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Artigo de Revisão

Blood Flow Restriction Resistance Training as An Alternative To Resistance Training Alone To Improve Strength In Elderly: A Systematic Review With Meta-Analysis

Treinamento Com Restrição Do Fluxo Sanguíneo Como Alternativa Ao Treinamento Resistido Tradicional Para A Melhora Da Força Em Idosos: Uma Revisão Sistemática Com Meta-Análise

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RESUMO

O objetivo deste estudo foi realizar uma revisão sistemática com meta-análise para comparar os efeitos do treinamento resistido com restrição do fluxo sanguíneo (RFS) aos efeitos do não treinamento (CON) e do treinamento resistido (TR) tradicional na força muscular em idosos. Esta foi uma revisão sistemática com meta-análise de ensaios clínicos randomizados (ECR’s), publicados em inglês, até fevereiro de 2022, conduzidos no MEDLINE (PubMed), EMBASE, Web of Science e Cochrane Library. A qualidade de evidência foi avaliada por meio do sistema GRADE. O risco de viés foi avaliado através da ferramenta RoB2. Diferenças médias padronizadas (SMD) e diferenças médias foram reunidas utilizando um modelo de efeitos aleatórios. Valores de $p<0,05$ foram considerados como diferença estatisticamente significativa. Oito ECR’s foram incluídos nesta revisão. Não foram encontradas diferenças nos efeitos da força muscular ao comparar os treinamentos com RFS e TR tradicional (SMD= -0,18 [-0,56 a 0,19]; p=0,34; I^2=12%). Por outro lado, nossos achados demonstraram que o efeito do treinamento com RFS foi superior ao CON para força muscular em idosos (SMD= 0,63 [0,24 - 1,01]; p=0,001; I^2=11%). O treinamento com RFS parece ser uma alternativa de treinamento eficaz no ganho de força muscular em idosos, tornando-se uma estratégia promissora para profissionais de saúde na abordagem dessa população com baixa tolerância ao TR

Palavras-chave: Kaatsu; Oclusão vascular; Treinamento de força; Força muscular; Idoso; Envelhecimento.

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ABSTRACT

The aim of this study was to perform a systematic review with meta-analysis to compare the effects of resistance training with blood flow restriction (BFR) to those of no training (CON) and traditional resistance training (RT) on muscle strength in aging. This was a systematic review with meta-analysis of randomized clinical trials (RCTs), published in English, until February 2022, controlled in MEDLINE (PubMed), EMBASE, Web of Science and Cochrane Library. The quality of evidence was assessed using the GRADE system. The risk of bias was assessed using the RoB2 tool. Standardized mean differences (SMD) and mean differences were pooled using a random effects model. Values of $p<0.05$ were considered a statistically significant difference. Eight RCTs were included in this review. No differences were found in the effects of muscle strength when comparing training with RFS and traditional TR (SMD= -0.18 [-0.56 to 0.19]; p=0.34; I^2=12%). On the other hand, our findings felt that the effect of training with RFS was superior to CON for muscle strength in the elderly (SMD= 0.63 [0.24 - 1.01]; p=0.001; I2=11%). Training with RFS seems to be an effective training alternative for gaining muscle strength in the elderly, making it a promising strategy for health professionals to approach this population with low tolerance to RT

Keywords: Kaatsu; Vascular occlusion; Strength training; Muscle strength; Older; Aging.

INTRODUÇÃO

The world's population, according to UN data, could reach 2.1 billion people over 60 years old by 2050. Given the upward trend in life expectancy, there is there is a growing need to identify alternative interventions that may maintain or enhance the health, functionality, and autonomy of aging individuals[1]. The aging process generates a sharp decline in strength production capacity, primarily influenced by neurological and musculoskeletal systems autonomy and, consequently, the quality of life of aging individuals[2]. The significance of muscle strength for the health of aging individuals has been widely acknowledged. There is an important relationship between this ability and the performance of simple daily tasks for this population[3,4]. The literature has shown that the reduction in the ability to produce strength may be related to several health conditions that negatively influence the quality of life of the aging individuals, such as an increased risk of limited mobility, dependence for activities of daily living (ADL), cognitive decline, and an increased risk of mortality [5-7].

Although the resistance training (RT) is referred to in the scientific literature as an effective strategy for preserving or improving muscle strength[4,8], the RT may not be feasible or well-tolerated in specific situations due to the intensity of this modality. These limitations may difficult the application and adherence to RT in these populations [8-10].

Over the last two decades, a training modality that has stood out in research around the world is resistance training combined with blood flow restriction (BFR)[11-14]. The BFR training is characterized by using tourniquets or cuffs, during exercises, which create a blockage in blood vessels in one or more members of the human body. [13].

Studies have shown similar gains in muscle strength when comparing BFR training with high intensity RT in young and aging populations [11]. However, the main advantage in using the BFR training as strategy is the ability to achieve strength improvements using significantly lower weights. This advantage may be interesting for populations that are unable to use high intensities in RT, due to joint limitations or other dysfunctions [13].

Studies show that the adequate intensity for the BFR to present more satisfactory results seems to be approximately between 20 and 50% of 1RM for young populations, values that are determined according to other variables, such as the choice of exercises, volume, and density of the training sessions[13]. These intensities have shown, in other populations, satisfactory and beneficial. Thus, BFR emerges as a viable alternative for a population that suffers from disorders of the neurological and musculoskeletal system, resulting in a lower risk of injury from RT and, therefore, justifying the need for a greater understanding of the efficiency of this intervention[14,15].

