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Effect of training with partial blood flow restriction in older adults: a systematic review

Efeito do treinamento com restrição parcial do fluxo sanguíneo em adultos mais velhos e idosos: Uma revisão sistemática

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Abstract – Low-intensity training with blood flow restriction (BFR) has been suggested as an alternative to physical training for older adults. The present study aimed to review the literature regarding the effect of training with BFR for older adults. The search strategy consisted of experimental studies aimed at verifying the effects of training with BFR on any outcome in older adults. An electronic search in PubMed / Medline, Bireme Scielo, Lilacs and Cochrane Library databases, published until December 2015 was conducted. Experimental studies that considered individuals aged 50 years and over published in English or Portuguese, were included. The Downs & Black scale was used to assess the methodological quality of articles. Of the 60 studies, 12 were included in the review. Training with BFR improved body mass, torque and muscle power; functional capacity; bone health; venous compliance; peak oxygen uptake; and blood flow; balance and overall performance. The methodological quality of studies had mean score of 16.2 points (SD = 1.6). The prescription of low-intensity exercises with BFR may be an alternative of training for older adults. However, future studies should address the methodological quality, especially external validity and power, the main gaps in articles reviewed in this study.

Key words: Chronic disease; Exercise; Health of the elderly; Muscle strength; Walking.

Resumo – *O treinamento de baixa intensidade com restrição do fluxo sanguíneo (RFS) tem sido sugerido como alternativa para o treinamento adultos mais velhos e idosos. Assim, o presente estudo objetivou revisar a literatura existente referente ao efeito do treinamento com RFS em adultos mais velhos e idosos. A estratégia de busca consistiu a partir de estudos experimentais que objetivaram verificar os efeitos do treinamento com RFS sobre qualquer desfecho em indivíduos com 50 anos ou mais. Foi realizada busca eletrônica nas bases de dados Pubmed/ Medline, Bireme, Scielo, Lilacs e Cochrane, publicados até dezembro de 2015. Foram incluídos estudos experimentais, publicados em inglês e português, com adultos com 50 anos ou mais. A escala Downs & Black foi utilizada para averiguar a qualidade metodológica dos artigos. Dos 60 estudos encontrados, 12 foram incluídos na revisão. O treinamento com RFS melhorou o grau de força, a massa, o torque e a potência muscular, a capacidade funcional, a saúde óssea, a complacência venosa, o consumo de oxigênio de pico, o fluxo sanguíneo e o equilíbrio e a performance geral. Quanto à qualidade metodológica os estudos apresentaram um escore médio de 16,2 pontos (DP=1,6). A prescrição de exercícios de baixa intensidade com RFS pode ser uma alternativa para o treinamento de adultos mais velhos e idosos. Porém, futuros estudos devem atentem para a qualidade metodológica, especialmente validade externa e poder, principais lacunas apresentadas pelos estudos revisados.*

Palavras-chave: *Caminhada; Doença crônica; Exercício; Força muscular; Saúde do idoso.*

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INTRODUCTION

The aging process is associated with innumerable unhealthy adaptations in human metabolism, such as cachexia, sarcopenia, increased oxidative stress, systemic inflammation, among others[1,2]. As a consequence, older adults may present worsening quality of life, reduced physical capacity and functional dependence, as well as increased risk of developing chronic non-communicable diseases[1,3].

On the other hand, physical exercise can reduce the effect of these adaptations, making aging healthier[1-3]. The American College of Sports Medicine (ACMS) recommends that older adults should perform 150-300 minutes of aerobic exercise per week and two weekly sessions of strength training, with volumes of 8-12 repetitions[4]. However, many individuals of advanced age may present physical impairment that makes it impossible to perform high training volumes and intensities, leading to adverse effects[5].

