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Review article

Blood flow restriction training - an intervention to counteract muscle loss caused by the Covid-19 pandemic

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Abstract

Introduction: Physical inactivity is a major unintended consequence of the social distancing imposed by the Covid-19 pandemic. Increased physical inactivity and sedentary behaviors have profound physiological impacts on muscular health, leading to muscle and strength losses that are associated with lower performance and higher mortality rates. In the so-called "new normal", exercise routines must find alternative ways to replace high-intensity resistance exercises, since resources are limited in home environments. Blood flow restriction (BFR) is a low-intensity training method involving compressive pressure of the vasculature by use of a tourniquet cuff in the proximal portion of the upper and lower limbs. BFR has been demonstrated to be a safe and efficient training modality to promote muscle and strength gains in different groups, including those under musculoskeletal rehabilitation, young and older adults, and athletes. Objective: This review aims to show that BFR training is an effective intervention for counteracting losses of muscle mass and function caused by Covid-19. Methods: A review of the scientific literature was conducted on electronic databases, such as PubMed, Scielo and Web of Science, covering the period 2000–2020. Results: We advocate the use of BFR training as an urgent counteracting intervention to prevent muscle and strength losses during social distancing and propose a progressive home-based protocol based on wide array of literature. Conclusion: This evidence can help practitioners, personal trainers, physical therapists, and physician assistants to implement an alternative exercise routine that may prevent the deleterious physiological effects of physical inactivity on muscle function during intermittent social distancing.

Keywords: Covid-19; Physical activity; Resistance exercise; Blood flow; Muscular system.

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Introduction

Since the World Health Organization (WHO) declared the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) outbreak to be a pandemic, on 11 March, 2020, governments have sought to minimize the mortality due to coronavirus disease 2019 (Covid-19) by avoiding an exponential number of new cases, managing the impact on the economy, and flattening the epidemic curve while awaiting widespread vaccination. Vaccine distribution, social distancing and mask use continue to be the most important approaches to control the Covid-19 pandemic.

Although widely recommended, social distancing has several unintended public health consequences. From more domestic violence against women, increases in mental health disorders, restrictions in access to food and adequate nutrition, to a sharp drop in treatment of other illnesses, social distancing imposes significant public health challenges.

Responsible for 6% of the burden of coronary heart disease, 7% of type 2 diabetes mellitus, 10% of breast and colon cancers and 9% of premature mortality, while killing more than 5 million people every year and having substantial social and economic impacts, physical inactivity is one of the most important unintended consequences of the social distancing imposed by the Covid-19 pandemic.[1, 2]

Even before Covid-19, levels of physical inactivity were as high as 70% in certain countries, due to changing transportation patterns, increased use of technology, and urbanization.[3] Worldwide, 1 in 4 adults, and 3 in 4 adolescents (aged 11–17 years), do not currently meet the global recommendations of 150 minutes per week of moderate-intensity physical activity, the performance of which has become even more challenging during the Covid-19 pandemic.[4]

Physical inactivity becomes even more important since clinical and epidemiological data have demonstrated a link between the recommended levels of physical activity and a reduction in the prevalence of hospitalization due to Covid-19, as well as in the severity of the disease. A study published by Sallis e cols. (2021), which analyzed 48,440 adults infected with SARS-COV-2, showed that those who did not meet the recommended levels of physical activity of 150 minutes per week presented higher rates of hospitalization, intensive care unit admissions and premature mortality, when compared to those considered active, after adjustment for demographic and other risk factors for severe Covid-19.[5]

Current physical activity guidelines recommend that physical exercise programs include neuromotor, stretching, aerobic and resistance activities. An optimal combination of frequency, intensity, duration, type, volume and progression of exercise, together with main goals, health status and fitness level of practitioners are mandatory aspects of an exercise program to improve physical fitness and health, without compromising safety.[6]

From clinical care to athletic performance at an elite level, resistance exercise is a core component of any training program. Guidelines recommend that resistance training (RT) should involve large muscle groups at least 2–3 times a week, with intensities associated to muscular adaptations ranging from 60 to 80% of one repetition maximum (1 RM), including 8–10 exercises, 2–3 sets per exercise, with 8–12 repetitions, and a resting interval of 2–3 minutes between sets.[6]

However, during the expected intermittent social distancing at home, concern arises about the application of exercise intensity, especially for RT, which usually requires specific equipment that is not readily available to most people in their homes. In other words, workloads with intensities ≥60–70% of 1RM, which are in turn associated with hypertrophic and neuromuscular adaptations, become more difficult to implement in home environments.