Although there are several studies that have been willing to understand the effects of BFR training on the capacity to produce strength, there are no systematic reviews that have evaluated the influence of BFR training on muscle strength in people over sixty years old. A systematic review by Centner et al. (2019) sought to compare the effects of BFR training to the effects of RT on muscle strength in aging individuals. However, the population included in this study consisted of people over fifty years old[16]. In our study, we restricted the research population to those over sixty years old, taking into account that this is a population that has very specific needs and limitations and that, in underdeveloped countries, people are considered elderly after sixty years old. Lastly, there is a lack in the literature that needs attention to help health professionals to better understand this intervention. Therefore, the aim of this systematic review with meta-analysis was to verify the effect of BFR training and compare it with RT traditional and/or non-training (CON) on muscle strength in people older than sixty years.

METHODS

Research registration

We conducted this systematic review with meta-analysis in accordance with PRISMA statement (see Supplemental Digital Content 1 that is a table with PRISMA check list)[17]. Search commission of Federal University of Health Sciences from Porto Alegre registration number: 084/2020. PROSPERO registration number: CRD42020220729.

EXPERIMENTAL APPROACH TO THE PROBLEM

This was a systematic review with meta-analysis based on a focused question described in a PICO format[18]. We established: Patient/Problem/Population = Elderly (age ≥ 60 years), Intervention = Resistance training with blood flow restriction, Comparison =

Resistance training/placebo/non-training, Outcomes = Strength and Study design = Randomized clinical trials.

All studies were screened and assessed for eligibility regarding our inclusion and exclusion criteria, which were based on the PICOS principle (i.e., extracting population, intervention, comparison intervention, outcome measures and study design information).

Data sources*.*

The electronic databases used were MEDLINE (PubMed), Web of Science, Cochrane Library, and EMBASE in February 2022. We used a comprehensive search strategy tailored to each database. In cases of missing data, authors of selected papers were contacted. When contacted authors did not answer, data were extrapolated from figures, using Image J software, or using available data and mathematics formulas provided by Cochrane's handbook as presented at section 2.4[19].

Search strategy

For identification of relevant studies, a systematic literature search was performed by two blinded researchers (Mallmann, ALS & Doria, LD). Keywords and medical subject headings (MeSH) for the terms "Blood flow restriction", "Kaatsu"; "Vascular occlusion", "Strength training", "Resistance Training", "Muscle strength", "Elderly", "Older" and "Aging" were selected. No filters were used to perform this search. The term OR was used for Union of MeSH terms and "entry terms", and the term AND was used to attach the terms. The complete string used at PUBMED and adapted for the other databases is fully described at Supplemental Digital Content 2. Study information, including title and abstract, were exported from the databases and stored in a citation manager (Mendeley1, version1.17.9). Before further processing of the studies all duplicates were removed.

PARTICIPANTS

Inclusion and exclusion criteria

We included: (1) Participants were older than 60 years old, (2) the study design allowed to compare resistance training combined with blood flow restriction to traditional resistance training and/or to a control group (without any intervention or placebo training, such as light stretching), and (3) muscle strength were assessed pre- and post-intervention. No restriction on publication date was imposed.

We excluded: (1) participants received any kind of substance that could interfere with study results, (2) manuscripts that were not written in English, Portuguese, or Spanish languages or (3) meta-analysis articles.

Tables with inclusion/exclusion decisions by reviewer and agreements may be accessed at Supplemental Digital Content 3

PROCEDURES

Data extraction and assessment of reviewer agreement

First, two researchers (Mallmann, ALS and Doria, LD) screened, independently, all the studies titles, then abstracts and, finally, the full text of the included papers. This process was made in three steps and the reviewers were blinded about the coworker screening. In case of any discrepancy, a third reviewer (Dos Santos, LP) was asked to find an agreement and decide to include or not the paper. The sheets of inclusion/exclusion process for Mallmann, ALS and Doria, LD is available at Supplementary material 2. All data from each study were screened using a bibliographic management program (Mendeley1, ver- sion1.17.9).

After screening of the studies, all relevant considered articles were assessed for eligibility based on their full texts. At this stage, we extracted information about (1) population characteristics, (2) primary outcome measures, (3) methods, (4) exercise/interventional characteristics and (5) the main result of the study. When intervention effects were assessed at multiple time points, only the very last time point was considered (as post-training value). When available, data were extracted in the form of delta mean ($mean_{change}$), delta standard deviation (SD_{change}), and sample size of the studies to perform the meta-analysis. In case of incomplete raw data availability, we contacted the corresponding author of the manuscript or extrapolated the data from figures, if the authors could not be reached. When the article reported baseline and post-intervention outcomes, however, without $mean_{change}$ and SD_{change}, we used the equation (Delta mean = post-training mean– baseline mean) to calculate the delta value. Considering Cochrane's handbook recommendations to calculate the SD_{change}, we used the correlation equals zero, since none of the selected papers provided the delta data as mean ± pattern deviation [19]. In order to find $SD_{change}$for selected studies, the following formula was used.

$$SD_{E,change} = \sqrt{SD_{E,baseline}^2 + SD_{E,final}^2 - (2\ x\ Corr\ x\ SD_{E,baseline}\ x\ SD_{E,final}} \quad (1)$$

Where Corr is correlation coefficient in the experimental group, $SD_{E,baseline}$is baseline standard deviation in the experimental group, $SD_{E,final}$ is final standard deviation in the experimental group and $SD_{E,change}$ is standard deviation of the changes in the experimental group. When data were presented by interquartile range (IQR), it was decided to transform these data in order to standardize the results of all studies in $mean_{change}$ and SD_{change}. The equation used to calculate the $mean_{change}$ is available below[20].

$$\underline{x} \approx \frac{q_1 + m + q_3}{3} \quad (2)$$

Where q1 is the first quartile, m is the median and q3 is the third quartile. Finally, to find the SD_{change} presented by IQR, we use the calculation available below[20].

$$S \approx \frac{q_3 - q_1}{1.35}$$

(3)

The choice for using these formulas was based on a previous Systematic Review with meta-analysis about effects of BFR training on strength, hypertrophy, and functionality for people with osteoarthritis and rheumatoid arthritis[21].

