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Research Article

Effect of 12-Week Resistance Training with Blood Flow Restriction on Arterial Stiffness in Octogenarian People with Low Gait Speed: A Randomized Controlled Trial

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Abstract

Aim: Aging is associated with loss of muscle mass and strength. Low-Intensity Resistance Exercise with Moderate Blood-Flow Restriction (LIRE-BFR) improves these outcomes, but the long-term effect on arterial stiffness and safety in elderly people with low gait speed is unknown.

Methods: This is a parallel, randomized controlled clinical study with 12 older adults (3 men; 9 women; 84.0 [76.0; 87.5] years old) who completed a 12-week training of traditional resistance exercise (TRE; n=6) or LIRE-BFR (n=6). All participants were evaluated at baseline and after 12 weeks by carotid-femoral aortic Pulse Wave Velocity (PWV).

Results: After 12 weeks of interventions, PWV decreased in TRE group (-2.9 [-8.1; 2.4] m/s) and increased slightly in LIRE-BFR group (1.1 [-3.2; 5.3] m/s) but no differences were observed between the groups (p=0.21 for group; Hedge's g: 0.52). Mean blood pressure was similar between TRE (86.2 [81.8; 90.9] to 85.8 [76.5; 96.3] mmHg) and LIRE-BFR (92.4 [82.1; 103.9] to 85.5 [79.2; 92.4] mmHg, p=0.462 for interaction). Gait speed increased significantly after 12 weeks in both groups (p<0.001 for time) with no differences between them (p=0.693 for groups).

Conclusions: Compared to TRE, LIRE-BFR increased PWV slightly, while gait speed increased similarly in both training modalities. Larger clinical trials including elderly people with low gait speed are needed to determine the clinical impact of these findings.

Keywords: Resistance training; Blood flow restriction; Vasodilation; Arterial stiffness; Elderly

Introduction

Aging is associated with loss of functional capacity, cardiovascular diseases, and frailty mainly in octogenarians. Exercise training is a non-pharmacological evidence-based therapy to counteract these outcomes in the elderly population. However, elderly people over 80 years of age are underrepresented in randomized clinical trials involving exercise training.

Moderate-intensity aerobic physical activity and muscle-strengthening activities at moderate or greater intensity are recommended for older adults [1]. However, frail elderly people often face major barriers to physical activity including cognitive decline, discomfort and pain, fear of injury or falling, past sedentary lifestyle, insufficient understanding of physical activity, and environmental restriction [2].

Frail octogenarians may benefit from an exercise training approach that addresses their limitations. For instance, physical activity guideline recommends resistance training to improve muscle strength in older persons at the intensity of 40%-50% of the 1-repetition maximum (1-RM) [1]. Lower intensity of resistance training (20%-50% of the 1RM) in older adults may improve power. Although these evidence-based recommendations can include frail population, additional studies are needed to provide definitive guidelines regarding exercise prescription in older individuals with frailty and low gait speed.

In healthy young adults, low-intensity resistance exercise with Blood Flow Restriction (BFR) improved muscle mass and strength similarly when compared to traditional high-intensity