Training with blood flow restriction (BFR) is an alternative, which is characterized by the performance of physical exercises with partial blood flow restriction through the placement of an inflatable band at the root of the limb. This method promises to provide relevant benefits with lower intensities and volumes - aerobic exercise sessions of 20 minutes duration with 50% of maximum aerobic capacity and strength training with intensities from 20% of 1 maximum repetition[6-13]. According to Libardi et al.[13], the performance of exercises with BFR provides important health advantages for older adults, since they are characterized as exercises with volumes and intensities lower than those recommended by ACMS, therefore causing less mechanical stress, especially in knee joints.

The main findings of the scientific literature have sought to support the use of training with BFR as a method alternative to traditional - conventional training - mainly with samples of healthy and young individuals, although the method is more recommended for populations that present weaknesses that make it impossible to perform exercises with high intensities and volumes, as individuals in rehabilitation and / or older individuals[14]. A meta-analysis conducted by Loenneke et al.[14] included 12 studies, of which only two with a sample composed only of individuals aged 50 years or older. In order to verify the effect of the method on muscle strength and hypertrophy, the authors concluded that low-intensity strength training with BFR promoted significant improvement in muscle strength and hypertrophy - effect size of 0.58 (95% CI: 0.40, 0.76) and 0.39 (95% CI 0.35, 0.43) respectively.

Therefore, since it is an alternative training method that promises to provide important benefits with low intensities, it is fundamental to carry out a review that synthesizes the findings of related studies in a robust way, assuring to adults older and professionals of the area a consistent and non-biased collection of existing content about the subject. Thus, the present study aimed at reviewing the existing literature regarding the effect of training with BFR on older adults and seniors.

METHODOLOGICAL PROCEDURES

Search strategy

In the systematic review, experimental studies aimed at verifying the effects of training with BFR on any outcome in older adults were selected. An electronic search was carried out in Pubmed/Medline, Bireme, Scielo, Lilacs and Cochrane databases between August 2015 and January 2016. Studies published until December 2015 were also included.

The selection of descriptors used throughout the review process was done according to the Medical Subject Headings (MeSH) and in the specialized literature. The following descriptors were used in the English language: blood flow restriction, vascular occlusion, Kaatsu, resistance training, strength training, weightlifting, low intensity training, walking, cycling, aged, elderly, older. In order to combine descriptors and terms used in the search, logical operators "AND" and "OR" were used.

Eligibility criteria and selection of studies

The review included studies with the following characteristics: experimental studies, full articles published in English or Portuguese and studies with individuals aged 50 years or over.

Two independent reviewers assessed all included studies. In addition, the Downs and Black[15] scale was used to assess the methodological quality of articles. The differences between reviewers were resolved in consensus among them, and there was no need for a third reviewer. The decision to include or exclude studies was initially made based on the analysis of the title, then through the abstract and - finally - the complete manuscript.

Data collection

The information was extracted from each study based on: 1) population - characteristics of study participants - age and diagnostic method; 2) intervention - characteristics of the intervention protocol - duration, frequency, intensity, volume and types of exercises, compared to a control group; 3) control - characteristics of the intervention protocol of the comparison group, when there was; and 4) outcome - type of outcome measured.

Analysis of study quality

Initially, a detailed report of scores achieved by studies in each item on the methodological quality scale proposed by Downs and Black[15] - communication, external validity, internal validity (bias and confounding factors) and power - was performed. Then, the percentage of points reached by each article of the maximum possible - 31 points - in each item was calculated. At the end, mean and standard deviation (SD) were obtained, as well as the median, amplitude and percentage of points reached. Data were entered in Excel 2013 and analyzed using the Stata 14.0 statistical package.

RESULTS

After searching for all the above mentioned keyword combinations, 73 articles were found, of which 60 were selected, 28 articles in Bireme, 17 in MedLine/PubMed, 15 in Cochranee databases, none in Lilacs and Scielo. Of these, 26 were duplicates, remaining 34 studies to read the titles. After reading, 13 articles were excluded (figure 1).