The extracted data of included studies are sample characteristics (number of participants, age, Body Mass Index (BMI), Duration of the intervention (weeks), frequency (sessions per week), sets, repetitions, interval (seconds), one maximum repetition percentual, blood flow restriction pressure (BFR mmHg) and the delta strength, resulting from interventions).

Methodological quality assessment

Evidence quality of reports was determined using the Grading of Recommendations Assessment, Development and Evaluation (GRADE). The peer reviewed analysis is available at supplementary material 4. For each of the 7 items of the GRADE scale, two reviewers (Mallmann, ALS and Doria, LD) assessed the studies independently. Disagreements about methodological quality were resolved by a third reviewer (Dos Santos, LP). The GRADE approach considers the risk of bias and the body of evidence to rate the certainty of the evidence into one of four levels:

High certainty: We are very confident that the true effect lies close to that of the estimate of the effect.

Moderate certainty: We are moderately confident in the effect estimate — the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

Low certainty: Our confidence in the effect estimate is limited — the true effect may be substantially different from the estimate of the effect.

Very low certainty: We have very little confidence in the effect estimate — the true effect is likely to be substantially different from the estimate of effect.

Studies were included independently of the evidence quality calculated.

Risk of bias

The risk of bias of the studies was assessed using the risk of bias tool 2.0 (RoB2) from Cochrane[22]. Two authors (Mallmann, ALS and Doria, LD) independently assessed the risk of bias. In the case of disagreement, the subject was discussed with another author (Dos Santos, LP). The evaluators analyzed the randomization process, deviations from intended interventions, missing outcome data, measurement of the outcome, and selection of the reported results. The studies were classified into low, moderate, or high risk of bias.

STATISTICAL ANALYSES

We conducted a meta-analysis using $mean_{change}$ and SD_{change} from each study. All outcome measures were continuous variables. Two meta-analyses, representing the effects of interventions, were performed: the random-effects model with the mean difference (MD) or standardized mean difference (SMD). MD was performed when studies reported outcomes with the same assessment scale or instrument. When the same outcomes between studies were evaluated but analyzed by different scales or instruments, we performed SMD[19]. The calculation of SMD is represented by dividing the difference in mean outcome between groups by the standard deviation of the result within the groups. The formula between groups within each study used is available below[21,23].

$$S_{within} = \sqrt{\frac{(n_1 - 1)\, S_1^2 \; + \; (n_2 - 1)\, S_2^2}{n_1 + n_2 - 2}} \tag{4}$$

The 95% confidence intervals (CI) were used, and the heterogeneity of the studies included in the meta-analysis was assessed using the inconsistency test (I^2). Inconsistency was considered as low, moderate or high when values were 25%, 50% and 75% or more respectively [19,24]. The software used for statistical analysis was RevMan (Review Manager 5.4.1, The Cochrane Collaboration, 2020), and we considered it significant statistically when $P < 0.05$.

RESULTS

Search strategy

The searches were performed in the five databases from beginning to 2022 and returned 6,956 (380 duplicates) (Fig 1). After removing duplicates, reading the titles, abstracts and full texts, eight studies, between 2013 and 2020, were kept for analysis. Six of them compared BFR training to a non-training group (CON)[25-30] and six of them compared BFR training to a group trained with traditional moderate or high intensity RT[25,27,29,31,32].