The lack of an optimal RT prescription is associated with a loss of muscle mass, the result of an imbalance between protein synthesis and degradation. This affects athletic performance, since studies show a reduction in fibrillar structure after 15 days of detraining,[7] changes of fast-type fibers into slow-twitch types after 4 weeks[8] and reductions of 7 to 12% in strength after a period of 8 to 12 weeks.[9] Even though some studies have shown that low-intensity RT to muscular failure can promote muscle hypertrophy, cross-sectional comparisons suggest that strength and skeletal muscle mass gains are not as great as those achieved with high-intensity RT.[10]

From a health perspective, regular RT has been demonstrated to be an independent predictor of all-cause mortality in the general population,[11] indicating the clinical importance of muscle health. In older adults, a high-risk group for severe illness from Covid-19,[12] declines in skeletal muscle mass and strength have been associated with functional impairment, physical dependence, poor quality of life, institutionalization, higher rates of hospitalization, and risk of morbidity and mortality.[13]

All these findings reinforce the importance of novel approaches to counteract muscle loss imposed by home social distancing. In the so-called "new normal", exercise routines must use alternative means to replace optimal RT intensities, since resources are limited. Below, we propose a home-based training method, considering recent findings associated to increases in muscle and strength gains even in the absence of high-intensity workloads.

In recent years, evidence has accumulated indicating that low-intensity RT performed with blood flow restriction (BFR) promotes increases in muscle mass and strength. Results are promising for several different groups, including subjects undergoing musculoskeletal rehabilitation, older subjects, young adults, athletes, and other clinical populations.[14]

BFR involves compressive pressure of the vasculature, using a tourniquet cuff in the proximal portion of the upper and lower limbs, which leads to a venous occlusion and a reduction of arterial blood flow in the distal portion of the cuff. Restriction levels vary among studies from 50 to 300mmHg and exercise workloads are usually set from 20 to 40% of individuals' maximal strength. BFR training has been mainly investigated with resistance exercises but is also associated with low-intensity aerobic (walking and cycling) exercise and passive activity, without exercise.[14]

Several groups have described different physiological pathways associated with acute and chronic muscle effects of BFR training. There is a consensus, however, that the hypoxia triggered by the mechanical compression of cuff inflation reduces intracellular pH levels and adenosine triphosphate (ATP) resphosphorylation, triggering a cascade of events associated with the regulation of cell energy-sensing mechanisms.[15]

Some of these physiological and molecular mechanisms are described as follows: a) increase in intramuscular metabolic stress (ATP hydrolysis, depletion of phosphocreatine, increases in inorganic phosphate, reduction of pH and increment of lactate); b) increase in plasma levels of several hormones and growth factors, such as growth hormone (GH), insulin-like growth factor 1 (IGF-1), testosterone and cortisol; c) recruitment of fast-twitch muscle fibers; d) activation of intracellular signaling pathways for muscle protein synthesis (mTOR pathway); e) decrease of mRNA gene expression of myostatin; f) increase of heat shock protein; and g) increase of nitric oxide synthase-1.[15] Figure 1 depicts an evidence-based theoretical model of the physiological responses associated with BFR.

These findings have important implications for individuals who cannot tolerate the mechanical stress of high-intensity RT, such as those undergoing musculoskeletal rehabilitation and older subjects. Moreover, considering the Covid-19 pandemic and the limitations in resources imposed by intermittent home distancing, BFR training can be considered as an alternative intervention for a larger group of people, comprising young adults, athletes, and older sub-groups, including fragile and sarcopenic subjects. In Table 1, we present some relevant well-designed studies of BFR training for these specific groups.

In general, these studies confirm the results of previous studies, which demonstrate increases in muscle mass and strength after a period of BFR training. It is noteworthy, however, that greater strength gains are usually observed in cases of high-intensity RT than in BFR, after adjustment for potential moderators.[16] Inversely, increases in muscle mass seem to be similar when results of high-intensity RT and low-intensity activity with BFR are compared, even when differences in occlusion pressure or cuff width are taken into account. Considering the similar gains in muscle mass and the fact that BFR training elicits superior strength gains when compared to low-intensity RT,[17] we advocate that this novel training method should be used for individuals unable to tolerate high-intensity

