated application of BFR reinforces that older women, for whom a conventional exercise program might be contraindicated due to comorbidities or high mechanical stress on the bones and joints, can perform this alternative training as an effective, tolerable, and potential clinical rehabilitation approach.

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Institutional Review Board Statement: The study was conducted according to the guidelines of the Declaration of Helsinki, and approved by the Ethics Committee of the Health Science Center of the Federal University of Paraíba (CAAE: 67125317.1.0000.5188; approved in May 29, 2017).

Informed Consent Statement: Patients who consented to participate in the present study signed an Informed Consent Form.

Data Availability Statement: The data presented in this study are available on request from the corresponding author. The data are not publicly available due to ethical restrictions.

Conflicts of Interest: The authors declare no conflict of interest.

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