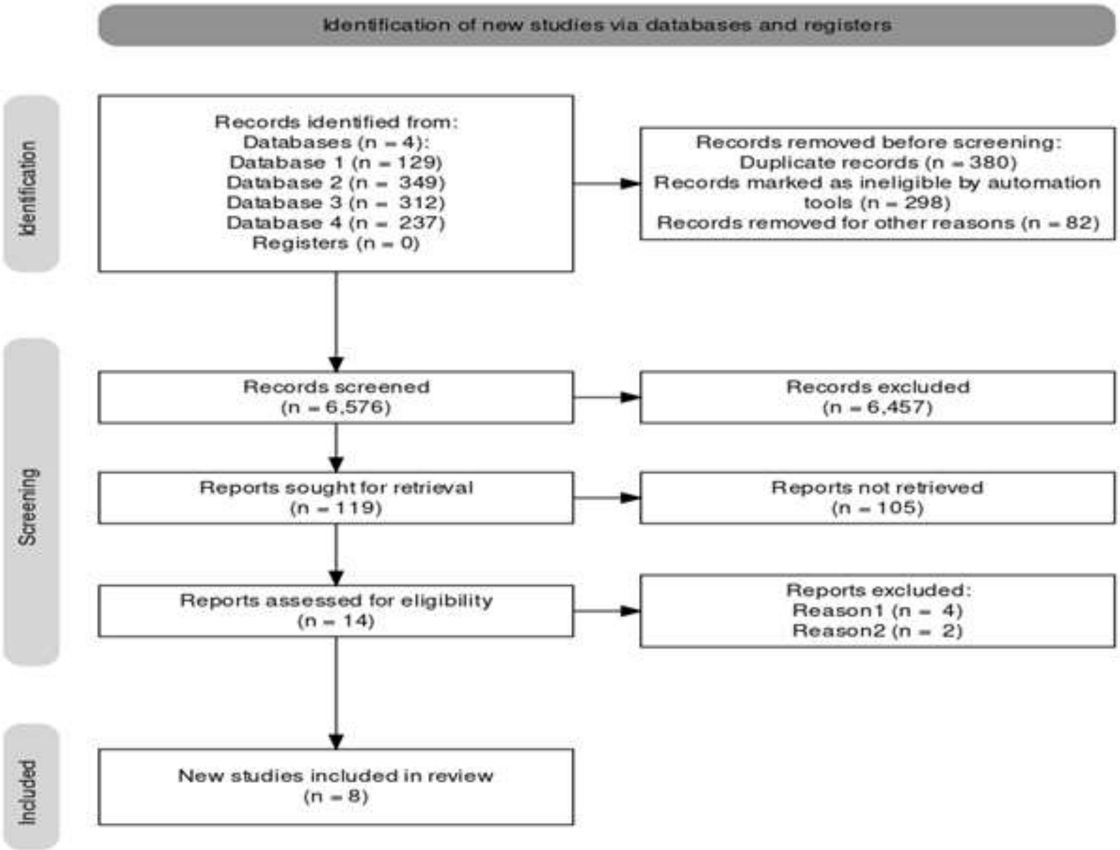

Fig 1. Flow chart including literature search and selection steps following PRISMA statement.

Studies Data

In table 1 the characteristics of the sample are presented. It is possible to notice that there is homogeneity between groups in each study in age and body mass index (BMI). The mean age across studies was 69,2±5,4, and the mean BMI 26,2±2,8. The total sample analyzed was 232 older (≥ 60 years old) men (76) and women.

Table 2 shows that there is no pattern in the duration of the training period (6 to 16 weeks), in the number of repetitions (from 10 to failure) or in the BFR pressure used (from 71 to 270 mmHg) for the included papers. However, it is possible to observe that the number of sets (2 to 4) and the interval between them (30 to 60 seconds) followed the ACSM recommendation for resistance training[4]. It is also possible to see that for resistance training using the BFR resource, the percentages of a maximum repetition (1RM) were lower (20-30% 1RM) than those of traditional resistance models (70-80% 1RM).

	Group	N	Gender	Age (y)	BMI (Kg/m²)	Occlusion Cuffs placement	Cuffwidth
Bigdeli et al, 2020	BFR	10	M	67.6(5.1)	25.4(3.2)	proximal portion of extremities	5cm
	RT	10		66.3(4.6)	25.7(1.7)	-	-
	CON	10		69.3(7.4)	26.2(2.8)	-	-
Cook et al, 2019	BFR	10	4M, 6F	76.4(6.6)	27.5(3.3)	proximal portion of the leg	6x83 cm
	RT	11	5M, 6F	76.3(8.7	26.5(3.0)	-	-
Cook et al, 2017	BFR	12	5M, 7F	76.5(4.2)	26.8(2.4)	Proximal portion of the leg	6x83 cm
	RT	12	5M, 7F	76.7(5.4)	26.8(2)	-	-
	CON	12	5M, 7F	74.8(5.1)	26.2(2.1)	-	-
Letieri et al, 2018	BFR	22	56F	68.7(4.7)	27.5(2.8)	Not described	Notdescribed
	RT	22		69.2(4.6)	29.1(4.2)		
	CON	12		69(6.4)	29.6(3.8)		
Vechin et al, 2015	BFR	8	14M, 9F	65(2)	27.4(6.2)	proximal portion of the thigh.	18 cm wide
	RT	8		62(3)	26.8(6)	-	-
	CON	7		66(5)	26.7(6.2)	-	-
Yasuda et al, 2016	BFR	10	F	70(6)	20.8(2.5)	most proximal portion of both thighs.	50mm
	MH-Tr	10		72(7)	20.9(2.1)	-	-
	CON	10		68(6)	22.3(2.8)	-	-
Yasuda et al, 2015	BFR	9	2M, 7F	71.8(6.2)	21.1(2.2)	most proximal portion of both arms.	(30mm)
	CON	8	1M, 7F	68.0(5.1)	22.0(3.0)	-	-
Yasuda et al, 2014	BFR	9	3M, 6M	71.3(7.1)	20.8(2.5)	most proximal portion of both legs.	50mm
	CON	10	2M, 8F	67.7(6)	21.3(2.8)	-	-

Table 1. Participant's characteristics at baseline

n: sample number; y: years; BMI: body mass index; kg: weight; m²: height squared; *BFR:* blood flow restriction training group; *RT*: resistance training group; *CON*: control group; *MH-Tr*: Moderate to High intensity resistance training; *M:* Male; *F;* Female; cm: centimeters; mm: millimeters; Values are reported as mean±standard deviation (SD) .

Group	Duration (weeks)	Frequency (sessionsper week)	sets	reps	interval (seconds)	Training	BFR pressure (mmHg)

							Intensity (%1RM)	
Bigdeli et al, 2020	BFR	6	3	2-4	10	60	25-35	50-70% AOP
	RT				10	60	25-35	-
	CON	-	-		-	-	-	-
Cook et al, 2019	BFR	12	2	1-3	42.9(14)	60	30-50	184(25)
	HL			1-3	23.5(5)	60	70	
Cook et al, 2017	BFR	12	2	3	Failure	60	30-50	184(25)
	RT				10	60	70	-
	CON	12	2	3	-	-	Light dumbells or elástic bands	-
Letieri et al, 2018	LI+BFR_H	16	3	3-4	15	30	20-30	185(5,45)
	LI+BFR_L			3-4	15	30	20-30	105(6,5)
	HI			3-4	6-8	60	70-80	-
	LI			-	-	-	-	-
	CON			-	-	-	-	-
Vechin et al, 2015	BFR	12	2	3-4	15	60	20-30	71+9
	RT				15	60	70	-
	CON	-					-	
Yasuda et al, 2016	BFR	12	2	4	15-30	30	-	161(12)
	MH-Tr			3	12-13	30	70-90	
	CON	12	-		-	-	-	-
Yasuda et al, 2015	BFR	12	2	4	15-30	30	-	196 (18)
	CON-T			4	15-30	30	-	
Yasuda et al, 2014	BFR	12	2	4	10-30	20	20-30	120-270
	CON		-		-	-	-	-

Table 2. Characterization of the training in the studies resulting from the search in the databases.