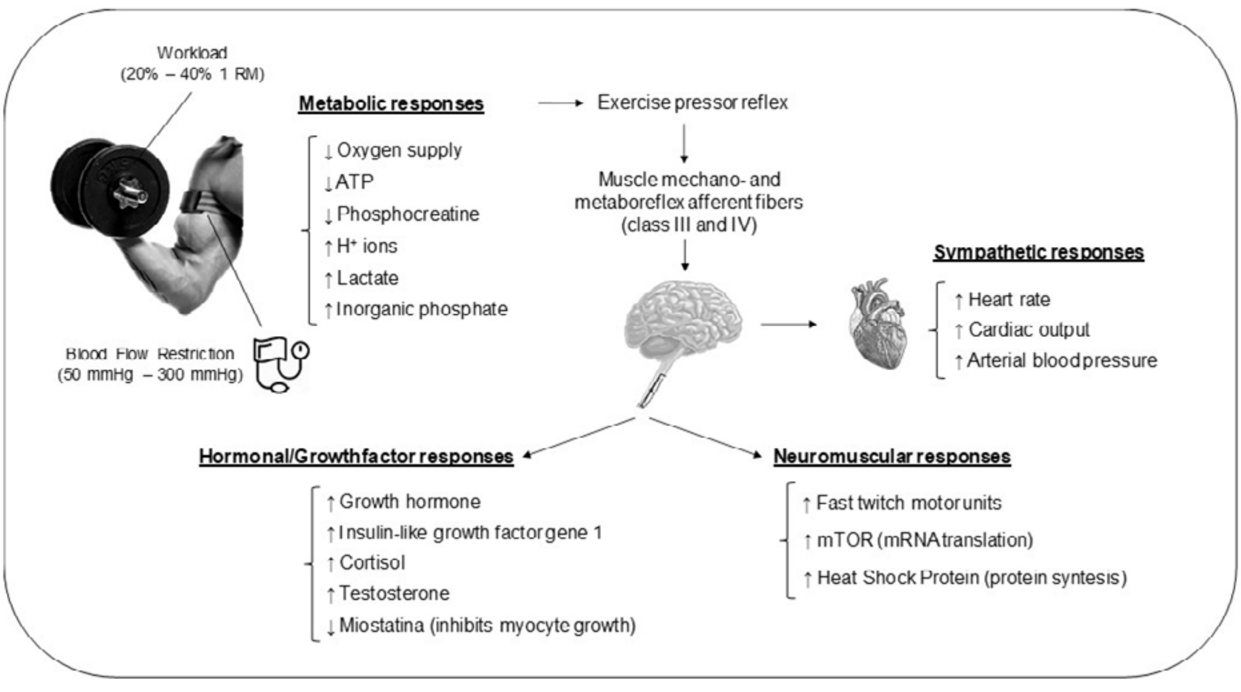

Figure 1. Physiological responses associated with blood flow restriction exercise

Legend: RM – repetition maximum, ATP - adenosine triphosphate, H+ ions – ions of hydrogen, mTOR - mammalian target of rapamycin.
Source: The authors (2022).

Table 1. Studies of BFR training in musculoskeletal rehabilitation, older subjects, subjects, young adults and athletes