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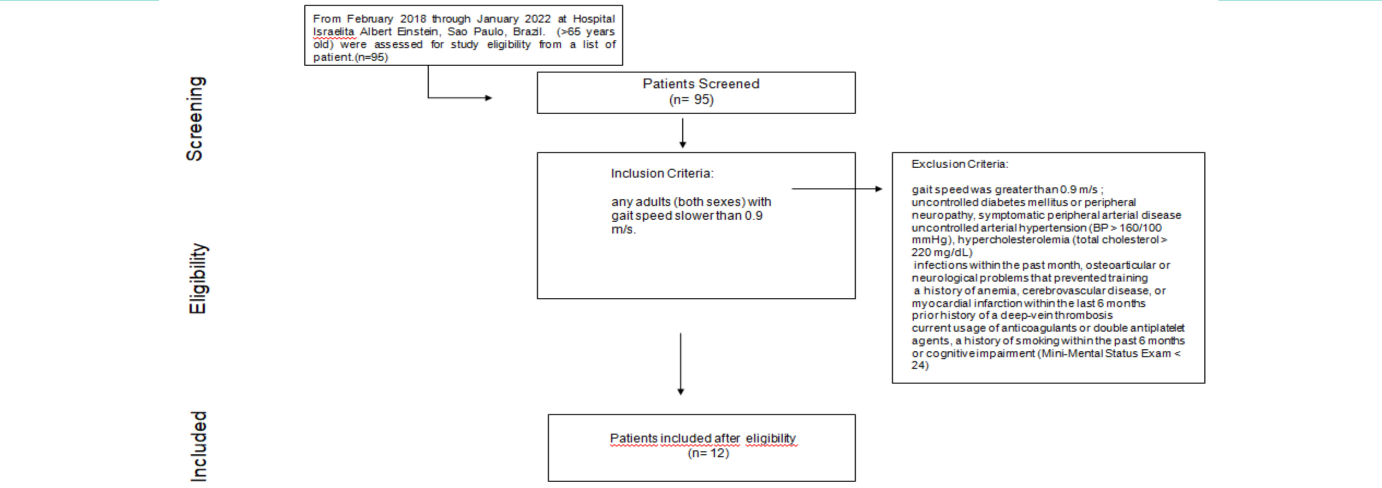

Figure 1: Fluxogram of intervention.

strength training [3,4]. Typically, BFR training uses low loads (20%-30% of 1RM) [5], which may be more appropriate to octogenarians, especially those who are sarcopenic. BFR combines resistance exercise with blood flow restriction on the limbs to reduce blood flow. Flow restriction-induced ischemia activates different mechanisms and has been associated with up- and down-regulated muscle genes expression, angiogenesis, muscle strength, and muscle hypertrophy [6-8]. Additionally, BFR has been proposed in cardiac rehabilitation of frail patients [9]. However, cardiovascular safety and possible harms are not known.

Recently, we demonstrated the acute effect of a single bout of Traditional Resistance Exercise (TRE) and BFR on arterial stiffness in older people with a mean age of 82 years with low gait speed [10]. TRE and BFR induced similar increases in Pulse Wave Velocity (PWV) without any adverse event. Previous study showed that four months of TRE reduces central arterial compliance in healthy men [11], but this association was not observed in middle-aged participants (≥40 years old) [12]. Therefore, the clinical significance of this mild resistance training-induced arterial stiffness is unclear, particularly in older persons.

Here, we described a proof-of-concept study to determine the chronic effect of 12 weeks of BFR on arterial stiffness in elderly people with low gait speed. Our hypotheses in this non-inferiority randomized study are that BFR elicits similar increase in gait speed and muscle strength as conventional resistance training with no detrimental effect on arterial stiffness.

Methods

Trial Design

This is an open label, non-inferiority, parallel, randomized controlled trial. The protocol of this study was published previously [13] and registered on ClinicalTrials (NCT03272737). The study was approved by the institutional review board (CAAE: 56798316.4.0000.0071) and all participants provided their informed written consent before enrollment. We followed the CONSORT checklist for randomized clinical trials [14].

Participants

We conducted the study from February 2018 through February 2020 at Hospital Israelita Albert Einstein, Sao Paulo, Brazil. Ninety-five older adults (>65 years old) were assessed for study eligibility from a list of patient records from the Hospital Israelita Albert Einstein.

Inclusion criteria were any adults (both sexes) with gait speed slower than 0.9 m/s. Adults were excluded from the study if their gait speed was greater than 0.9 m/s or any of the following was uncovered in their patient records or clinical examination: uncontrolled diabetes mellitus or peripheral neuropathy, symptomatic peripheral arterial disease, uncontrolled arterial hypertension (BP >160/100 mmHg), hypercholesterolemia (total cholesterol >220 mg/dL), infections within the past month, osteoarticular or neurological problems that prevented training, a history of anemia, cerebrovascular disease, or myocardial infarction within the last 6 months, a prior history of a deep-vein thrombosis, current usage of anticoagulants or double antiplatelet agents, a history of smoking within the past 6 months or cognitive impairment (Mini-Mental Status Exam <24). After screening, twelve older adults were included in the study (Figure 1).