AOP: Arterial Oclusion Pressure an exception for mmHg; *%1RM:* percentage of one maximum repetition; *mmHg:* mercury millimeters; *BFR:* Blood flow restriction resistance training; *RT*: Resistance training; *HL*: High load training;*LI+BFR_H:* low intensity blood flow restriction high pressure; *LI+BFR_L:* low intensity blood flow restriction low pressure;*HI:* high intensity; *LI:* low intensity; *MH-Tr:* Moderate to High intensity resistance training; *CON-T:* Control training; *Reps:* Repetitions per set; BFR pressure showed in mean±standard deviation.

Meta-analysis data

Fig 2(A) shows the comparison of BFR with RT for selected papers. Only studies with similar methodologies were included in this analysis, minimizing the risk of biasing findings. Studies were included in our meta-analysis if the assessments of muscle strength were made preferentially with bilateral knee extension (KE) exercise. We also included, for this meta-analysis, papers that evaluated participants with Leg press and unilateral KE exercises. A Sensitivity analysis, represented by figure 2(B), was made by excluding the study from Letieri et al. 2018 because the training was slightly different from the others for the use of unilateral KE, whereas the other authors compared bilateral KE for both groups. Nevertheless, there were no significant differences between training methodologies, even without considering said study[27].

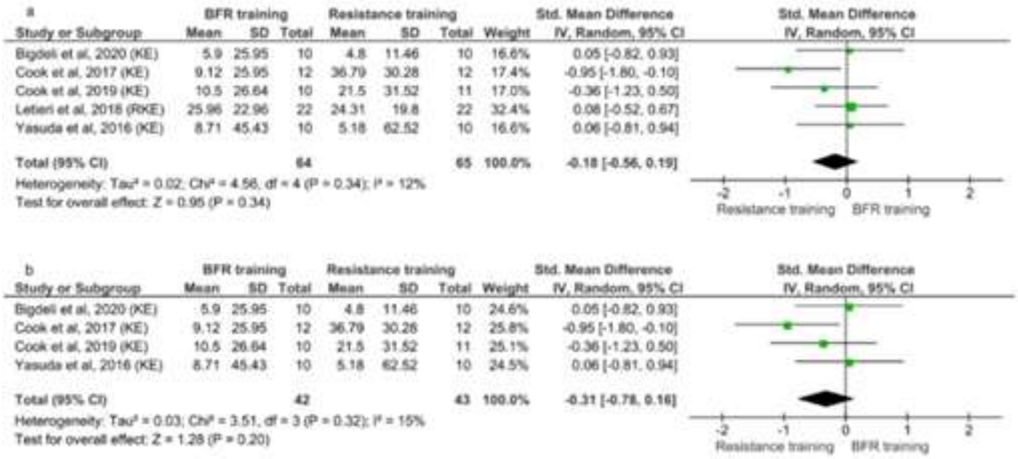

Fig 2. Forest plot graph of the strength of elderly trained with BFR versus Resistance training. A: comparison for all studies with similar methodology including unilateral and bilateral KE; B: sensitivity analysis excluding the paper from Letieri et al, 2018 that used unilateral knee extension; *KE:* knee extension; *BFR:* blood flow restriction; *I^2:* inconsistency test (heterogeneity); *SD:* standard deviation; *Std:* Standardized, *95% CI:* confidence interval, *IV:* inverse variance, *Random:* random effects model

Fig 3 shows the comparison between BFR and CON and its sensitivity analysis. Figure 3 (A) is the overall comparison between all studies that included groups without any intervention between assessments or applied placebo training (e.g., light stretch training). Figure 3 (B, C and D) illustrates the sensitivity analysis we made to minimize the bias of that comparison. Were excluded papers with methodological differences that could interfere with the results. First (B) we excluded studies from Letieri et al. 2018 and Vechin et al. 2015 for using unilateral KE and Leg Press (LP), respectively. Second (C) we reintroduced only the study from Vechin et al. 2015. (D) Third, we excluded the study by Vechin et al. 2015 and reintroduced it from the one by Letieri et al. 2018. Although, the difference between groups remained significant in favor of BFR training.