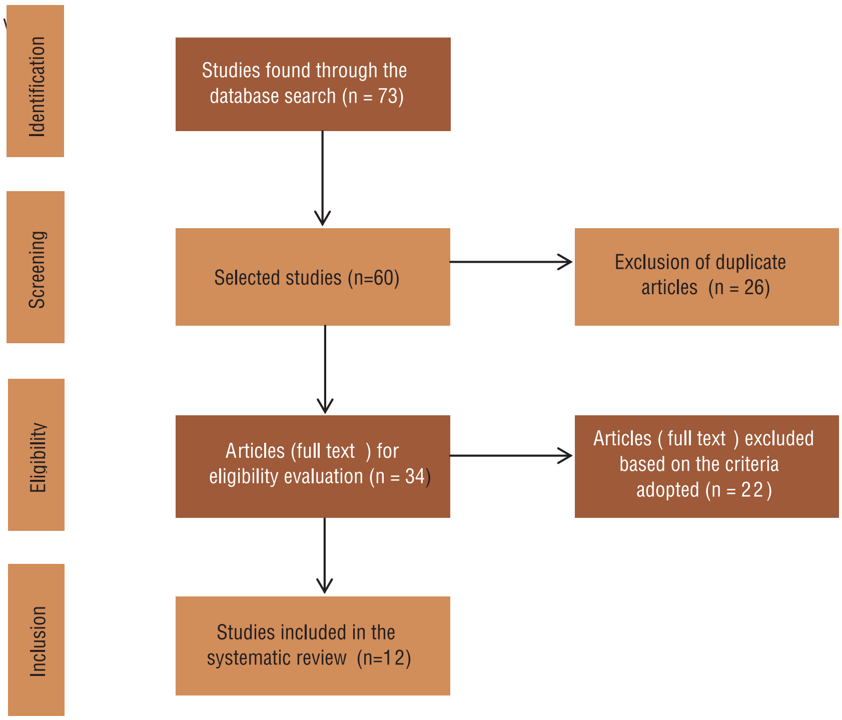

Figure 1. Flowchart of the search process of scientific articles.

Of the 22 studies qualified for critical reading of abstracts, ten were excluded because subjects were not older adults or because they assessed the acute effect of training with BFR on some outcome. Thus, a total of 12 studies were included in the review[6-10,12,13,16-20].

As can be seen in table 1, interventions lasted from 4[17] to 12 weeks[9,10,13] and presented a weekly frequency of two[8-10] to five sessions[12]. The sample size ranged from 10[17] to 51[8] individuals. As for the intervention protocol, eight studies[6,10,16,17,19] applied BFR in low-intensity strength exercise, two studies[12,18] in low-intensity walking, and one study[13] in the combination of walking with strength exercises, both of low intensity.

Among the most studied outcomes of chronic responses of training with BFR in older adults, muscle strength was considered in seven articles[7-10,13,17,19] and muscular hypertrophy in 5 articles[7,9,10,12,13]. The results found by the reviewed studies indicated that low-intensity training was effective to increase strength and promote muscle hypertrophy when performed with BFR.

Training with BFR performed by older adults and/or seniors also promoted increased muscle torque[12], improved functional capacity[12], improved