Randomization

Participants were randomized into one of the two groups: Low-Intensity Resistance Exercise with Moderate Blood-Flow Restriction (LIRE-BFR) or Traditional Resistance Exercise (TRE) using the website “randomizer.org” (available online: http://www.randomizer.org/). The researchers who performed the experiments at baseline and after 12 weeks were blinded to the participant’s group allocation. However, the blood flow restriction specialist (S.A.) who conducted the exercise session was not blinded.

Interventions

Exercise training consisted of two 10-minute sessions per week for 12 weeks. LIRE-BFR and TRE performed 2 sets of 15 repetitions on the leg press and the leg extension machines.

LIRE-BFR group participants performed both exercises at 20% of 1RM throughout the study, while the TRE group performed at 60% of 1RM throughout the study. The rest interval between exercises was 60 seconds for both groups, and rest interval between sets was 20 seconds for the LIRE-BFR group and 60 seconds for the TRE group. The exercise duration of each repetition was 2.0 seconds (1.0 second concentric and 1.0 second eccentric lifting cadence). The exercise volume was increased to 3 sets for both groups in the fifth week of training. A load adjustment was carried out in training sessions 9 and 18.

LIRE-BFR was performed by KAATSU Nano device (KAATSU

Global) that automatically detects the pressure needed on the limbs to reduce blood flow. Baseline pressure was calculated according to the age and general physical condition of the participants. This is the pressure observed after manually tightening the pneumatic cuffs on the upper legs. The cuffs were placed around both upper legs, and a cycle function was started that comprises 8 cycles of 20 seconds inflation and 5 seconds deflation of the cuffs. After this step, the instructor removed the cuffs and placed the leg cuffs on both lower limbs and inflates the cuffs up to the optimal pressure that did not cause pain or discomfort. The optimal pressure values are calculated from a combination of age, level of fitness, limb circumference, and tests standardized by the methodology as previously described in our protocol [13]. Participants remained with the cuffs on the lower limbs from the beginning to the end of the exercise session.

LIRE-BFR and TRE groups trained under the supervision of an exercise physiologist (S.A.) at the hospital and all participants required at least 80% adherence to interventions.

Measurement of Arterial Stiffness

Arterial stiffness was estimated from the carotid-femoral aortic Pulse Wave Velocity (PWV) as described in the protocol [13]. The carotid-femoral aortic pulse waves were recorded by tonometry (SphygmoCor, AtCor Medical). Electrocardiogram registered the wave transit time. Two distances were measured: the recording point between the carotid artery and the sternal furcula (distance 1); and between the sternal furcula and the recording point in the femoral artery (distance 2). The distance traveled by the pulse wave was calculated as "distance 2−distance 1".

The carotid-femoral aortic pulse wave velocity was calculated as follows: carotid-femoral aortic pulse wave

velocity=¼(×) distance traveled by the pulse wave (m)/transit time (seconds).

Pulse Wave Analysis

A non-invasive applanation tonometry of radial artery (SphygmoCor device, AtCor Medical, Sydney, Australia) was used to assess arterial pulse wave [15]. Radial artery pressure waveforms were recorded in the right wrist using a pencil-type high-fidelity micromanometer (Millar Instruments, Houston, Texas). The radial artery pressure curve was calibrated using brachial blood pressure. Aortic pressures, aortic augmentation index (AIx), and AIx adjusted for a heart rate of 75 beats per minute (AIx75) were obtained from the pulse wave analysis of the aortic pressure waveform. Aortic pressure waveform and augmentation index (AIx) were calculated by using the transfer function of SphygmoCor device. Aortic AIx was calculated as follows: $AIx=\Delta P/PP$, $\Delta P=P2-P1$ (P2: peak systolic pressure, P1: inflection point that indicates the beginning upstroke of the reflected pressure wave).

Speed Gait Test

To measure gait speed, all participants walked 4.6 m and the time needed to cover this distance was recorded. The mean of 3 attempts was calculated and divided by the distance.

Participants had to achieve an average of less than 0.9 m/s on the walk test.

Handgrip Strength

Muscle strength was assessed by handgrip dynamometer (Model J00105; Jamar Hydraulic Hand Dynamometer) using the dominant hand in a supinated position with elbow flexed at 90°. There was 1 minute rest interval between efforts, and the maximum value of three attempts was used [16].