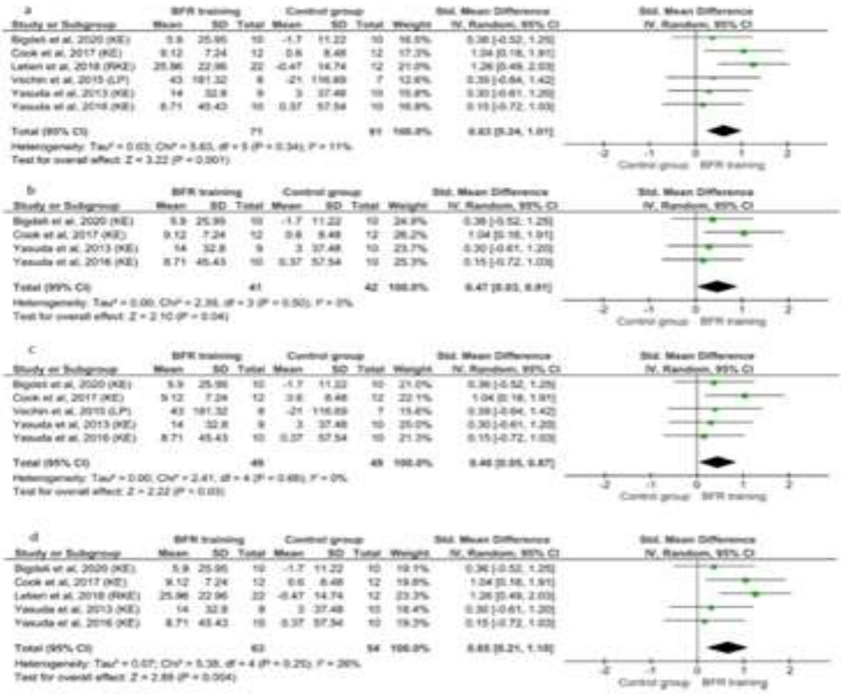

Fig 3. Forest plot graph of the strength of elderly trained with BFR versus Control group (without training or placebo training).A: comparison for all studies with similar methodology including LP, unilateral and bilateral KE; B: sensitivity analysis excluding the papers that used unilateral KE and LP; C: sensitivity analysis excluding only the study from Letieri et al, 2018 that used unilateral KE; D: sensitivity analysis excluding only the article from Vechin et al, 2015 that used LP; *KE:* knee extension; *BFR:* blood flow restriction; I^2*:*inconsistency test (heterogeneity); *SD:* standard deviation; *Std:* Standardized, *95% CI:* confidence interval, *IV:* inverse variance, *Random:* random effects model.

Risk of Bias

All selected studies were analyzed for their risk of bias according to the GRADE Approach tool, by Cochrane Collaboration. The data presented were analyzed using RoB 2 software.

Among the analyzed fields, shown in Figure 4, the greatest risk of bias was found in the random sequence generation field, with one study that did not present such a variable (12%). In the field about measurement of the outcome, most studies (75%) were classified as “some concerns”.. All selected studies were included in the systematic review, independently of quality assessment results.

For more details about risk of bias, see figures 4 and 5 (for complete peer reviewed risk of bias see the figure at Supplemental Digital Content 4).

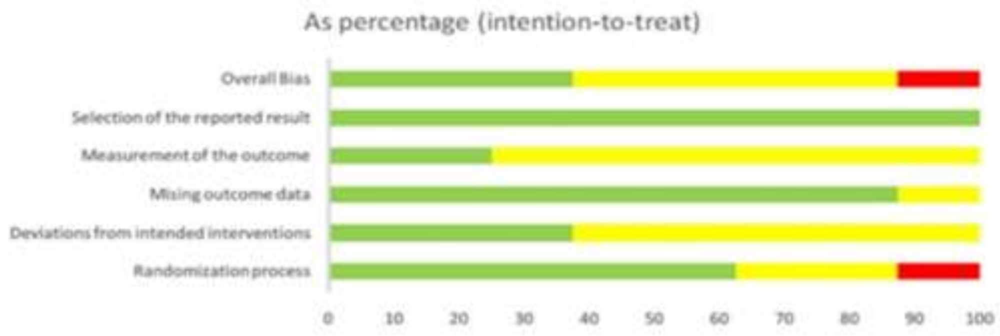

Fig 4. Risk of bias graph considering all studies pooled.

. **Fig 5.** Risk of bias for individual studies and according to the different criteria assessed

Quality assessment

Overall studies quality assessment show that the evidence presents low quality, in accordance with the GRADE tool. The lowest quality shown is for risk of bias domain since a study presented high risk of bias for randomization process. For complete data, see table at Supplemental Digital Content 5 with each reviewer quality assessment.

Study / measure		BFR Training n	BFR Training pre	BFR Training post	BFR Training Deta	RT n	RT pre	RT post	RT Delta	CON n	CON pre	CON post	CON Delta
Bigdeli et al, 2020													
KE		10	31.7 ± 9.9	37.6 ± 9.4	5.90 ± 25.95	10	31 ± 8.2	35.8 ± 8	4.80 ± 11.46	10	29.5 ± 6.7	27.8 ± 9	-1.7 ± 11.22
CP			31.4 ± 11	37.8 ± 12.2	6.40 ± 16.43		31.9 ± 10.2	37.2 ± 12,4	14.25 ± 16.06		26.2 ± 10.2	23.7 ± 10.8	-2.5 ± 14.86
Cook et al, 2019													
KE		10	36.6 ± 17.6	47.1 ± 20	10.5 ± 26.64	11	39 ± 18.8	60.5 ± 25.3	21.5 ± 31,52				
KF			28.5 ± 10.2	33.2 ± 12.6	4.7 ± 16.21		26 ± 10.3	34.8 ± 8	8.8 ± 13.04				
Cook et al, 2017													
KE		12			9.12 ± 25.95	12			36.79 ± 30.28	12			0.6 ± 8.48
LC					5.38 ± 15.56				8.23 ± 14.71				0.4 ± 2.47
LP					18.70 ± 71.29				22.50 ± 77.85				-0.2 ± 18.02
Letieri et al, 2018													
RKE	LI+BFR_H		93.51 ± 17.43	119.47 ± 14.4	25.96 ± 22.96		91.7 ± 13.48	116.01 ± 14.5	24.31 ± 19.8		80.54 ± 9.86	80.07 ± 10.96	-0.47 ± 14.74
	LI+BFR_L	22	94.77 ± 14.97	109.7 ± 14.2	14.93 ± 20.63	22				12			
LKE	LI+BFR_H		94.35 ± 16.08	118.13 ± 15.02	23.78 ± 22		89.4 ± 13.4	116.57 ± 13.7	27.17 ± 18.91		77.48 ± 10.38	78.35 ± 12.09	0.87 ± 15.93
	LI+BFR_L		92.65 ± 16.16	110.21 ± 15.21	17.56 ± 22.19								
Vechin et al, 2015													
Leg Press		8	273 ± 114	316 ± 141	43.00 ± 181.32	8				7	224 + 81	203 + 84	-21 + 116.69
Yasuda et al, 2016													
KE (MVC)			91.82 ± 19.71	103.36 ± 22.12	11.54 ± 29.63		91.39 ± 32.69	101.44 ± 37.02	10.05 ± 49.39		108.16 ± 65.81	112.24 ± 61.73	04.08 ± 90.23
KE 1RM		10	68.32 ± 30.8	77.03 ± 33.39	8.71 ± 45.43	10	65.03 ± 45.14	70.21 ± 43.26	5.18 ± 62.52	10	50.81 ± 40.32	51.18 ± 41.05	0.37 ± 57.54
LP 1RM			244.85 ± 79.95	304.11 ± 87.47	59.26 ± 118.5		249.55 ± 79.01	312.57 ± 90.29	63.02 ± 119.98		211.06 ±	215.85 ± 149.78	4.79 ± 208.47
Yasuda et al, 2015													
EF		9	79.6 ± 85.82	100.74 ± 98.26	21.14 130.46	8	59.71 ± 98.25	58.47 ± 110.7	-1.24 ± 148.01	8			
EE			84.42 ± 69.34	106.53 ± 70.35	22.11 ± 98.78		68.34 ± 45.23	70.35 ± 47.24	02.01 ± 65.40				
Yasuda et al, 2013													
KE		9	50 ± 20	64 ± 26	14.00 ± 32.8	10				10	52 ± 26	55 ± 27	3 ± 37.48
LP			145 ± 47	191 ± 56	46.00 ± 73.11						143 ± 56	142 ± 51	-1 ± 75.74