Authors	Population studied	Age (yrs)	Study design	Exercises	Duration	Frequency	Intensity	Number of sets and repetitions	Restriction level	Assessments		Main findings
										Hypertrophy	Strength	
MUSCULOSKELETAL REHABILITATION												
Ferraz et al. (2017)	48 women with knee osteoarthritis	50 to 65	RCT	Leg press and knee extension	12 weeks	2 days/week	HI: 80% of 1RM LI: 30% of 1RM LI-BFR: 30% of 1RM	4–5 sets of 10 reps 4–5 sets of 15 reps	97.4 ± 7.6 mmHg (70% of occlusive pressure)	Tomography for quadriceps CSA	1RM leg press, 1RM knee extension	HI: ↑ 1MR of leg press in 33% and of knee extension in 22% LI-BFR: ↑ 1MR of leg press in 26% and of knee extension in 23% HI: ↑ Quadriceps CSA in 8% LI-BFR: ↑ Quadriceps CSA in 7%
Rodrigues et al. (2019)	48 women with rheumatoid arthritis	46 to 67	RCT	Leg press and knee extension	12 weeks	2 days/week	HI: 70% of 1RM LI-BFR: 30% of 1RM	HI: 4–5 sets of 10 reps LI-BFR: 4–5 sets of 15 reps	108.9 ± 14.6 mmHg (70% occlusive pressure)	Tomography for quadriceps CSA	1RM leg press, 1RM knee extension	HI: ↑ 1MR of leg press in 24% HI: ↑ 1MR of knee extension in 24% LI-BFR: ↑ 1MR of leg press in 23% LI-BFR: ↑ 1MR of knee extension in 20% HI: ↑ Quadriceps CSA in 10.8% LI-BFR: ↑ Quadriceps CSA in 9.5%
Ladlow et al. (2018)	28 men with lower-limb injury	19 to 49	Single-blind RCT	Deadlift, back squat and lunges - HI Leg press and knee extension - LI-BFR	3 weeks	HI: 3 days/ week LI-BFR: twice/day	HI LI-BFR: 30% of 1RM	HI: 4 sets of 6-8 reps LI-BFR: 4 sets of 15, 15, 15 and 30 reps	124 ± 13 mmHg (60% of limb occlusive pressure)	MRI for quadriceps CSA	5RM leg press and 5RM knee extension	LI-BFR: ↑ CSA in 7% HI: ↑ CSA in 5% LI-BFR ↑ strength by leg press in 16% and knee extension in 40% HI: ↑ strength by leg press in 25% and knee extension in 24%
Segal et al. (2015)	41 men knee injury	56.1 ± 7.7	Double-blind RCT	Bilateral leg press	4 weeks	3 days/week	30% of 1RM	4 sets of 30, 15, 15 and 15 reps	100 - 200 mmHg		1RM leg press	CON: ↑1MR of leg press in 4.7% "LI-BFR: ↑1MR of leg press in 3.1%"
Segal et al. (2015)	40 women with knee osteoarthritis	45 to 65	Double-blind RCT	Bilateral leg press	4 weeks	3 days/week	30% of 1RM	4 sets of 30, 15, 15 and 15 reps	100 - 140 mmHg	MRI of quadriceps	1RM leg press	LI-BFR: ↑ 1MR of leg press in 28 ± 4 kg CON: ↑ 1MR of leg press in 15 ± 4 kg ↔ Quadriceps volume in both groups
OLDER SUBJECTS												
Vechin et al. (2015)	14 men and 9 women	59 to 71	RCT	45° leg press exercise	12 weeks	2 days	LI-BFR: 20–30% of 1RM HI: 70–80% of 1RM	1 set x 30 reps + 3 sets x 15 reps 4 sets x 10 reps	50% of the maximum tibial arterial pressure (average cuff pressure = 71 mmHg)	Quadriceps CSA	1RM leg press	LI-BFR: ↑1MR of leg press in 17% HI: ↑ 1MR of leg press in 54% LI-BFR: ↑ quadriceps CSA in 6.6% HI: ↑ quadriceps CSA in 7.9%
Libardi et al. (2015)	25 healthy men	64.7 ± 4.1	RCT	45° leg press exercise	12 weeks	2 days	CT-BFR: 20–30% of 1RM CT-HI: 70–80% of 1RM	1 set x 30 reps + 3 sets x 15 reps 4 sets x 10 reps	50% of resting occlusion pressure (average pressure = 67 ± 8.0 mmHg)	Quadriceps CSA	1RM leg press	CT-BFR: ↑ CSA in 7.6% CT-HI: ↑ CSA in 7.3% CT-BFR: ↑ 1MR of leg press in 35.4% CT-HI: ↑ 1MR of leg press in 38.1%
Cook et al. (2017)	36 (men and women)	73.4 to 78.5	RCT	Leg extension, leg curl and horizontal leg press machine	12 weeks	2 days	LI-BFR: 30–50% of 1RM HI: 70% of 1RM	3 sets to failure	1.5 times brachial SBP (average pressure=184±25 mmHg)	Quadriceps CSA	Leg extension - isokinetic dynamometer - MVC 1RM leg extension and leg press	LI-BFR: ↑1MR tests (leg extension in 24% and leg press in 12%) LI-BFR: ↑ CSA in 4.3% HI: ↑ MVC in 16% HI: ↑ CSA in 3.6%
Karabulut et al. (2013)	36 healthy older males	56.6 ± 0.6	RCT	Latissimus pull down, shoulder press, biceps curl, leg press and knee extension	6 weeks	3 days	HI: 80% of 1RM LI-BFR: 20% of 1RM	1 set x 30 reps + 2 sets x 15 reps	160 - 240 mmHg	Tomography for quadriceps CSA		LI-BFR: ↑ CSA in 1.3 ± 0.7% HI: ↑ CSA in 3.7 ± 0.8% CON: ↑ CSA in 1.5 ± 0.4%
Letiere et al (2018)	56 active women	68.8 ± 5.09	Double-blind RCT	Squat, leg press, knee extension and leg curl	16 weeks	3 days					Knee Extension - Isokinetic dynamometer	LI-BFR high: ↑ peak torque of knee extension in 27.2 and 25.2% LI-BFR high: ↑ peak torque of knee flexion in 36.7 and 35.8% LI-BFR low: ↑ peak torque of knee extension in 15.7 and 18.9% LI-BFR low: ↑ peak torque of knee flexion in 22.8 and 24.9% HI: ↑ peak torque of knee extension in 13.8 and 30.4% HI: ↑ peak torque of knee flexion in 34.9 and 26.1% LI and CON: ↔ peak torque
Karabulut et al. (2010)	37 healthy older males	50 to 64	RCT	Lat pull down, biceps curl, shoulder press, leg press, and leg extension	8 weeks	3 days	HI: 80% of 1RM LI-BFR: 20% of 1RM	3 sets of 8 reps 1 set of 30 reps and 2 of 15 reps	Mean restrictive pressure = 205.4 ± 4.3 mmHg		1RM Lat pull down, biceps curl, shoulder press, leg press and leg extension	HI: ↑ 13.2% (lat pull down), ↑ 9.6% (shoulder press), ↑ 20.4% (leg press) LI-BFR: ↑ 15.9% (lat pull down), ↑ 8.6% (shoulder press), ↑ 19.3% (leg press) HI: ↑ 22.9% (biceps curl), ↑ 31.2% (leg extension) LI-BFR: ↑ 19.3% (biceps curl), ↑ 19.1% (leg extension)
Takarada et al. (2000)	24 healthy postmenopausal women	47 to 67	RCT	Single-arm dumbbell curl exercises	16 weeks	2 days	LI: 50% of 1RM BFR: 50% of 1RM HI: 80% of 1RM	3 sets until failure	110 ± 7.1 mmHg	MRI of brachii	Isokinetic dynamometer	LI-BFR: ↑ CSA of biceps brachil in 20.3% LI: ↑ CSA of biceps brachil in 6.9% HI: ↑ CSA of biceps brachil in 18.4% LI-BFR: ↑ torque of elbow flexion in 18.4% LI: ↑ torque of elbow flexion in 1.04% HI: ↑ torque of elbow flexion in 22.6%

Legend: BFR: blood flow restriction. CON: control condition. RCT: randomized controlled trial. CSA: cross-sectional area. MRI: Magnetic Resonance Imaging. CT: concurrent training. EMG: electromyography. HI: high-intensity exercise. HT: hypoxic training. LI: low intensity exercise. MDS: maximum dynamic strength. Min: minute. MVC: maximum voluntary contraction. RM: repetition maximum. Rep: repetition. SBP: systolic blood pressure. S: second. ↑: increased. ↔: maintained. ↓: decreased.