One-Repetition (1-RM) Maximum Assessment

The 1-RM assessment was performed for each exercise. Leg press (VR4860, Cybex International Inc., Medway, MA, USA) was performed before leg extension (VR2, Cybex International Inc., Medway, MA, USA). Five minutes of rest was allocated after determining the 1-RM in the leg press before moving onto the leg extension. The testing protocol consisted of a specific warm-up with 50% of the participant's estimated 1-RM. One minute of rest was given and then each participant performed one set of three repetitions of their estimated 70% 1-RM. After a 3 minutes rest period, the participants had up to five attempts to achieve their 1-RM. Loads were determined subjectively and a successful repetition was defined as movement of the knee joint from 90º to 0º of flexion in the exercise. If the participant successfully completed the repetition, three minutes of rest were allocated, and a minimal amount of additional weight was added. This process was repeated until a 1-RM was achieved.

Adverse Events and Risks

BFR exercise may cause headache, red spots, redness, pain, and numbness in lower limbs during or after exercise sessions. All these possible adverse events were computed throughout the study.

End Points

The primary end point was the change in arterial stiffness evaluated by carotid-femoral aortic pulse wave velocity. The secondary end point was the change in the gait speed test, handgrip strength, and one-repetition maximum test (knee extension and seated leg press).

Statistical Analysis

The sample size was calculated with Stata software (StataCorp LP) based on previous reports and was described in the study protocol [13].

Baseline data were described using absolute and relative frequencies for categorical variables and by medians and quartiles, in addition to minimum and maximum values for numerical variables. The distributions of numerical variables were evaluated by histograms, QQ plot and Shapiro–Wilk tests. Comparisons between groups regarding baseline measurements were performed using Fisher's exact tests for qualitative variables and Mann-Whitney tests for quantitative variables. To assess exercise-induced changes, generalized linear mixed models were performed considering groups (LIRE-BFR and TRE), moment (pre- and post-exercise) and the interaction between factors.

To calculate the effect size, we used the absolute variations observed between the moments in the intervention groups. We used the estimates of average variations in the post evaluation in relation to the pre-intervention moment obtained by generalized mixed models for each group. Standard deviation estimates were obtained from the standard errors estimated by the models, and we calculated the Hedge-adjusted effect size

Table 1: Characteristics and baseline data of the elderly with low gait speed.

Variables	Total(n=12)	Interventions		p-value
		TRE(n=6)	LIRE-BFR(n=6)	
Sex				>0.999"
Female	9(75.0%)	5(83.3%)	4(66.7%)	
Male	3(25.0%)	1(16.7%)	2(33.3%)	
Age(years)				0.699S
Median(IQR)	84.0(76.0; 87.5)	82.5(74.0; 88.0)	85.5(78.0; 87.0)	
Minimum; Maximum	70.0; 89.0	70.0;89.0	71.0;89.0	
Comorbidities				
Alzheimer				>0.999
No	11(91.7%)	5(83.3%)	6(100.0%)	
Yes	1(8.3%)	1(16.7%)	0(0.0%)	
Diabetes				>0.999
No	10(83.3%)	5(83.3%)	5(83.3%)	
Yes	2(16.7%)	1(16.7%)	1(16.7%)	
Fracture				>0.999
No	11(91.7%)	5(83.3%)	6(100.0%)	
Yes	1(8.3%)	1(16.7%)	0(0.0%)	
Osteoporosis				>0.999
No	9(75.0%)	5(83.3%)	4(66.7%)	
Yes	3(25.0%)	1(16.7%)	2(33.3%)	
Osteoarthrosis				>0.999
No	10(83.3%)	5(83.3%)	5(83.3%)	
Yes	2(16.7%)	1(16.7%)	1(16.7%)	
Dyslipidemia				0.182
No	3(25.0%)	3(50.0%)	0(0.0%)	
Yes	9(75.0%)	3(50.0%)	6(100.0%)	
Hypertension				0.455
No	2(16.7%)	2(33.3%)	0(0.0%)	
Yes	10(83.3%)	4(66.7%)	6(100.0%)	
Medications				
Antiparkinsonian				0.455
No	10(83.3%)	6(100.0%)	4(66.7%)	
Yes	2(16.7%)	0(0.0%)	2(33.3%)	
Anxiolytic				
No	12(100.0%)	6(100.0%)	6(100.0%)	
Anticonvulsant				>0.999
No	10(83.3%)	5(83.3%)	5(83.3%)	
Yes	2(16.7%)	1(16.7%)	1(16.7%)	
Statins				>0.999
No	5(41.7%)	3(50.0%)	2(33.3%)	
Yes	7(58.3%)	3(50.0%)	4(66.7%)	
Oral hypoglycemic				0.545
No	8(66.7%)	3(50.0%)	5(83.3%)	
Yes	4(33.3%)	3(50.0%)	1(16.7%)	
Antipsychotic				>0.999
No	11(91.7%)	5(83.3%)	6(100.0%)	
Yes	1(8.3%)	1(16.7%)	0(0.0%)	
Drugs for Dementia				>0.999
No	11(91.7%)	5(83.3%)	6(100.0%)	
Yes	1(8.3%)	1(16.7%)	0(0.0%)	
Antiplatelet Drugs				>0.999
No	7(58.3%)	3(50.0%)	4(66.7%)	
Yes	5(41.7%)	3(50.0%)	2(33.3%)	
Antidepressant				>0.999
No	7(58.3%)	4(66.7%)	3(50.0%)	
Yes	5(41.7%)	2(33.3%)	3(50.0%)	
Antihypertensive				0.455
No	2(16.7%)	2(33.3%)	0(0.0%)	
Yes	10(83.3%)	4(66.7%)	6(100.0%)	
Other medications				0.455
No	2(16.7%)	2(33.3%)	0(0.0%)	
Yes	10(83.3%)	4(66.7%)	6(100.0%)	