Table 3. Summary of strength results for selected studies

BFR: Blood flow restriction resistance training; *RT*: Resistance training; *CON:* Control; *LI+BFR_H:* Low Intensity blood flow restriction high pressure; *LI+BFR_L:* Intensity blood flow restriction low pressure; *KE*: knee extension; *KF:* knee flexion; *CP:* chest press; *LC:* leg curl; *LP:* leg press; *RKE:* right knee extension; *LKE:* left knee extension; *EF:* elbow flexion; *EE:* elbow extension; *Delta:* Pos – pre; Data in mean ±standard deviation; Short training protocols describing for each study are presented at Supplemental Digital Content 6.

DISCUSSION

It is important to note that this was the first systematic review with meta-analysis to consider previous studies with active and non-active people aged 60 years or older, who performed BFR training compared to RT alone, or with people who did not do any intervention or just stretching. Our main finding is that BFR was similar to RT, as well as better than non-training, for muscle strength improvement which justifies the applicability of BFR for people that presents any kind of intolerance to traditional RT.

Our results show no statistically significant differences between groups trained with BFR or RT alone and these findings are in consistency with previous literature[33]. In some cases, BFR showed bigger strength improvements than RT alone, while in other studies the results from RT were better than BFR for strength improvement.

In line with that, the study from Loenneke *et al.*, (2012) show that BFR present better results for strength improvement, with a bigger effect size, when intervention has longer duration, with ten or more weeks from baseline to post-intervention assessments [33]. It is important to note that the intervention duration varied from 6 to 12 weeks among included papers, that is, only 2 weeks more than the study from Loenneke *et al.*, (2012) found as a time cut point for better strength improvements, resulting from BFR training[25, 26, 28, 33].

Although BFR presents less neural drive, our findings show that there is no difference in strength gains between this methodology and RT. A systematic review with meta-analysis from 2020 found inconclusive results comparing muscle activation between low load BFR training (LL-BFR) and HL-RT, but most of the studies included in this paper lasted for less than 10 weeks [34]. If the neural drive, as mentioned, is smaller with the application of BFR training than with RT, it is important to try to understand how BFR brings strength improvements similar to RT. The literature has shown the physiological mechanisms that could explain these gains and, thus, enabling new hypotheses for future research with greater direction regarding BFR training to control the loss of strength in the aging individuals[35,36].

Studies show that must be a strong relationship between the metabolic response, arising from BFR training, and gains, both in muscle strength and muscle hypertrophy. The study by Loenneke et al. (2010) was the first to clarifies that the main mechanisms related to gains arising from BFR are apparently the accumulation of metabolites, such as blood lactate, plasma lactate and muscle cell lactate, in addition to being related to activation of fast twitch muscle fibers (FT), even when training intensity is low. And, last but not least, gains may be related to increased expression of mammalian target of rampamycin (m-TOR)[36].

When we look for the comparison between BFR and non-training, we find consistency in the literature. A study from Centner *et al.*, (2019) compared BFR combined with collagen hydrolysate (BFR+CH) against BFR combined with placebo (BFR+PLA) and to a third group that only consumed the protein supplementation (CH). Both groups with BFR training show improvements in strength capacity while CH group demonstrated a decrease in strength gains, suggesting that BFR is better than non-training to strength capacity, even when participants have protein supplementation[35].

Our results show that BFR can be an alternative to physiotherapists and other health professionals who needs to find a tolerable training strategy to work with aging patients and/or patients with joint injury, pain or any disorder that makes RT not recommendable. This is part of our main finding because, since muscle strength can be improved with the application of the BFR and this, in turn, requires a much lower intensity than the RT, it can be assumed that this modality would become making exercises with weights more tolerable for people with osteoarticular, neurological and/or musculoskeletal disorders that may or not be an aging result.