Table 1. Studies of BFR training in musculoskeletal rehabilitation, older subjects, subjects, young adults and athletes (cont.)

Authors	Population studied	Age (yrs)	Study design	Exercises	Duration	Frequency	Intensity	Number of sets and repetitions	Restriction level	Assessments		Main findings
										Hypertrophy	Strength	
YOUNG ADULTS												
Yasuda et al. (2014)	9 healthy men	23 to 41	RCT	Triceps extension and biceps flexion exercises using elastic band	3 weeks	1 day	BFR: 15 to 20% of 1 RM	1 set of 30 reps and 3 sets of 15 reps	170 to 260 mmHg		EMG	BFR: ↑ muscle activation in 46% triceps extension and in 69% biceps flexion CON: ↔ muscle activation in 12% triceps extension and in 23% biceps flexion
Lixandrão et al. (2015)	26 Inactive men		RCT	Unilateral knee extension	12 weeks	2 days	BFR 20/40: 20% of 1RM BFR 20/80: 20% of 1RM BFR 40/40: 40% of 1RM BFR 40/80: 40% of 1RM HI: 80% of 1RM	2 to 3 sets of 15 rep 2 to 3 sets of 15 rep 2 to 3 sets of 15 rep 2 to 3 sets of 15 rep 2 to 3 sets of 10 rep	40% of occlusion pressure (55.5 ± 7.6 mmHg) 80% of occlusion pressure (109.6 ± 9.4 mmHg) 40% of occlusion pressure (54.5 ± 4.6 mmHg) 80% of occlusion pressure (105.0 ± 18.5 mmHg)	Quadriceps muscle CSA	1 MR knee extension - MDS	BFR 20/40: ↑ CSA in 0.78 % and ↑ MDS in 10.30% BFR 20/80: ↑ CSA in 3.22 % and ↑ MDS in 13.20% BFR 40/40: ↑ CSA in 4.45 % and ↑ MDS in 12.20% BFR 40/80: ↑ CSA in 5.30 % and ↑ MDS in 12.70% HI: 80 ↑ CSA in 5.90 % and ↑ MDS in 21.60%
Clark et al. (2011)	16 young, healthy adults	18 to 30	RCT	Bilateral knee extension	4 weeks	3 days	LI-BFR: 30% of 1RM HI: 80% of 1RM	3 sets ultil failure 3 sets until failure	30% above the resting brachial SBP		Knee extension dynamometer (MedX)	LI-BFR: ↑ strength in 8% HI: ↑ strength in 13%
Shinohara et al. (1998)	5 untrained males	19 to 29	Controlled experimental study	One-legged voluntary isometric knee extension	4 weeks	3 days	40 % of MVC	3 sets x 3 min	Ischemia at > 250 mmHg		Knee extension - MVC	LI-BFR: ↑ MVC 9% in 2 weeks and 26% in 4 weeks
ATHLETES												
Takada et al. (2012)	12 trained males (sprinters and endurance runners)	19 to 20	RCT	Unilateral plantar flexion exercise	1 week	2 days	LI: 20% of 1RM for 2 min HI: 65% of 1RM for 2 min LI-BFR: 20% of 1RM for 2 min (L-BFR) LI-BFR: 20% of 1RM for 3 min (prolonged-BFR)	30 reps per min	130% of resting SBP	Recruitment of fast-twitch fibers		LI-BFR: ↑ intramuscular phosphocreatine in edurance runners 24.6 ± 1.4% LI-BFR: ↑ intramuscular phosphocreatine in sprinters 32.0 ± 3.2% HI: ↑ inorganic phosphate in 100% L-BRF: ↑ inorganic phosphate in 33.3 % Prolonged-BFR: ↑ inorganic phosphate in 83.3%
Manimmanakorn et al. (2012)	30 female netballers	20.2 ± 3.3	RCT	Bilateral knee extensions and flexions	5 weeks	3 days	20% of 1RM CON, LI-BFR and LI-HT	3 sets of knee extensions and 3 sets of knee flexions to failure	Increased by 10 mmHg each day: day 1 (160 mmHg) and day 8 (230 mmHg)	MRI of quadriceps	1RM knee extension and flexios	LI-BFR: ↑ MVC 3 seconds in 11.0 ± 11.9% LI-HT:↑ MVC 3 seconds in 15.0 ± 13.1% LI-BFR: ↑ CSA extensors in 5.7 ± 4.0% LI-HT: ↑ CSA extensors in 2.8 ± 1.8% CON: ↑ CSA extensors in 2.4 ± 1.7% LI-BFR:↑ CSA flexors muscles in 7.7 ± 5.0% LI-HT: ↑ CSA flexors muscles in 10.0 ± 5.0% CON: ↑ CSA flexors muscles in 3.4 ± 3.4%
Takarada et al. (2002)	17 male rugby athletes	Around 27	"Controlled experimental study"	Bilateral knee extension and leg press	8 weeks	2 days	50% of 1RM	4 sets / mean rep in each set = 16.3 ± 0.7	196 ± 5.7 mmHg	MRI of quadriceps	1 MR knee extension and leg press	LI-BFR: ↑ strength in 14.3 ± 2.0% LI: ↑ strength 3.2 ± 2.3% untrained-CON ↔ strength LI-BFR: ↑ CSA 15% in knee extensors untrained-CON ↔ CSA in knee extensors
Cook et al. (2014)	20 male rugby athletes	21.5 ± 1.4	RCT	Leg squat, bench press, and weighted pull-up	3 weeks	3 days	70% of 1RM	5 sets of 5 rep	180 mmHg		1 MR leg squat and bench press	BFR: ↑ bench press in 8.6 ± 5.8 kg (+ 1.4% compare to CON) BFR: ↑ leg squat in 12.0 ± 6.7 kg (+ 0.4% compare to CON)
Takarada et al. (2000)	6 young male athletes	22 to 22	RCT	Bilateral knee extension	4 weeks	1 day	20% of 1RM	5 sets, until exhaustion (mean rep per set = 14.4 ± 1.6)	214 ± 7.7 mmHg.		1RM bilateral leg extension exercise in the seated position (EMG)	LI-BFR: ↑ iEMG in 1.8 times