LIRE-BFR: Low-Intensity Resistance Exercise with Moderate Blood-Flow Restriction; TRE: Traditional Resistance Exercise: IQR: Interquartile Range; #: Fisher's exact test; S: Mann Whitney test

measures (adjusted Hedges' g) as described by Bernards et al [17]. The analyzes were performed using the SPSS statistical package (version 24.0), considering a significance level of 5%.

Results

The characteristics of the participants are described in Table 1. We did not observe significant differences between groups at baseline. Body weight did not change significantly between TRE (68.4 [57.7; 81.1] to 68.1 [56.9; 81.4] kg) and LIRE-BFR (72.5 [66.0; 79.7] to 72.6 [66.7; 79.0] kg, p=0.597 for interaction). Similarly, BMI did not change significantly between TRE (28.7 [24.1; 34.2] to 28.6 [23.8; 34.3] kg/m^2) and LIRE-BFR (29.0 [27.0; 31.1] to 29.0 [26.9; 31.3] kg/m^2, p=0.479 for interaction). There were no exercise-related adverse events. Additionally, all participants had more than 80% of adherence to interventions.

Primary Outcomes (arterial stiffness)

After 12 weeks, PWV decreased in TRE group (-2.9 [-8.1; 2.4]

Table 2: Primary and secondary outcomes.

	Interventions		p-value		
	TRE	LIRE-BFR	Group	Time	Interaction
Primary outcomes					
PWV (mis)			0.980	0.574	0.217
Baseline	13.0(8.8; 19.2)	10.9(9.9; 12.1)			
12-week	10.2(9.5;10.8)	12.0(8.4 ; 17.2)			
Secondary outcomes					
Gait speed (m/s)			0.693	<0.001	0.008
Baseline	0.74(0.65; 0.83)	0.62(0.51;0.74)			
12-week	0.82(0.67; 0.97)	0.86(0.68;1.05)			
Handgrip strength (kg)			0.018	0.018	0.359
Baseline	13.7(11.1; 16.7)	19.3(15.2;24.5)			
12-week	17.4(14.5; 20.7)	21.5(18.7;24.7)			

Values are expressed by mean and 95% confidence interval. LIRE-BFR: Low-Intensity resistance exercise with moderate blood-flow restriction; TRE: Traditional resistance exercise; PWV: pulse wave velocity.

Table 3: Maximum strength tests as secondary outcomes.