Table 1. Summary of studies on training with partial blood flow restriction

Author	Sample	Aim	Intervention	Main results
Abe et al.[12]	19 individuals (60-78 years)	Investigate the effects of walking training with BFR on muscle size, strength and functionality	GBFR: walking with BFR; GC – walking without BFR.	Isometric (11%) and isokinetic (7% -16%) knee extension and flexion torque, transverse musculoskeletal area (5.8% and 5.1% for thigh and leg respectively), as well as muscle mass estimated by ultrasound (6.0% and 10.7% for total and thigh respectively) improved in GBFR (P <0.05), but not in GC. Functional capacity also significantly improved in GBFR (P <0.05).
Iida et al.[18]	16 women (59 – 78 years)	Examine the influence of walking with BFR on venous compliance in older women.	GBFR: Walking with BFR; GC: Hiking without BRF.	Venous compliance (Pre: 0.0518 ± 0.0084, post: 0.0619 ± 0.0150 ml / 100 ml / mmHg (P <0.05) and maximum venous flow (pre: 55.3 ± 15.6 , post: 67.1 ± 18.9 ml / 100 ml / min (P <0.01) increased significantly in GBFR but not in GC.
Karabulut et al.[19]	37 men (50-64 years)	Compare the effect of two types of strength training on the adaptation of muscular strength in older men	GTT - High intensity strength training without BFR; GBFR - Low intensity strength training with BFR; GC - No exercise.	GTT and GBFR groups showed significantly greater strength improvements in the legpress exercise when compared to GC (p <0.05), with similar gains between GTT and GBFR. In the leg extension exercise, GTT presented significantly greater force gain than GBFR (p <0.05).
Karabulut et al.[16]	37 men (50-64 years)	Compare the effect of different types of strength training on the concentration of bone markers in older men	GTT - High intensity strength training without RFS; GBFR - Low intensity strength training with BFR; GC - No exercise.	A significant effect was detected on bone alkaline phosphatase in exercise groups (p <0.05), 21%, 23% and 4.7% for LIBF, HIT and GC respectively. HIT and LIBFR groups presented significantly greater gains when compared to GC (p <0.05), except for the leg extension exercise (HIT> LIBFR> GC, p <0.05).
Karabulut et al.[6]	37 men (50-64 years)	Compare the effect of different types of strength training on anabolic hormones, damage markers and inflammatory markers in older men.	GTT - High intensity strength training without BFR; GBFR - Low intensity strength training with BFR; GC - No exercise.	There were no significant differences between groups in the resting levels of CK, IL-6, IGF-I, IGFBP-3 and Testosterone. In addition, there were no significant changes in the cross-sectional area of the muscle, but a trend towards a significant decrease in percentage changes in subcutaneous thigh flexion.
Libardi et al.[13]	25 individuals (64 ± 4.1 years)	Investigate the effects of concurrent training with BFR and non-BFR on aerobic fitness, muscle mass and muscle strength in a cut of older individuals.	GTT: high intensity strength training without BFR (2 days / week). GBFR: low intensity strength training with BFR (2 days / wk)	GTT and GRFS showed similar increases in thigh muscle transverse area in the post-test (7.3% and 7.6%, respectively), maximal strength (38.1% and 35.4%, respectively) and VO2max (9.5%, P = 0.04, 10.3%, P = 0.02, respectively).
Patterson et al.[17]	10 individuals (62-73 years)	Check strength training response with and without BFR on calf strength	Low intensity force training. One leg with BFR and another without.	Maximum strength, maximal voluntary isometric contraction, and isokinetic strength at 0.52 rad / s increased more after training with BFR than without BFR Peak blood flow post BFR increased after training with BFR, compared to no change after training without BFR.
Thiebaud et al.[7]	14 women (61±5 years)	Check the effects of different strength training intensities with and without BFR on strength and muscle mass.	GBFR: Low intensity strength training with BFR; GC: Low intensity strength training without BFR.	Maximum seated bench press (P = 0.01), shoulder pressure (P = 0.02) and sitting row (P = 0.01) force increased significantly, but no differences were found between groups. Only greater thickness of the pectoral muscle was found (P = 0.04).
Vechin et al.[9]	23 older adults (64.04±3.81 years)	Compare the effects of different types of training on quadriceps muscle strength and muscle mass in the elderly.	GTT: High intensity strength training without BFR; GRFS: Low intensity strength training with BFR; GC: without exercise.	Both training protocols were effective in increasing maximal strength in legpress (GTT: 54%, p <0.001; GRFS: 17%, p = 0.067) and quadriceps cross-sectional area (GTT: 7.9%, p <0.001 ; GRFS: 6.6%, p <0.001); however, traditional high-intensity training seems to induce greater strength gain.