Legend: BFR: blood flow restriction. CON: control condition. RCT: randomized controlled trial. CSA: cross-sectional area. MRI: Magnetic Resonance Imaging. CT: concurrent training. EMG: electromyography. HI: high-intensity exercise. HT: hypoxic training. LI: low intensity exercise. MDS: maximum dynamic strength. Min: minute. MVC: maximum voluntary contraction. RM: repetition maximum. Rep: repetition. SBP: systolic blood pressure. S: second. ↑: increased. ↔: maintained. ↓: decreased.

RT. In a context of intermittent social distancing, these recommendations are further extended to all those with limited resources in their home environments in which to implement high-intensity RT routines.

As is the case in conventional RT, the optimal prescription of BFR must take into account common training variables and goals, as well as the health status and fitness level of practitioners. In addition, the application of BFR should also consider cuff pressures (restriction level and duration), width, and material. Considerations on BFR methodology and application were published in a recent review by Patterson e cols., where all these aspects are presented for three different modalities of BFR, as follows: a) voluntary resistance BFR exercise; b) voluntary aerobic BFR exercise; and c) passive BFR without exercise. In general, BFR training may be performed 2–3 times a week, and, in light of the faster recovery associated with the low-intensity variant, can be applied once or twice a day, regardless of the modality.[14] Cuff pressure is recommended to range from 60 to 80% of the arterial occlusion pressure (AOP), regardless of cuff width and material. This range represents a safe and effective pressure according to many results in the literature. Cuff pressures above occlusion or resting systolic blood pressure have been associated with higher cardiovascular responses and greater discomfort during and after exercise.[18]

In the case of passive BFR without exercise, however, higher pressures (80 to 100% of AOP) may be required to prevent muscle atrophy.[19] From subjects under rehabilitation to athletes, workloads corresponding to 20 to 40% of 1RM are recommended for gains in muscle strength and muscle mass. When aerobic BFR exercises are performed, the intensity may be lower than 50% of maximal oxygen uptake or heart rate reserve. For passive BFR, where exercise is absent, adjustment of the cuff pressure and restriction time (5 minutes duration) is essential to achieve better results.[14] In all BFR modalities, unilateral or bilateral exercises can be performed for both arms and legs.

Home-based progressive protocol of BFR training

Based on the evidence and recommendations, we propose a simple progressive home-based BFR protocol that takes into account the limited resources and the safety of practitioners. In Table 2, four different BFR training protocols are described as phases. However, progress through the phases is not mandatory; depending on their clinical status and goals, subjects may stay in a single phase for weeks. The Borg scale should be used in each session of exercises to rank participants' perceived exertion and to measure progress in each phase. Weekly messages must be sent to reinforce the usage instructions. Remote supervision (through explanatory videos, text messages and phone calls) of subjects must be performed by physical education professionals and physiotherapists in order to provide instructions about the methodology and application of BFR training.

Passive BFR training is designed for individuals with musculoskeletal disorders, lower limb injuries or pain with limited range motion, including older subjects. This group may include subjects waiting for knee surgery at home, since many elective surgeries have been postponed due to the Covid-19 pandemic. In the first week, passive BFR may be performed with 1 or 2 sets with 5 minutes of restriction, at 40% of AOP. In the following weeks, the number of sets and the pressure may be increased according to the guidance presented in Table 2. As patients proceed to surgery and wait for musculoskeletal rehabilitation, they can progress to phase 2, in which BFR is associated with walking or stationary cycling.