	Interventions		p-value		
	TRE	LIRE-BFR	Group	Time	Ineraction
Leg press			0.818	<0.001	0.272
Familiarization	126.7 (95.8; 167.5)	133.3 (111.1; 160.0)			
Session 9	152.1 (121.9; 189.8)	148.3 (130.3; 168.9)			
Session 18	157.8(110.3; 225.7)	171.7 (152.9; 192.7)			
Leg extension			0.987	0.004	0.925
Familiarization	71.7(53.9; 95.2)	70.8(55.8; 89.9)			
Session 9	78.9(61.2; 101.9)	80.0 (63.6; 100.6)			
Session 18	76.1(57.4; 101.0)	76.7(63.6; 92.5)			

Values are expressed by mean and 95% confidence interval.

Table 4:

	Interventions		p-value		
	TRE	LIRE-BFR	Group	Time	Interaction
Aortic SBP (mmHg)			0.417	0.03	0.236
Baseline	119.3(110.2; 129.2)	131.7(117.5; 147.6)			
12-week	113.6(103.1; 125.2)	111.5(101.7; 122.2)			
Aortic DBP (mmHg)			0.037	0.226	0.664
Baseline	63.5(57.5; 70.1)	69.7(65.3; 74.5)			
12-week	58.3(50.4; 67.5)	67.0(61.1; 73.5			
Aortic MBP (mmHg)			0.508	0.015	0.430
Baseline	85.7(79.0; 92.9)	92.2(84.5; 100.7)			
12-week	80.0(71.6; 89.4)	80.7(71.1; 91.5)			
Aortic PP (mmHg)			0.530	0.080	0.099
Baseline	55.8(50.1; 62.3)	61.7(50.9; 74.9)			
12-week	55.3(44.9; 68.2)	44.5(36.1; 54.9)			
Radial SBP (mmHg			0.798	0.081	0.241
Baseline	129.8(121.1; 139.2)	139.3(124.7; 155.6)			
12-week	126.2(113.8; 139.9)	120.5(110.0; 132.0)			
Radial DBP (mmHg)			<0.001	0.055	0.289
Baseline	62.7(56.7; 69.3)	70.2(65.6; 75.1)			
12-week	52.0(44.3; 61.1)	66.5(60.4; 73.2)			
Radial MBP (mmHg)			0.246	0.041	0.694
Baseline	85.7(79.0; 92.9)	92.7(84.6; 101.5)			
12-week	80.2(71.8; 89.5)	84.0(76.9; 91.8)			
Radial PP (mmHg)			0.268	0.208	0.146
Baseline	67.2(61.3; 73.6)	69.8(58.3; 83.5)			
12-week	68.4(54.8; 85.4)	54.0(44.2; 66.0)			
Aortic Augmentation Index (%)			0.035	0.017	0.212
Baseline	33.3(28.8; 38.6)	46.4(37.6; 57.4)			
12-week	30.0(25.6; 35.2)	33.3(26.4; 42.1)			
Alx75 (%)			0.384	0.074	0.029
Baseline	28.0(21.0; 37.4)	38.2(30.6; 47.7)			
12-week	28.9(22.4; 37.2)	28.0(22.4; 35.0)			

Values are expressed by mean and 95% confidence interval. SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; MBP: Mean Blood Pressure; PP: Pulse Pressure; Alx75: Index Normalized for a Heart Rate of 75 bpm.

m/s) and increased slightly in LIRE-BFR group (1.1 [-3.2; 5.3] m/s) but no statistical differences were observed between the groups (p=0.980 for group and p=0.217 for interaction, Table 2; effect size - Hedge's g: 0.52). Mean blood pressure was similar between TRE (86.2 [81.8; 90.9] to 85.8 [76.5; 96.3] mmHg) and LIRE-BFR (92.4 [82.1; 103.9] to 85.5 [79.2; 92.4] mmHg, p=0.462 for interaction).

Secondary Outcomes

Gait speed increased significantly after 12 weeks (p<0.001 for time and p=0.008 for interaction) and the multiple comparisons showed no differences between the groups (p=0.693 for groups, Table 2). Handgrip strength increased similarly after 12 weeks of interventions in TRE and LIRE-BFR groups (p=0.018 for time, Table 2). Leg press and leg extension strength increased similarly after 12 weeks of interventions in TRE and LIRE-BFR groups (p<0.001 for time) but with no differences were found between the groups (Table 3).