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Author	Sample	Aim	Intervention	Main results
Yasuda et al.[10]	17 individuals (61-85 years)	Examine the effect of strength training with BFR on muscle size and arterial stiffness.	GC: Low intensity strength training without BFR; GRFS: Low intensity strength training with BFR;	Flexor (17.6%) and elbow extensors (17.4%) cross-sectional area increased, as well as maximal isometric voluntary contraction of flexors (7.8%) and elbow extensors (16.1%) improved in GRFS, but not in GTT. There were no changes in the ankle cardiovascular index and ankle-brachial pressure index in both groups.
Yokokawa et al.[8]	51 individuals (65 years or more).	To compare the effects of two types of training in the elderly.	GRFS: Low intensity strength training with BFR; GED: Dynamic balance training.	Improvements were found in overall performance and balance after training programs, but there were no differences between groups. Muscle strength in the lower limbs increased significantly in GRFS, but not in GED. Growth hormone concentration increased significantly in GRFS.
Shimizu et al.[20]	40 individuals (71 ± 4 years)	Investigate the effects of training with BFR on endothelial function and circulation in the elderly	GRFS: Low intensity strength training with BFR; GC: Low intensity strength training without BFR.	The lactate, norepinephrine and growth hormone concentrations increased significantly more in GRFS than in GC. GRFS showed significant improvement in endothelial function and peripheral blood circulation. There was no difference in muscle strength between groups, but both increased the strength of the lower limbs.

VO2max = Maximum oxygen uptake; LCA - Anterior Cross Ligament. GRFS – Low-intensity force or walk training group with blood flow restriction. GTT - Traditional Training Group - High Intensity Strength Training. GED - Dynamic Balance Training Group. BFR - blood flow restriction of; GC - Control group.

bone health[16], increased venous compliance[18], improved peak oxygen uptake (VO_2), increased blood flow[17,18] and improved balance, overall performance, and increased growth hormone concentration[8].

According to criterion proposed by Downs and Black[15], the average methodological quality score assigned to the articles selected was 16.2 points (SD = 1.6) and the median score was 17 points, with 18 points being the maximum value reached and 13 the minimum, of a maximum total possible of 31 points. Based on this scale, an article with 18 points[17] and seven with 17 points[6-8,10,16,19,20] were highlighted. From the quintile categorization of the quality of studies evaluated by the Downs & Black scale, it was observed that all studies are in the intermediate quintile (12.9 to 19.2 points). Table 2 describes in detail the distribution of the methodological quality of studies according to the following items: communication, external validity, internal validity (bias and confounding factors) and power, as well as the percentage of points reached by each article of the total possible in each item. The median percentage of the maximum score among studies was 54.9 points. The lowest scores were on items external validity and power, in which all studies reached 1 point in each of the possible 3 elements in external validity and five in power.

DISCUSSION

Of the 12 studies that fully met the inclusion criteria and were included in this review, seven evaluated the response of low-intensity strength training with BFR on strength and all found a significantly positive effect on the increase of this variable, regardless of whether the weekly frequency was two or three times and the protocol duration of 4 or 12 weeks. In addition,

Table 2. Methodological quality of studies according to the Downs and Black15 criteria

Study	Communication	External validity	VI (bias)	VI (confounding factor)	Power	Total	Percentage
Abe et al.[12]	6	1	3	4	1	15	48.4
Iida et al.[24]	5	1	3	3	1	13	41.2
Karabulut et al.[19]	7	1	3	5	1	17	54.9
Karabulut et al.[16]	7	1	3	5	1	17	54.9
Karabulut et al.[6]	7	1	3	5	1	17	54.9
Shimizu et al.[20]	7	1	4	4	1	17	54.9
Yokokawa et al.[8]	8	1	3	4	1	17	54.9
Yasuda et al.[10]	7	1	4	4	1	17	54.9
Vechin et al.[9]	6	1	4	4	1	16	51.6
Thiebaud et al.[7]	7	1	3	5	1	17	54.9
Patterson et al.[23]	7	1	4	5	1	18	58.1
Libardi et al.[13]	4	1	3	4	1	13	41.2

VI: internal validity.

when low-intensity training with BFR was compared with traditional training (high-intensity without BFR), the results were similar between groups[13,19]. Thus, it is possible to affirm that strength training with BFR performed 2 to 3 times a week is effective for improving strength in older adults. Among the factors associated with this improvement, the literature presents neuromuscular adaptations caused by training, such as improvement in neuromuscular and / or nerve coordination, greater recruitment of fast fibers and their motor units and greater muscle activation[10,21-23].