In this phase, we include inactive adults with more than 6 months without RT and older subjects with preserved functional autonomy. Since studies demonstrate[20, 21] that low intensity (≤50% of heart rate reserve) is associated with increases in muscle mass and strength, we suggest, in a context of limited resources, that a self-perceived comfort pace is applicable to all subjects in this phase. As these groups become more comfortable with BFR, they can pass to phase 3 and initiate a RT program with BFR. A combination of walking and RT-BFR is possible. Designed for subjects with low fitness levels, we do not recommend that cuff pressures exceed 60% of AOP and workloads 20% of 1RM in this phase.

Finally, considering the lack of support at home from a personal trainer or a physical therapist, we suggest that only active adults with higher fitness levels and a history of RT and athletes proceed to phase 4, following the recommendations in Table 2. Although safe, whenever possible, telehealth support is recommended to all who wish to implement this program, especially those that proceed to phase 4.

Two important aspects must be considered before implementing a BFR routine. Firstly, the calculation of the correct percentage of AOP to set cuff restriction

Table 2. Home-based progressive model of BFR training

1 - PASSIVE BFR	2 - WALKING with BFR	3 - RT BFR (low fitness level)	4 - RT BFR (high fitness level)
Target Groups All under MSR* - limited range motion Older subjects - joint pain Older subjects - limited range motion Cuff pressure First week: 40% of AOP Next weeks: 80% of AOP Number of sets First week: 1 to 2 Next weeks: 3 to 5 Repetitions Passive (without exercise) Restriction time 5 min interval (3 min of resting)	Target Groups Subjects after MSR Physically inactive adults Older subjects Cuff pressure First week: 40 to 50% of AOP Next weeks: 60 to 80% of AOP Number of sets First week: 1 to 2 Next weeks: 3 to 4 Repetitions Walking or stationary cycling Restriction time 5 min interval (1min rest) Intensity Comfortable pace	Target Groups Subjects after MSR Physically inactive adults Older subjects Cuff pressure First week: 40% to 50% of AOP Next weeks: 60% of AOP Number of sets First week: 1 to 2 Next weeks: 3 Repetitions 30x15x15x15 (1min rest) Intensity 20% of 1 MR	Target Groups Physically active adults Athletes Cuff pressure First week: 50% of AOP Next weeks: 80% of AOP Number of sets First week: 2 to 3 Next weeks: 4 to 5 Repetitions Concentric failure (30secs rest) Intensity 30 to 40% of 1 MR

Legend: BFR: blood flow restriction. MSR: musculoskeletal rehabilitation. AOP: arterial occlusion pressure: RM: repetition maximum. * Patients after major orthopedic surgery, hip or long bone fractures must contact the physician assistant before implementing this program.
Source: Authors (2022).

for both upper and lower limbs and, secondly, the correct workload, expressed as percentage of 1 MR. We recommend the purchase of two commercially available standard aneroid sphygmomanometers that fit both thighs and arms for pressure settings and training. We suggest the following steps to set up the cuff pressure: 1) finding the AOP—to find the AOP, subjects should position the cuff in the proximal portion of the limbs (preferably in the exercise position) and inflate the cuff until they do not fell radial (arm) and popliteal or dorsalis pedis (leg) pulses. Detailed information on how to assess the radial, popliteal, or dorsalis pedis pulses is available from Hill and Smith;[22] 2) calculation of the training cuff pressure (% of AOP)—after finding the AOP, simple mathematical calculations can be applied to set the recommended % of cuff pressure, according to the type and phase of BFR training in Table 2. Calculation of the workload in the home environment is not simple because it requires a maximal repetition test. In the social distancing context, however, we recommend two alternatives. The first applies to those who used to perform RT before social distancing, who may utilize their previous workloads as a parameter to estimate the % of 1RM for the BFR training. As an example, suppose that the 10 RM workload for someone's leg extension exercise is 50kg. Considering that 10 RM is the equivalent of approximately 75% of 1RM, after a simple mathematical calculation, we may assume that the proportional 20% of 1RM would be 13 kg. The same calculation can be applied for a biceps curl exercise. Considering a 10 RM workload of 12kg, 20% of 1RM for BFR training would be approximately 3kg. The second alternative applies to patients with musculoskeletal disorders awaiting surgery or in post-surgery awaiting rehabilitation, since previous workloads are invalid, and for those who did not have their previous workloads measured. In these cases, we recommend the use of the repetition perceived scale as a proxy of very light or light intensity.[23] To keep these recommendations as simple as possible, we suggest a sequence of 5 exercises (phases 3 and 4), as follows: a) dumbbell biceps curl; b) dumbbell triceps extension; c) leg extension (sit on a chair), d) standing leg curl; and e) calf exercise (exercises 4 and 5 are better performed with arm support for balance). A description of how to perform these exercises may be found from Clay.[24] Highly trained adults and athletes may add other exercises, since they are familiar with the execution and safety of more complex programs.