Aortic and radial blood pressure, pulse pressure, and aortic augmentation index are described in Table 4. Although we observed an increase in PWV in LIRE-BFR as described above, this did not reflect harmful changes in hemodynamic parameters. In fact, TRE and LIRE- BFR groups showed lower aortic and radial blood pressure at 12 weeks of training with no difference between the groups (Table 4).

Discussion

In this single-center, non-inferiority, parallel, randomized controlled trial we tested the chronic effect of 12 weeks of BFR on arterial stiffness in elderly people with low gait speed. Our hypotheses were that BFR would elicit similar increase in gait speed and muscle strength as conventional resistance training with no detrimental effect on arterial stiffness. PWV increased slightly in the LIRE-BFR group when compared to TRE, although it was not statistically different. However, we should consider an effect size of 0.52 as a medium effect for PWV and larger randomized control studies are needed to determine this alteration in arterial stiffness. In a systematic review and meta-analysis with 20 studies included, low-load BFR training elicited greater muscle strength than low-load training alone, but low-load BFR was less effective than heavy-load training [18]. Thirteen of the included studies evaluated older adults at risk of sarcopenia. Improvement in muscle strength is an important physical function in older adults with low gait speed but BFR training may elicit possible adverse effects. Recently, we published the acute effect of a single bout of TRE and LIRE-BFR on arterial stiffness in this same sample of individuals [10]. Both modalities of training had similar responses regarding hemodynamic parameters and PWV in older people with slow gait speed. In the present study, we extend this knowledge showing the long-term effects of LIRE-BFR on arterial stiffness.

The safety of BFR training is poorly reported in clinical trials and there is no large or long enough study in elderly individuals. Rare cases of muscle damage, blood clots, and rhabdomyolysis have been reported [18,19]. Additionally, cardiovascular system (central and peripheral), oxidative stress, and nerve conduction velocity responses are important concerns of BFR training in elderly [20]. However, most studies that reported adverse events were conducted in young population. Four weeks of BFR training did not alter nerve or vascular function, and a single bout of BFR and high-load resistance exercise increased fibrinolytic activity without altering selected markers of coagulation or inflammation in healthy young individuals [3].

Comparing young (22±1 years) and older adults (69±1 years), BFR training presented slightly greater hemodynamic stress than the traditional control exercise in both groups without differences between young and older participants [21]. This hemodynamic stress response was lower for walking than leg-press exercise. However, exercise-induced hemodynamic stress assessed this response acutely and the long-term hemodynamic effect is unknown.

In our study, we found that 12 weeks of BFR training was relatively safe with no serious adverse events; and the increase in PWV after BFR training may not represent an important clinical change. TRE and LIRE-BFR groups showed lower aortic and radial blood pressure at 12 weeks of training with no difference between the groups, which means that a meaningful adverse cardiovascular event is unlikely. However, we encourage larger randomized trials for a definitive recommendation. More importantly, both types of training increased gait speed above the average considered clinically significant (>0.8 m/s) [22], and this result suggests that LIRE-BFR might be incorporated in cardiac rehabilitation settings. Patients over 80 years of age often report joint pain, which limits them from doing muscle-strengthening exercise with greater loads. And this limitation can reduce adherence to exercise and worsen muscle mass and sarcopenia. Therefore, BFR training may be a good training method with better adherence in this population in the long term.

Limitations

We recognize limitations in the present study. Our protocol changed because of the COVID-19 pandemic and the estimated sample size was smaller than planned [13]. Consequently, the trial was not adequately powered to show modest differences but suggests that clinically meaningful adverse events is unlikely. Most of the participants included were women and the outcomes tested here should be adequately investigated in men.

Author Statements

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Conflict of Interest

Samuel Amorim is the representative of the KAATSU brand in Brazil. The other authors declare no conflict of interest.

Authors' Contributions

Marcelo Rodrigues dos Santos (writing and final discussion).

Samuel Amorim (Study design, data collection, writing and final discussion).

Alexandra Passos Gaspar (Study design, data collection, writing and final discussion).

Raphael Mendes Ritti-Dias (writing and final discussion).

Gabriel Grizzo Cucato (writing and final discussion).

Luciana Diniz Nagem Janot De Matos (Study design, data collection, writing and final discussion).

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