A secondary finding proposed by our group was to compare different protocols of BFR and its effects on strength in elderly. Although, we could not perform any kind of statistical analysis due to heterogeneity of selected papers for BFR protocols, which is a limitation of this review, as well as the small number of studies about BFR and its effects on strength for this specific population, making it difficult to carry out subgroups analysis, like comparing men against women.

It should be observed that the volume (sets x repetitions) and frequency found at the primary studies selected for this review are similar to the guidelines provided by ACSM, except for one paper[4, 30]. We could not compare different training volumes, intensities and rest intervals. In the same line, it must be noted that there were no comparisons between different occlusion protocols. Only one study compared two different levels of pressure applied on individuals trained with BFR[27]. Although, it was not possible to elicit the best protocol with just one study. A systematic review from 2018 did this comparison, with a different meta-analysis for each of the BFR characteristics (i.e., cuff width, absolute occlusion pressure, test specificity and occlusion pressure prescription method) and found results in favor of high load resistance training (HL-RT) for all the comparisons. Although, it must be observed that the population of said paper was composed of young people[34]. Our group sought to perform the same comparison, but with the elderly population, in order to determine whether musculoskeletal deterioration, inherent to aging, could interfere with the strength gains arising from BFR training.

A systematic review from 2012 compared several variables of the BFR training, in order to ascertain their influence on the results obtained with this modality. The authors' first analysis demonstrates that BFR training could be better utilized when associated with low-intensity resistance exercise than when associated with high-intensity. The researchers compared different occlusion pressures and, according to the survey data, there was no significant difference between groups using higher pressures and groups with lower pressures in strength gains and hypertrophy. Thus, it could be suggested that the pressure used for training may, perhaps, be much lower than that practiced in other studies[33].

By comparing these recommendations to the data obtained from our research, we can draw some conclusions. Regarding training intensity, all studies selected for this review evaluated BFR training associated with similar intensities, ranging between 20 and 35% of 1RM. As for the occlusion pressure, there are some inconsistencies between our findings and the literature [33]. The article by Letieri et al, (2018) obtained greater strength gains using BFR training with both high and low occlusion pressure when compared to traditional RT[27]. On the other hand, the study by Vechin *et al*. (2015) was the one that obtained the worst outcomes from the BFR compared to the RT, although it used the lowest occlusion pressure of all selected studies[28]. Another important training variable is the weekly frequency that is, in most of selected studies composed by 2 sessions per week, with the exception of two papers and, casually, these works found a tendency of higher strength improvements for BFR groups than the RT[25, 27]. A previous systematic review with similar population also found papers with 2 to 3 weeks of duration and, although the authors have not statistically analyzed this variable, results did not show trends to any duration variance as a predictor of better results for strength improvement[39].

It is important to understand the influence of time under ischemic conditions. From selected studies, four training protocols[28-30, 32] made participants remain with inflated cuffs during exercise sets and intervals with an approximate time under ischemic condition of 11 minutes, while three training protocols[26, 27, 31] maintained participants under ischemia during exercises and intervals, but deflated during exercises transitions with an approximate time under pressure of 5 minutes per exercise. Last but not least, one training protocol[25] deflated cuffs between sets and between exercises. Comparing our findings with previous literature[40, 41], we find no pattern for these training variables that may have some influence on training results.

There are several limitations of our systematic review. First, the heterogeneity of BFR training and assessments protocols. In some cases, we needed to perform analysis with different exercises (e.g., Leg press and Knee Extension). New papers should be conducted with similar protocols, making it viable to other researchers to compare the same exercises and bring new insights to scientific literature. In the same line, we could not compare BFR parameters, such as AOP, cuff positioning, time under occlusion, high or low intensity with BFR and others because of the wide range of protocols in a few studies. More research must be made with different protocols and, at the same time, similar protocols, so that systematic reviews can be performed comparing subgroups with different BFR training parameters.

Also, we found high risk of bias and low quality of evidence among included papers. These findings are limitations that health professionals must take under consideration before using BFR with their patients.

CONCLUSION AND PRACTICAL APPLICATIONS

Our findings suggest that BFR may be an alternative methodology of training for the aging individuals over 60 years old. In this sense, BFR training may serve as a possible strategy to increase muscle strength in this population, as it has been shown to be similar to RT traditional and better than CON.

New research should be conducted with the aim to compare different BFR protocols and a better description of methodology, in order to make possible a meta-analysis comparing, for example, occlusion pressures, higher or lower intensities, volumes and densities associated with BFR. Furthermore, it would be interesting for researchers to adopt a pattern regarding the choice of exercises, so that it is possible to compare the BFR and RT using data from multiple studies, making feasible a meta-analysis with these two types of training as comparators.

DECLARATIONS

CONFLICT OF INTEREST

All authors declare that they have no conflict of interest relevant to the content of this review.

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DATA AVAILABILITY STATEMENT

All raw data supporting this systematic review are from previously reported studies, which have been cited. Additional processed data that support the findings of the current review are available from the corresponding author upon request.

ETHICS APPROVAL

The research was submitted for the Research Committee from Federal University of Health Sciences from Porto Alegre, Brazil with the register number 23103.205151/2020-51. Because it is a review study, it is not necessary to submit for ethics committees.

AUTHOR CONTRIBUTIONS

ALSM: conceptualization; data curation, investigation, methodology, project administration, resources, software, validation, visualization, roles/writing – original draft;

LPS: data curation, formal analysis, methodology, software, validation;

LDD: formal analysis, investigation, methodology, software;

LFF: Conceptualization, investigation, methodology, visualization;

TRR: conceptualization, methodology, supervision, visualization, writing – review & editing;

LHTR: conceptualization, data curation, methodology, supervision, validation, visualization, writing – review & editing.

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