It is important to note that this home-based protocol is not intended to replace high-intensity

RT indefinitely. On the contrary, this protocol is only recommended as an alternative approach to counteract losses in muscle mass and strength during periods of social distancing imposed as a result of the Covid-19 pandemic. As governments re-open services following the safety procedures of health and scientific authorities, all these groups should return to their previous, supervised exercise routines or rehabilitation.

Safety Considerations

Concerns associated with BFR are usually related to central and peripheral cardiovascular responses and muscle damage. Detailed discussions of these aspects have been published in several review studies and are beyond the scope of the current study.[14, 25-27] However, considering the fact the present study proposes a home-based BFR protocol, some safety aspects will now be presented. The effect of BFR on the central cardiovascular response depends on the level of BFR and mode of application (i.e., continuous *vs.* intermittent). Studies in which cuff pressure is maintained during rest intervals (continuous BFR) have generally found increases in heart rate, systolic blood pressure and diastolic blood pressure when compared with the same exercise in free flow conditions[28-31]]. On the other hand, when compared to conventional RT, central cardiovascular responses during BFR are significantly lower.[32-35] In addition, prior studies have demonstrated that greater relative restrictive pressures increase the central cardiovascular responses to BFR[18] and therefore the potential risk associated with the combination of RT and BFR. This is important since our protocol proposes the application of progressive and restrictive levels up to 80% of AOP, which can reduce the central hemodynamic stress. All these aspects suggest that BFR with occlusion levels below AOP is safe, at least in terms of central hemodynamic responses.

Regarding peripheral risks associated with BFR training, there is an inherent caution regarding the formation of deep vein thrombosis due to external compression of the vasculature. Many trials using BFR have not directly measured venous thromboembolism formation or used diagnostic imaging. However, minimal adverse events pertaining to venous thromboembolism have been reported. Madarame e cols. assessed blood coagulation markers in patients with a history of ischemic heart disease. Although elevated, D-dimer and C-reactive protein remained within normal clinical ranges when compared with free flow conditions.[36] Again, it is important to note that all studies investigating the peripheral risks associated with BFR exercises have applied high levels of occlusive pressure, which is not the case of the present protocol. A recent study published by Kambic e cols. aimed to evaluate the safety and efficacy of BFR resistance training in patients with coronary artery disease compared to usual care.[37] The following outcomes were assessed before and after 8 weeks of BFR with intensity set at 30–40% 1 MR (unilateral knee extension) and occlusion of 15–20mmHg above resting brachial blood pressure: i) ultrasonographic assessment of vastus lateralis diameter and systemic flow-mediated dilation (brachial artery); ii) markers of inflammation (CD40 and TNF-α); iii) fasting glucose and insulin levels. The BFR improved muscle strength and was considered safe. It has therefore been put forward as an alternative option to aerobic exercise in patients with coronary artery disease. In short, aspects related to the risks of BFR were carefully considered when designing our training protocol.

Given the exposure, we believe that the current protocol is safe, especially because of the low level of occlusion applied to elicit BFR. Nonetheless, considering the need for more studies and the lack of in-person professional support imposed by social distancing, contraindications may apply for those with peripheral artery disease, clotting disorders, heightened risk of venous thromboembolism (pregnancies and after major orthopedic surgery, hip or long bone fractures), renal impairment and uncontrolled hypertension. In addition, since one of the unintended consequences of the Covid-19 pandemic is the interruption of treatment of many chronic diseases,[38] we strongly recommend that those subject to these conditions control their clinical status before implementing BFR or any other training regimen. For this purpose, telehealth technology may be applicable.[39] Our research group has accumulated ten years of experience in application of BFR, mostly with older subjects, without any serious clinical intercurrence to date. This includes a 91-year old sedentary man presenting exhaustion, lower-limb weakness, history of hypertension and multiple falls, diagnosed with sarcopenia who underwent 12 weeks of BFR with workloads corresponding to 30% of 1RM and cuff pressures set at 50% of resting systolic blood pressure (mean cuff pressure of 65 mmHg), three times a week. After the training period, appendicular skeletal mass, handgrip and isokinetic strength of knee extension and endothelial function were improved without any clinical intercurrence.[40]

In the present study, we propose a progressive home-based protocol of BFR training that may be helpful in mitigating the muscle and strength losses associated with the social distancing imposed by the Covid-19 pandemic. The main limitation of this study is that the suggested program was not tested during the pandemic scenario. However, it is important to mention that it is supported by robust literature. Therefore, this protocol is believed to be safe and efficient, while recognizing that it should be applied carefully and gradually over time to ensure protective adaptations associated with risk reductions. Another limitation is related to individual limb characteristics, especially the width of the lower limb. A bigger limb requires a wider sphygmomanometer to perform BFR training. The presence of another person may be required to help to adjust the cuff on the limb and to inflate the cuff to the percentage of blood flow restriction necessary with or without exercise under the protocol. Finally, we strongly suggest that subjects respect their comfort zones, and stay alert to any adverse events. In this case, they should stop their training routines and contact their physician.

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