Regarding muscle mass increase, three studies investigated the effect of strength training with BFR on the cross-sectional area[9,10,13]. The three studies concluded that low-intensity strength training with BFR was effective in improving this variable, with results similar to high-intensity traditional training recommended by ACSM[9,13], and more effective than low-intensity training without BFR[10]. Previous studies have found that training with BFR optimizes protein synthesis by increasing skeletal muscle myocytes and promoting increased muscle swelling, which, in addition to being associated with protein synthesis, reduces proteolysis[10,24,25].

In addition to neuromuscular responses, the process of hypertrophy and increased muscle strength promoted by training with BFR is due to metabolic and endocrine responses. The metabolic stress promoted by hypoxia associated with exercise leads to the translocation of type-4 Glucose Transporter (GLUT-4), stimulating the absorption of muscle glucose [26]. In addition, exercise with BFR provides a longer duration of metabolic acidosis, which stimulates the systemic release of the growth hormone (GH) and the consequent increased release of Insulin-1 Growth Factor (IGF-1)[23].

One study analyzed the response of low-intensity training with BFR on immune system and muscle damage parameters[6] and found no statistically significant changes in creatine kinase (CK) and interleukin-6 (IL-6) serum concentrations. It is important to emphasize that the inflammatory markers analyzed presented values considered normal at baseline, that is, they could not be modified after intervention with physical exercises. The positive point was that training with BFR did not induce additional inflammatory changes. In addition, among the limitations presented by the authors, the lack of control of the participants' diet stood out, a factor that may significantly contribute to the responses in the studied variables, and the last exercise session may have influenced the parameters evaluated, especially CK and IL -6, since blood collection was performed one day after the last exercise session. Depending on the subject's physical fitness level, cytokine and CK levels may remain altered for many hours after the exercise session[6].

Karabulut et al.[16] studied the response of low-intensity training with BFR on bone health[16]. The results indicated that training with BFR showed significant improvements in the concentration of bone health markers when compared to the group that did not exercise (bone alkaline phosphatase - 21%, C-Telopeptide - 7.6%). Training with BFR can positively affect the secretory function of endothelial cells, which may promote bone remodeling through the synthesis and release of different molecules, such as free radicals and growth factors, which may inhibit osteoclast activity and stimulate osteoblast activity[27,28]. In addition, the increase in muscle strength itself may be associated with improvements in bone health markers[29].

It is noteworthy that the studies included in the present review presented some common limitations. Although the need for custom prescription of pressure application to obtain adequate BFR according to limb circumference for effective performance during training with BFR[30] is well documented, none of the reviewed studies presented this concern. It is possible that some studies have made this mistake because they were carried out before the publication of the study that standardized the methodology.

The methodological quality presented by studies included in the present review (median score of 17) evaluated through the Dows and Black[15] scale is another important factor that should be discussed. Studies present some restriction mainly on external validity and power (all studies reached only one point of three possible in external validity and one point of five possible in power). Despite the positive results of training with BFR on different outcomes in older adults, especially hypertrophy and muscular strength, the methodological evaluation carried out leads to a cautious interpretation of the findings of studies. However, for allowing the performance of lower intensity exercises and less mechanical stress, especially in the knee joints, training with BFR may provide an interesting advantage for older adults, especially those with joint limitations[13].

FINAL COMENTS

The results suggest that the prescription of low-intensity exercises with BFR may be an alternative to improve strength, muscle mass, functional capacity, bone health, venous compliance and peak VO_2 without generating excessive muscle damage and inflammatory response in older adults and seniors. However, it is important to note that due to the methodological quality presented by original studies, the findings should be interpreted with caution. Thus, despite the potential benefits of training with BFR in older and seniors, future studies should aim at methodological quality, especially external validity and power, the main gaps in articles reviewed in this study.

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